

Supplementary Materials

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Supplementary file 1

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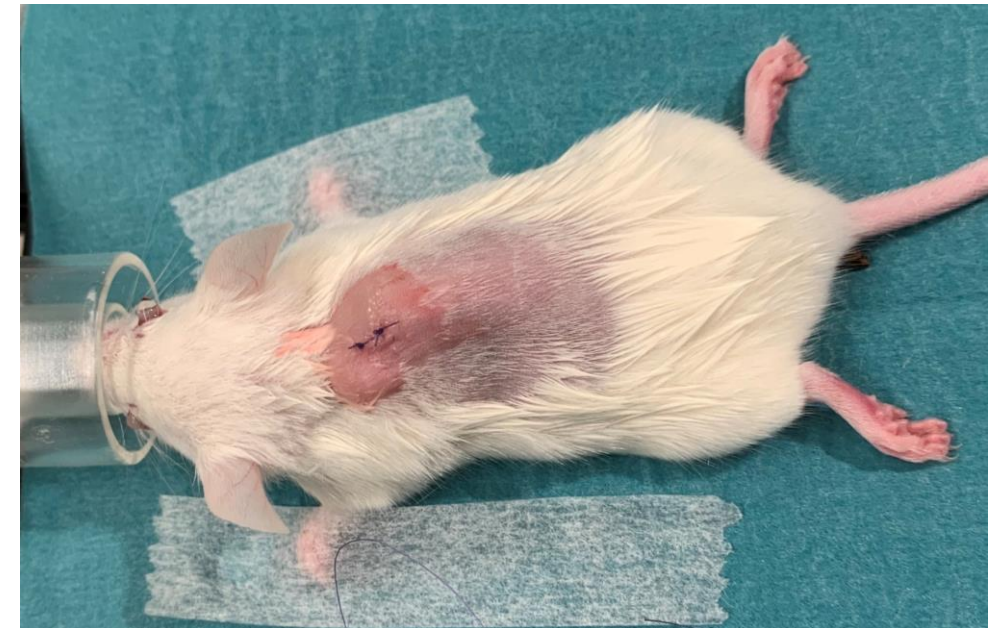
Mouse 12

- Surgery date: 01.04.19
 - Age (weeks) 11
 - Weight (g) 20.5
 - Tumor fragment P3-1A
 - Ear marks 1
 - Fragment size 4*4 mm

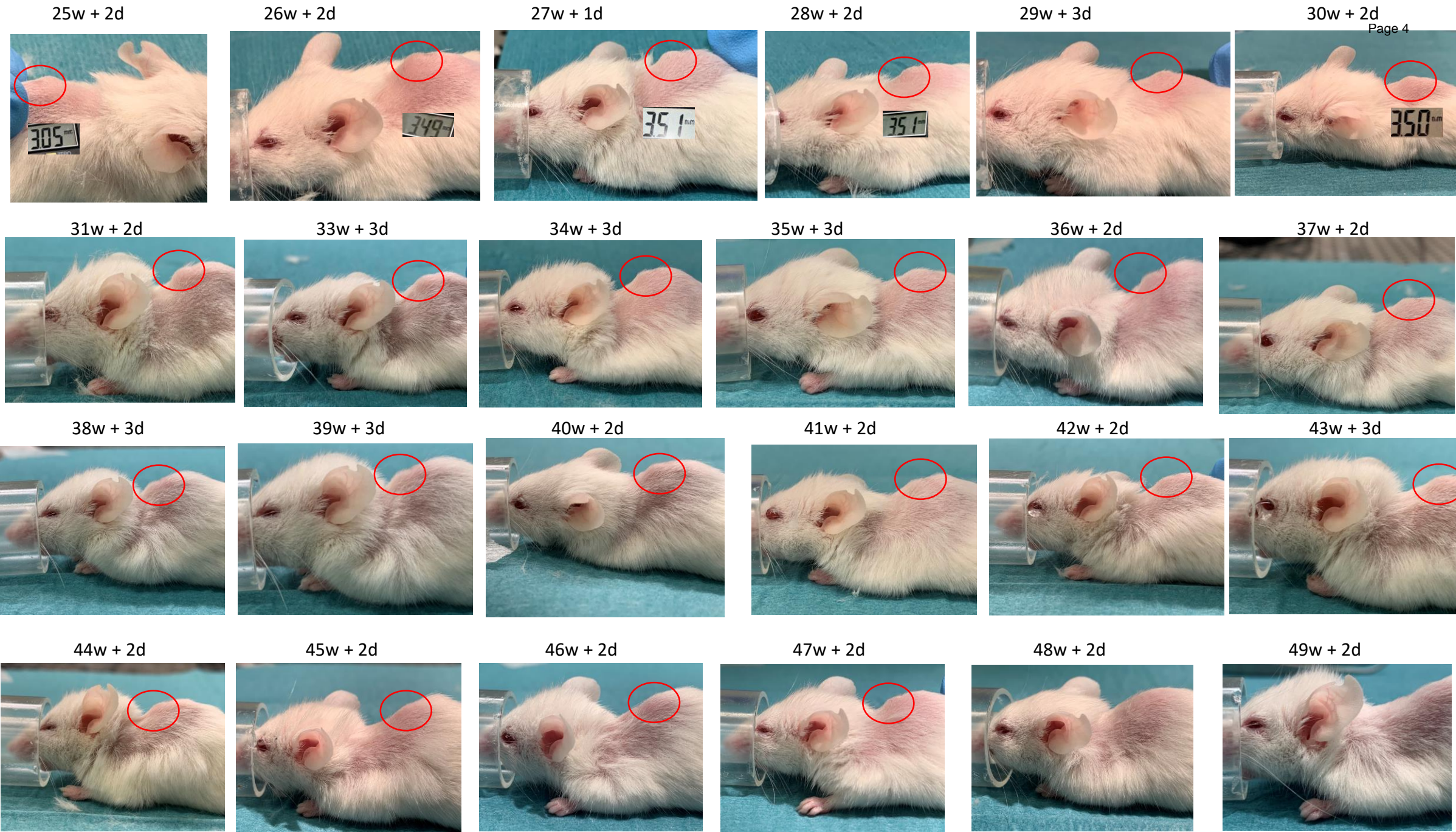
Page 3

MUS			FOTS
Kjønn ♀	Stamme CIEA NoG	Alder/vekt 6u	Antall 1
Bruker Caroline H. Pettersen			Ankomst dato 25/2-19
# 12			
01.04.19 Sett inn xenograft P3-1A mus 1			

Supplementary figure 1-12-1.
Pictures from the engraftment day.



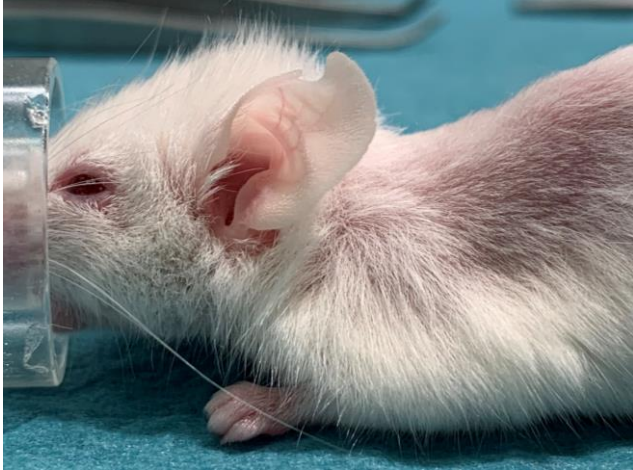
Supplementary figure 1-2. Pictures from follow up and tumor size measurement



Treatment:

- Mouse 12 was used as a «social mouse» during treatment with Smartfish containing fish oil for mouse 17
 - Did not have growing xenograft at that time, were suspected to have removed xenograft itself

Supplementary figure 1-12-3. Pictures from euthanization of mouse 12 (11.03.2020 / 49w + 2d)



Xenograft almost not visible



Necropsy

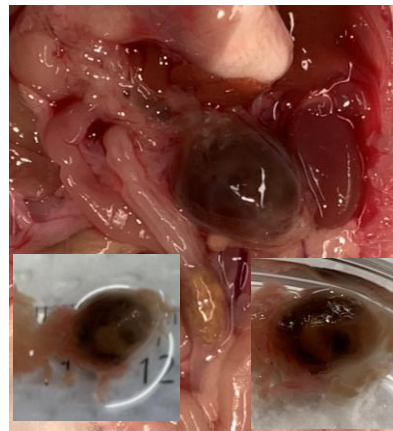


Necropsy

AUTOPSY CARD					
NUMBER 12 (P3-1a)klipp1	Male	Female	STRAIN CIEA NUG	BIRTH DATE	EXPERIMENT PDX - xenograft 1/4/19
AGE AT DEATH	DEATH MODE DATE 11.03.20			GROUP Pottersen, Caroline	
CLINICAL SYMPTOMS AT DEATH Fresh/healthy					
ORGAN WEIGHT		SECTION TAKEN			
ORGAN	WEIGHT	ORGAN	YES	GROSS OBSERVATION	
Femur	CH	1) Lung + Heart	X	Sent som histe/lunge or nie som ansvaret, fjell lunge og mformalin	
Liver	L	2) Liver	X	Liten, bare litten litten?	
		3) Kidney	X	Normal	
		4) Adrenal			
Spleen		5) Testis/Ovary			
	MP	6) Spleen + pancreas	X	Size? ca 1,3mm normal, pancreas m/blet/humer?	
Kidney		7) Lymph nodes			
		8) Bone marrow			
Testis/Ovary	X	9) xenograft	X	visible? en liten forhegning under huden, tatt ut til HES	
	T	10) thymus	X		
		11)			
		12)			
		13)			
Notes: Blodhort ✓ Blodplasma ✓ Bilder ✓					



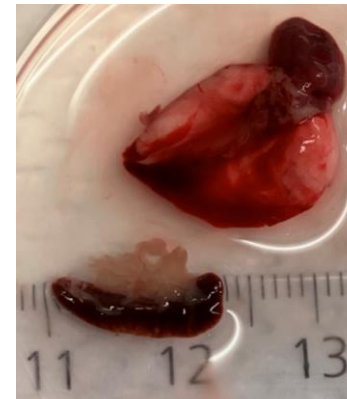
Only small trace visible of xenograft



Undefined dark «bladder» with liquid close to pancreas.



Lungs filled with formalin



Spleen, lungs and heart

Autopsy card modified from:

http://www.pathbase.net/Necropsy_of_the_Mouse/

Supplementary figure 1-12-4. Pictures of scoresheets

NTNU Score sheet FOTS: Avdeling for komparativ medisin (AKM) Responsible researcher: xengraft 1/4-19 Animal ID: 1 (P3 1a) (12)

Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0	2.4.19	3.4	5.4	11.4	24.4	30.4	7.5.19	15.5.19	21.5	4/6
	Reduced grooming	1		0	0	0	0	0	0	0	0	
	Minor distention of abdomen, rough hair coat	3										
	Hunchback or distended abdomen, inactive	18										
Behaviour (Level of activity)	Normal	0										
	Slightly reduced	1	1	1	0	0	0	0	0	0	0	
	Moderately reduced	3										
	Distressed behaviour due to growing tumour	3										
	Obviously reduced	5										
	Isolated, inactive, lethargic	18										
Body weight (Compared to body weight before experiment)	Body weight:		20.2			20.2	21.5	21.6	21.5	21.8	22.9	24.3
	No loss	0				0	0		0	0	0	
	Loss < 5%	1										
	Loss 5-9%	3										
	Loss 10-14%	5										
	Loss ≥ 15%	18										
Clinical signs (Infection, bleeding, discoloration)	Normal	0	0		0	5x5mm x-ray	5x5mm x-ray	5x5mm x-ray	5x5mm x-ray	5x5mm x-ray	5x5mm x-ray	4x4
	Minor irritation around surgical wound	1										
	Moderate irritation/infected surgical wound	3										
	Infected/open surgical wound	4 *										
	Tumour > 1.0 cm in diameter	10										
	Tumour > 1.5 cm in diameter	18										
	Ulcerous tumour	18										
	Total:											
Comments, treatments etc:												

NTNU Score sheet FOTS: Avdeling for komparativ medisin (AKM) Responsible researcher: xengraft 1/4-19 Animal ID: 1 (P3 1a) (12)

Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0	11/6-14	14/6	18/6	25/6	09/7	7/7	13/8	19/8	26/8	4/9
	Reduced grooming	1										
	Minor distention of abdomen, rough hair coat	3						0		0		
	Hunchback or distended abdomen, inactive	18										
Behaviour (Level of activity)	Normal	0										
	Slightly reduced	1										
	Moderately reduced	3										
	Distressed behaviour due to growing tumour	3						0				
	Obviously reduced	5										
	Isolated, inactive, lethargic	18										
Body weight (Compared to body weight before experiment)	Body weight:		23.1		21.9	23	23.7	21.7	22.7	23.6	22.3	22.7
	No loss	0										
	Loss < 5%	1										
	Loss 5-9%	3										
	Loss 10-14%	5										
	Loss ≥ 15%	18										
Clinical signs (Infection, bleeding, discoloration)	Normal	0										
	Minor irritation around surgical wound	1										
	Moderate irritation/infected surgical wound	3										
	Infected/open surgical wound	4 *										
	Tumour > 1.0 cm in diameter	10										
	Tumour > 1.5 cm in diameter	18										
	Ulcerous tumour	18										
	Total:											
Comments, treatments etc:												

NTNU Score sheet FOTS: Avdeling for komparativ medisin (AKM) Responsible researcher: xengraft 1/4-19 Animal ID: 1 (P3 1a) (12)

Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0	12/4	9/9	11/9	13/9	16/9	18/9	23/9	25/9	30/9	4/10
	Reduced grooming	1										
	Minor distention of abdomen, rough hair coat	3										
	Hunchback or distended abdomen, inactive	18										
Behaviour (Level of activity)	Normal	0										
	Slightly reduced	1										
	Moderately reduced	3										
	Distressed behaviour due to growing tumour	3										
	Obviously reduced	5										
	Isolated, inactive, lethargic	18										
Body weight (Compared to body weight before experiment)	Body weight:		22.7	22.9	23.3	23.5	22	21.9	22.3	22.7	21.8	21.9
	No loss	0										
	Loss < 5%	1										
	Loss 5-9%	3										
	Loss 10-14%	5										
	Loss ≥ 15%	18										
Clinical signs (Infection, bleeding, discoloration)	Normal	0										
	Minor irritation around surgical wound	1										
	Moderate irritation/infected surgical wound	3										
	Infected/open surgical wound	4 *										
	Tumour > 1.0 cm in diameter	10										
	Tumour > 1.5 cm in diameter	18										
	Ulcerous tumour	18										
	Total:											
Comments, treatments etc:												

NTNU Score sheet FOTS: Avdeling for komparativ medisin (AKM) Responsible researcher: xengraft 1/4-19 Animal ID: 1 (P3 1a) (12)

Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0	4/10	8/10	11/10	14/10	16/10	18/10	21/10	23/10	23/10	1/11
	Reduced grooming	1										
	Minor distention of abdomen, rough hair coat	3										
	Hunchback or distended abdomen, inactive	18										
Behaviour (Level of activity)	Normal	0										
	Slightly reduced	1										
	Moderately reduced	3										
	Distressed behaviour due to growing tumour	3										
	Obviously reduced	5										
	Isolated, inactive, lethargic	18										
Body weight (Compared to body weight before experiment)	Body weight:		21.9	22.2	21.7	21.6	22.5	23	22.8	22.8	21.7	21.5
	No loss	0										
	Loss < 5%	1										
	Loss 5-9%	3										
	Loss 10-14%	5										
	Loss ≥ 15%	18										
Clinical signs (Infection, bleeding, discoloration)	Normal	0										
	Minor irritation around surgical wound	1										
	Moderate irritation/infected surgical wound	3										
	Infected/open surgical wound	4 *										
	Tumour > 1.0 cm in diameter	10										
	Tumour > 1.5 cm in diameter	18										
	Ulcerous tumour	18										
	Total:											
Comments, treatments etc:												

Supplementary figure 1-12-4. Pictures of scoresheets

NTNU Score sheet FOTS: Avdeling for komparativ medisin (AKM) Responsible researcher: Pettersen Animal ID: 1 (P3) 12

Xenograft 1/4-19

Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0	4/11	6/11	12/11	13/11	15/11	18/11	20/11	25/11	27/11	2/12	5/12
	Reduced grooming	1											
	Minor distention of abdomen, rough hair coat	3											
	Hunchback or distended abdomen, inactive	18											
Behaviour (Level of activity)	Normal	0											
	Slightly reduced	1											
	Moderately reduced	3											
	Distressed behaviour due to growing tumour	3											
	Obviously reduced	5											
Body weight (Compared to body weight before experiment)	Isolated, inactive, lethargic	18											
	Body weight:		21,9	23,2	23,4		22,1	17,8	20,9	22,2	25,7	27,1	20,6
	No loss	0											
	Loss < 5%	1											
	Loss 5-9%	3											
Clinical signs (Infection, bleeding, discoloration)	Loss 10-14%	5											
	Loss > 15%	18											
	Normal	0											
	Minor irritation around surgical wound	1	3,5x3,5	3,7x	3,7	3,5	3,5	3,5	3,5	3,5	3,5	3,5	3,5
	Moderate irritation/infected surgical wound	3											
	Infected/open surgical wound	4 *											
Total:	Tumour > 1,0 cm in diameter	10											
	Tumour > 1,5 cm in diameter	18											
	Ulcerous tumour	18											
	Comments, treatments etc:												

0-3: Normal
4-9: Pay attention to health state and consider treatment
10-13: Pay close attention to health state, consider treatment or euthanasia
14-18: Euthanasia *Start treatment with antibiotics. If no effect within 3 days, euthanize the animal

NTNU Score sheet FOTS: Avdeling for komparativ medisin (AKM) Responsible researcher: Pettersen Animal ID: 1 (P3) 12

Xenograft 1/4-19

Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0	9/12	11/12	13/12	16/12	18/12	20/12	24/12	26/12	30/12	31/12	6/1/2021
	Reduced grooming	1											
	Minor distention of abdomen, rough hair coat	3											
	Hunchback or distended abdomen, inactive	18											
Behaviour (Level of activity)	Normal	0											
	Slightly reduced	1											
	Moderately reduced	3											
	Distressed behaviour due to growing tumour	3											
	Obviously reduced	5											
Body weight (Compared to body weight before experiment)	Isolated, inactive, lethargic	18											
	Body weight:		20,6	21	20,8	21,6	22,3	21,9	22,2	21,3	21,9	21,9	22,6
	No loss	0											
	Loss < 5%	1											
	Loss 5-9%	3											
Clinical signs (Infection, bleeding, discoloration)	Loss 10-14%	5											
	Loss > 15%	18											
	Normal	0											
	Minor irritation around surgical wound	1											
	Moderate irritation/infected surgical wound	3											
	Infected/open surgical wound	4 *											
Total:	Tumour > 1,0 cm in diameter	10											
	Tumour > 1,5 cm in diameter	18											
	Ulcerous tumour	18											
	Comments, treatments etc:												

0-3: Normal
4-9: Pay attention to health state and consider treatment
10-13: Pay close attention to health state, consider treatment or euthanasia
14-18: Euthanasia *Start treatment with antibiotics. If no effect within 3 days, euthanize the animal

NTNU Score sheet FOTS: Avdeling for komparativ medisin (AKM) Responsible researcher: Pettersen Animal ID: 1 (P3) 12

Xenograft 1/4-19

Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0	13/1	15/1	17/1	20/1	22/1	24/1	27/1	27/1	30/1	3/2	5/2
	Reduced grooming	1											
	Minor distention of abdomen, rough hair coat	3											
	Hunchback or distended abdomen, inactive	18											
Behaviour (Level of activity)	Normal	0											
	Slightly reduced	1											
	Moderately reduced	3											
	Distressed behaviour due to growing tumour	3											
	Obviously reduced	5											
Body weight (Compared to body weight before experiment)	Isolated, inactive, lethargic	18											
	Body weight:		22,4	22	22,3	23	23,5	23,5	21,9	22,5	22,3	21,4	22,3
	No loss	0											
	Loss < 5%	1											
	Loss 5-9%	3											
Clinical signs (Infection, bleeding, discoloration)	Loss 10-14%	5											
	Loss > 15%	18											
	Normal	0											
	Minor irritation around surgical wound	1											
	Moderate irritation/infected surgical wound	3											
	Infected/open surgical wound	4 *											
Total:	Tumour > 1,0 cm in diameter	10											
	Tumour > 1,5 cm in diameter	18											
	Ulcerous tumour	18											
	Comments, treatments etc:												

0-3: Normal
4-9: Pay attention to health state and consider treatment
10-13: Pay close attention to health state, consider treatment or euthanasia
14-18: Euthanasia *Start treatment with antibiotics. If no effect within 3 days, euthanize the animal

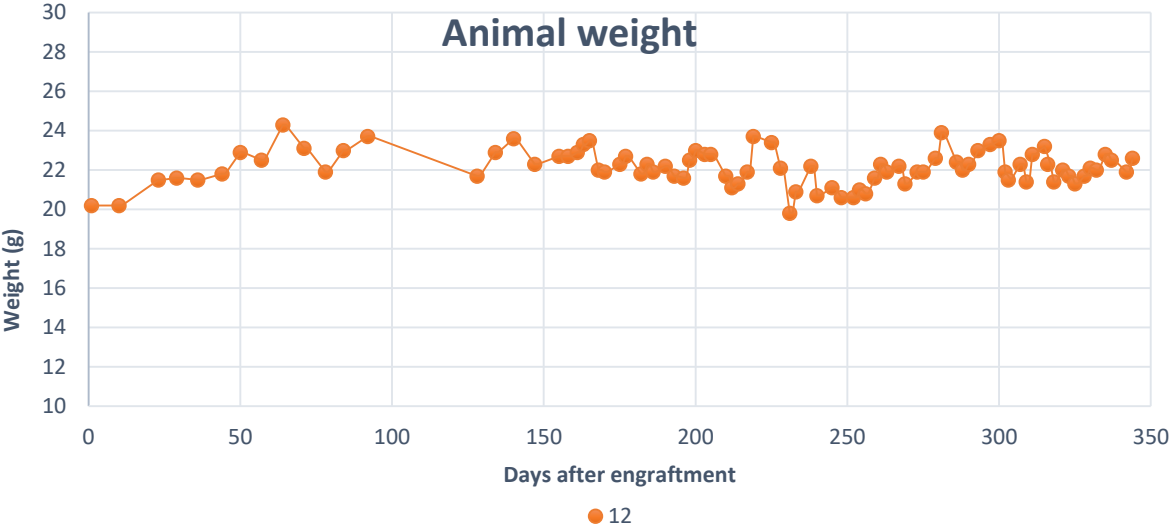
NTNU Score sheet FOTS: Avdeling for komparativ medisin (AKM) Responsible researcher: Pettersen Animal ID: 1 (P3) 12

Xenograft 1/4-19

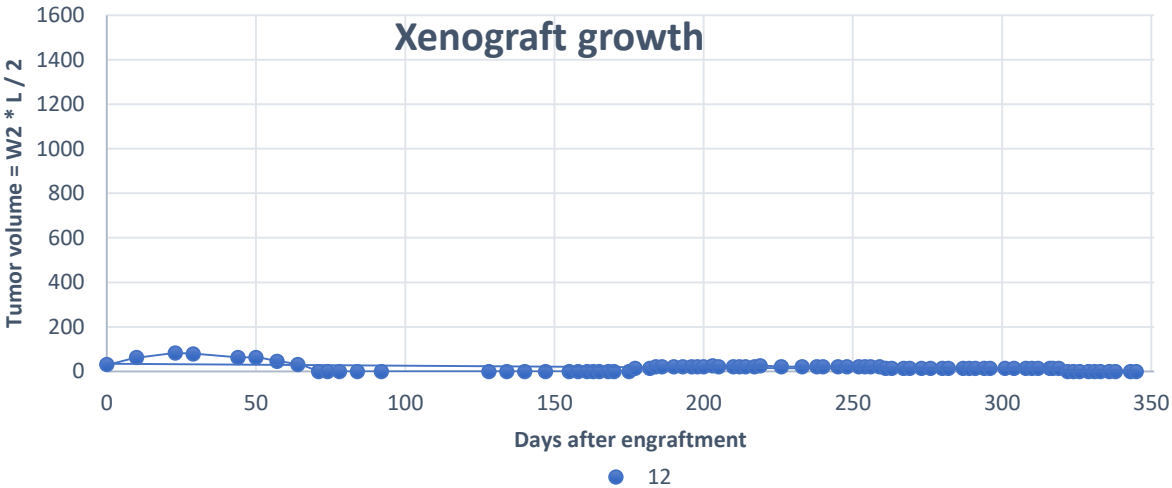
Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0	11/2	12/2	14/2	17/2	19/2	21/2	24/2	26/2	28/2	31/2	4/3
	Reduced grooming	1											
	Minor distention of abdomen, rough hair coat	3											
	Hunchback or distended abdomen, inactive	18											
Behaviour (Level of activity)	Normal	0											
	Slightly reduced	1											
	Moderately reduced	3											
	Distressed behaviour due to growing tumour	3											
	Obviously reduced	5											
Body weight (Compared to body weight before experiment)	Isolated, inactive, lethargic	18											
	Body weight:		23,2	22,3	21,4	22	21,7	21,3	21,7	22,1	22	22,8	22,5
	No loss	0											
	Loss < 5%	1											
	Loss 5-9%	3											
Clinical signs (Infection, bleeding, discoloration)	Loss 10-14%	5											
	Loss > 15%	18											
	Normal	0											
	Minor irritation around surgical wound	1											
	Moderate irritation/infected surgical wound	3											
	Infected/open surgical wound	4 *											
Total:	Tumour > 1,0 cm in diameter	10											
	Tumour > 1,5 cm in diameter	18											
	Ulcerous tumour	18											
	Comments, treatments etc:												

0-3: Normal
4-9: Pay attention to health state and consider treatment
10-13: Pay close attention to health state, consider treatment or euthanasia
14-18: Euthanasia *Start treatment with antibiotics. If no effect within 3 days, euthanize the animal

Weight curve



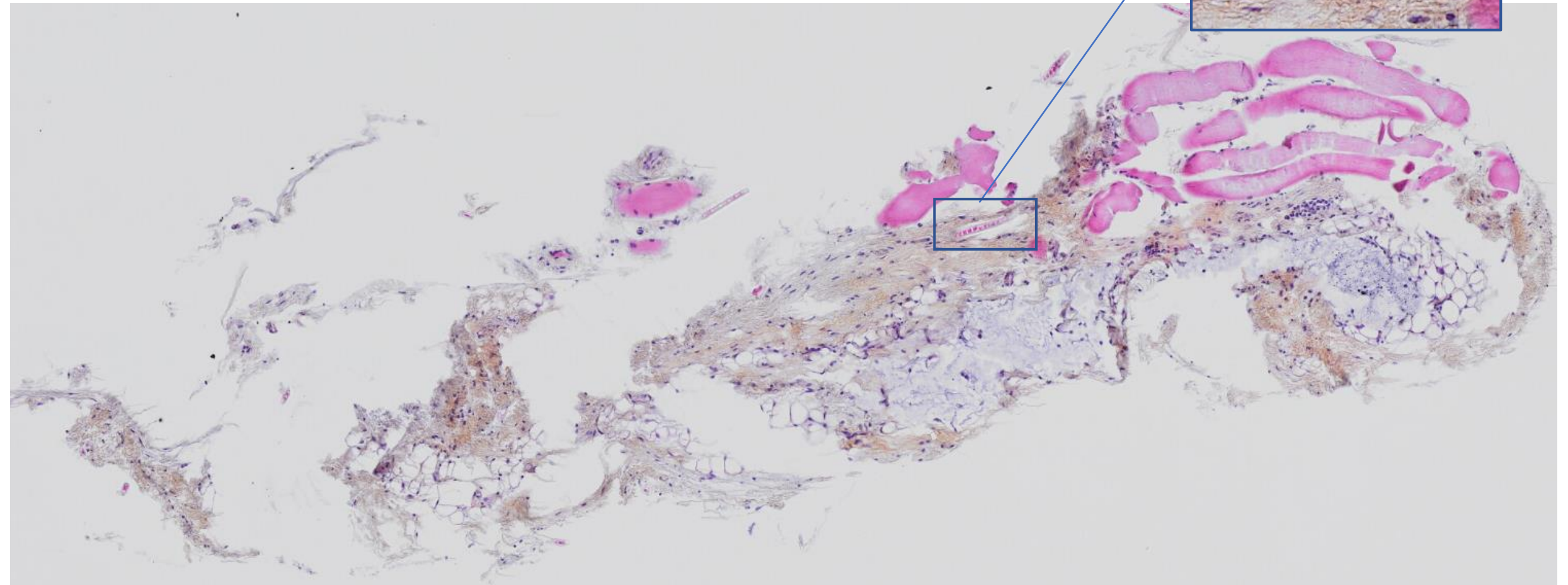
Xenograft growth curve



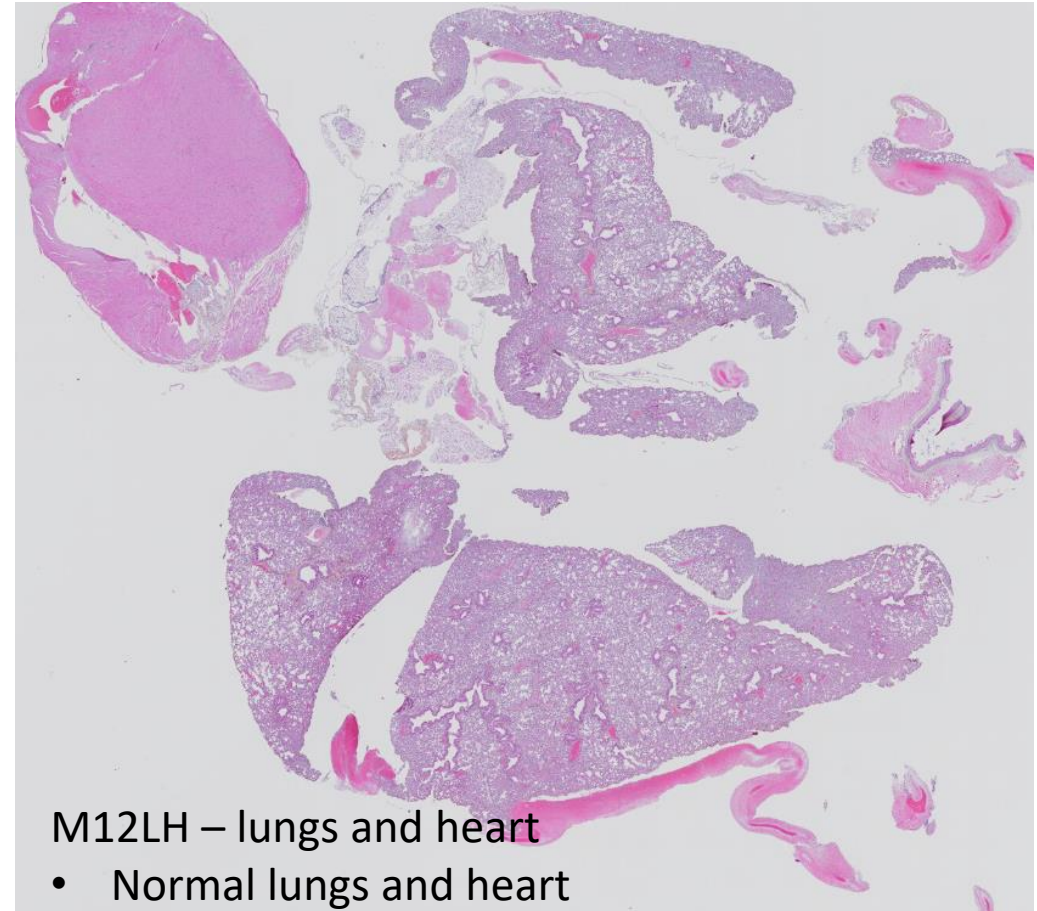
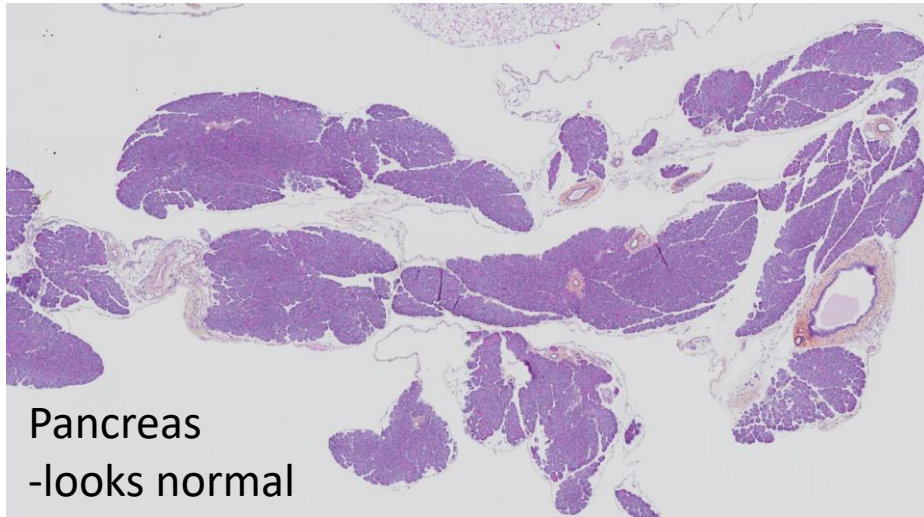
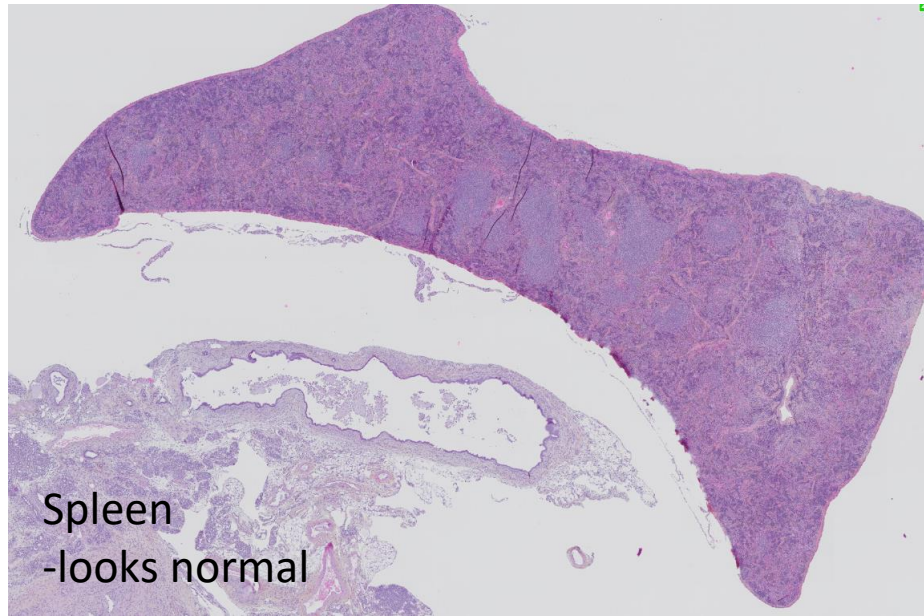
Supplementary figure 1-12-6. Histology pictures

M12X – tissue spot at surgery location at euthanization (thought to be remainings of engrafted tumor material)

- Stained with hematoxylin, eosine and saphron (HES)
- Probably not xenograft tissue
- No tumor cells found
- Muscle cells, fat, mucus, connective tissue
- Traces of plant cells outside but also inside tissue? Possibly paper leftovers.



Supplementary figure 1-12-6. Histology pictures

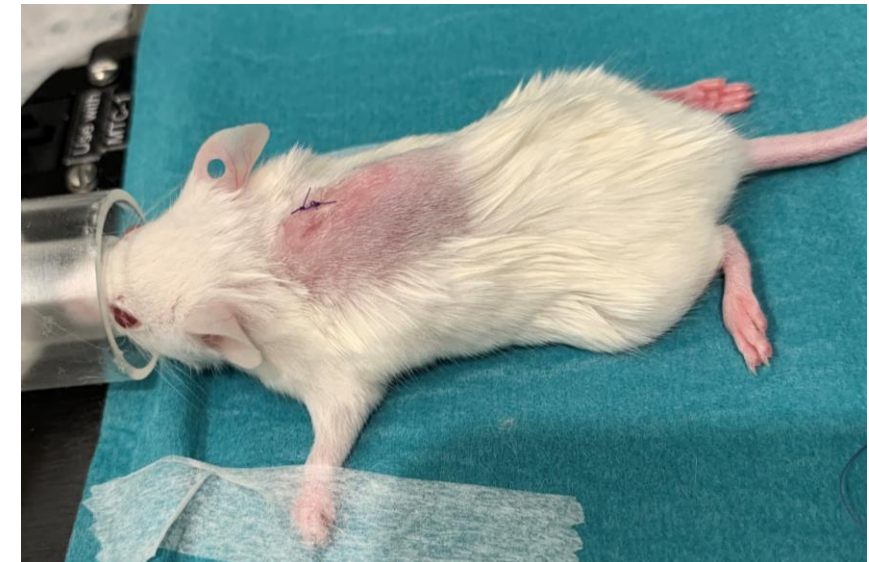


Mouse 15

- Surgery date: 01.04.18
 - Age (weeks) 11
 - Weight (g) 18.5
 - Tumor fragment P3-1B
 - Ear marks 2

MUS			FOTS
Kjønn	♀	Stamme	C1EA NOG
Alder/vekt	6u	Antall	1
Bruker	Caroline H. Pettersen		Ankomst dato
15			25/2-19
01.04.18 Satt inn xenograft P3-1B Mus 2			

Supplementary figure 1-15-1. Pictures from the engraftment day

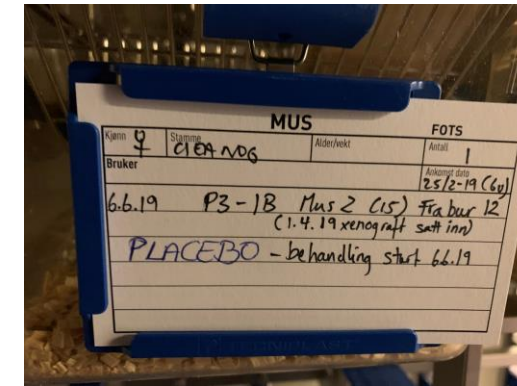


Supplementary figure 1-15-2. Pictures from follow up(14.06.19) and score sheets



Blood sample and treatment

- Blood samples before and after treatment
 - Before: Vena Saphena
 - After: heart
- Placebo treatment



Supplementary figure 1-15-3. List over treatment with placebo. Numbers are weight in grams before and after provided to the mice.

PLACEBO BUR 16

Vekt m/ drikke og tut

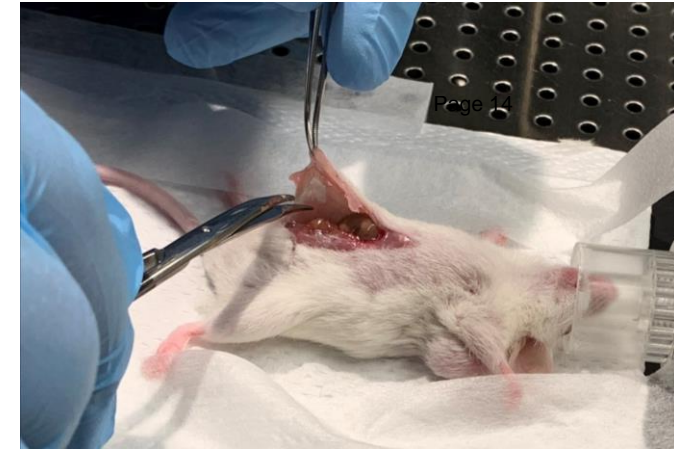
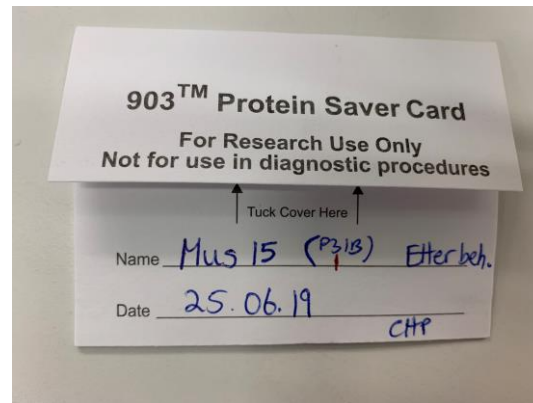
Antall gram per flaske før og etter 7 timer

	Weight (g)		ID mus	ID mus	ID mus	ID mus	ID mus	ID mus
	Start	End						
	08.00	15.00						
05.06.2019								
06.06.2019	131,6	126,3	15					
07.06.2019	129,0	122,6						
10.06.2019	—							
11.06.2019	136,4	127,2		20				
12.06.2019	134,3	124,4						
13.06.2019	133,2	121,2						
14.06.2019	132,4	121,0						
17.06.2019	135,1	125,1						
18.06.2019	133,6	125,2						
19.06.2019	135,0	119,2						
20.06.2019	134,2	116,8						
21.06.2019	133,9	121,1						
24.06.2019	133,2	121,6						
25.06.2019	131,1							
26.06.2019								
27.06.2019								
28.06.2019								
01.07.2019								

Start muggsopp i buret!

Supplementary figure 1-15-4. Pictures from euthanization (25.06.19)

- Necroscopy
 - Xenograft size 15.5 x 10
 - Blood sample (blood card and plasma)
 - Tumor tissue for
 - Histology
 - RNA isolation
 - Protein isolation



Supplementary figure 1-15-5. Pictures of score sheets

NTNU

Score sheet FOTS:

Avdeling for komparativ medisin (AKM)

Responsible researcher:

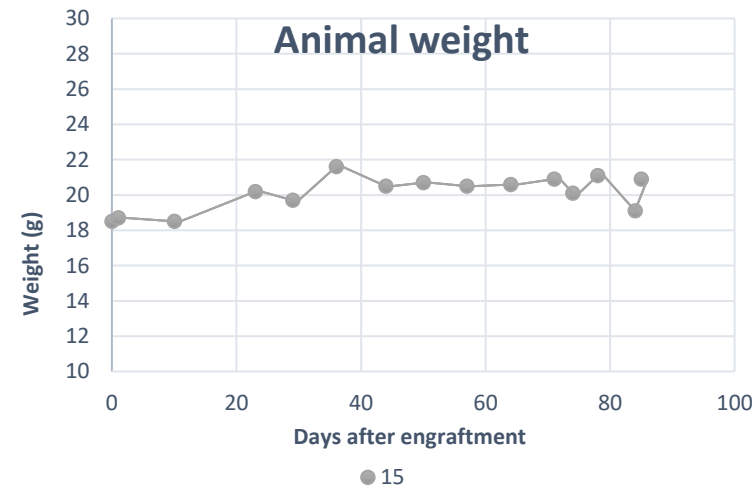
Animal ID: Xenograft 14-1 2 (P3) 15

Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date		
General appearance	Normal	0	2.4.19	3.4	5.4	11.4	24.4	30.4	7/5/19	15/5	21/5/19	28/5	4/6.19		
	Reduced grooming	1			0		6		6	6	6	0	0		
	Minor distention of abdomen, rough hair coat	3				6									
	Hunchback or distended abdomen, inactive	18													
Behaviour (Level of activity)	Normal	0	0		0	6	6		0	0	0	0	0		
	Slightly reduced	1													
	Moderately reduced	3													
	Distressed behaviour due to growing tumour	3													
	Obviously reduced	5													
	Isolated, inactive, lethargic	18													
Body weight (Compared to body weight before experiment)	Body weight:		18.7			18.5	20.2	19.67	21.6	20.5	20.7	20.5	20.6		
	No loss	0				0	6		6	0	0	0			
	Loss < 5%	1													
	Loss 5-9%	3													
	Loss 10-14%	5													
	Loss ≥ 15%	18													
Clinical signs (Infection, bleeding, discoloration)	Normal	0	0		1								6.5		
	Minor irritation around surgical wound	1											8.5		
	Moderate irritation/infected surgical wound	3													
	Infected/open surgical wound	4*													
	Tumour > 1.0 cm in diameter	10													
	Tumour > 1.5 cm in diameter	18													
	Ulcerous tumour	18													
	Total:														
Comments, treatments etc:			<div>3 operative open for 3d 0.1 lit Amn: U26</div> <div>5x55 5x55 4x4</div> <div>ser xenograft 7d met. 3d ser. 1d sister ut</div> <div>ca 9x4.5 4.5 6 (lung) res. over on lung</div> <div>6.5 8 8.5</div> <div>12.5 9.5 4.5 2.5</div> <div>234/ 587</div> <div>mm³</div> <div>1</div> <div>14 15</div> <div>15.5 17</div> <div>13.5 (9)</div> <div>179.6 mm³</div> <div>234.8 mm³</div> <div>or euthanasia Tect within 3 days, euthanize the animal</div>												

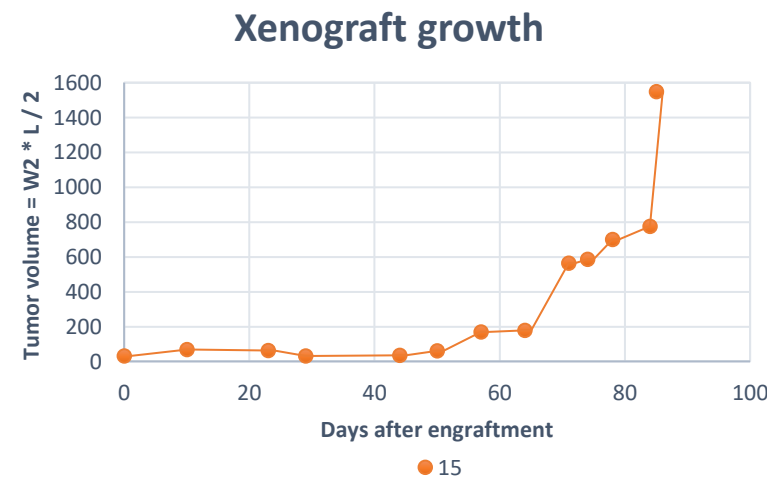
0-3: Normal
4-9: Pay attention to health state and consider treatment
10-13: Pay close attention to health state, consider treatment or euthanasia
14-18: Euthanasia *Start treatment with antibiotics. If no effect within 3 days, euthanize the animal

$$\frac{(8.5 \cdot 6.5^2)}{2} = 179.6 \text{ mm}^3$$
$$\frac{(6.5 \cdot 8.5^2)}{2} = 234.8 \text{ mm}^3$$

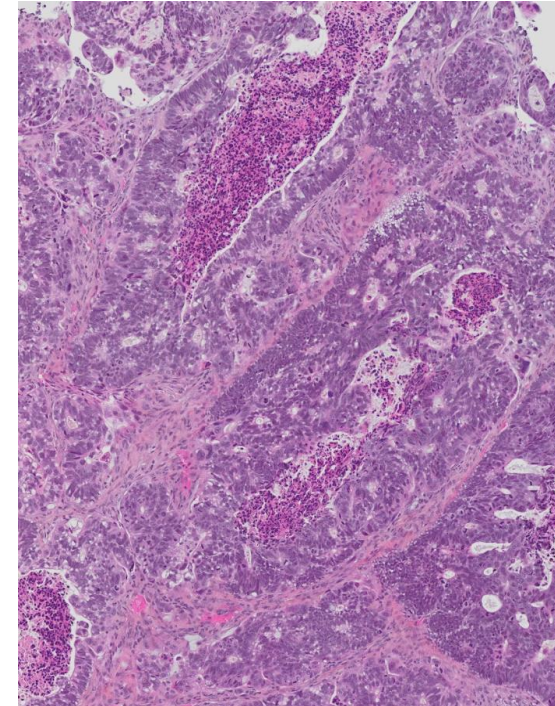
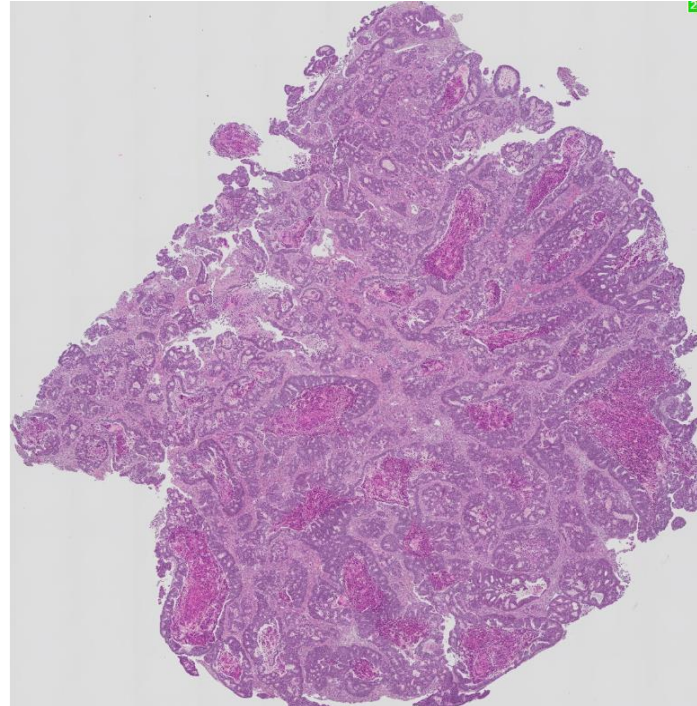
Weight curve



Xenograft growth curve



M15X



- Typical colorectal adenocarcinoma
- Very similar to the HES staining of patient tumor 3
- Gland forming cells
- Necrotic debris within glandular lumen

Mouse 16

- Surgery date: 01.04.19
 - Age (weeks) 11
 - Weight (g) 18.2
 - Tumor fragment P3-2A
 - Ear marks 3

MUS			FOTS
Kjønn	♀	Stamme	Antall
		CIEA N06	1
Bruker		Alder/vekt	Ankomst dato
Caroline H. Pettersen		6 u	25/2-19
16 #			
1.4.19 satt inn xenograft P3-2A Musnr3			

Supplementary figure 1-16-1.
Pictures from the engraftment day



Supplementary figure 1-16-2.
Pictures from follow up (14.06.19)



Blood sample and treatment

- Before: Vena Saphena
- After: heart 04.06.19
- Treatment: Smartfish with fishoil (OMEGA-3)

MUS		FOTS	
Kjønn	♀	Stamme	CIEA NOS
Alder/vekt		Antall	1
Bruker		Ankomst dato	
6.6.19 - P3-2A Mus 3 (16) Fra Bur 12		25/19 (6u)	
c. 1.4.19 xenograft satt inn			
Smartfish - behandling start 6.6.19			

Smartfish - OMEGA3 - BUR 17

Antall gram per flaske før og etter 7 timer Vekt m/drikke og tut

	Weight (g)		ID mus	ID mus	ID mus	ID mus	ID mus	ID mus
	Start	End						
05.06.2019								
06.06.2019	134	128,3	16					
07.06.2019	133,7	126,2						
10.06.2019								
11.06.2019	138,5	130		22				
12.06.2019	138	132,8						
13.06.2019	138,5	131,9						
14.06.2019	142,5	134,6						
17.06.2019	137,8	130,6						
18.06.2019	137,4	129,0						
19.06.2019	139,2	132,3						
20.06.2019	138,8	131,6						
21.06.2019	140,6	134,7						
24.06.2019	139,1	130,5						
25.06.2019	138,2							
26.06.2019								
27.06.2019								
28.06.2019								
01.07.2019								
02.07.2019								
03.07.2019								

← Papiret kan bryte flaska

Supplementary figure 1-16-3. List with weight registrations of the drinking bottle (with Smartfish Remune Peach drink) before and after provided to the mice

Supplementary figure 1-16-4. Pictures from euthanization

- Xenograft size 13 x 11.5
- Xenograft partly liquid
- Visiable blood vain formation
- Blood sample (blood card and plasma)
- Tumor tissue for
 - Histology
 - RNA isolation
 - Protein isolation



903TM Protein Saver Card
For Research Use Only
Not for use in diagnostic procedures

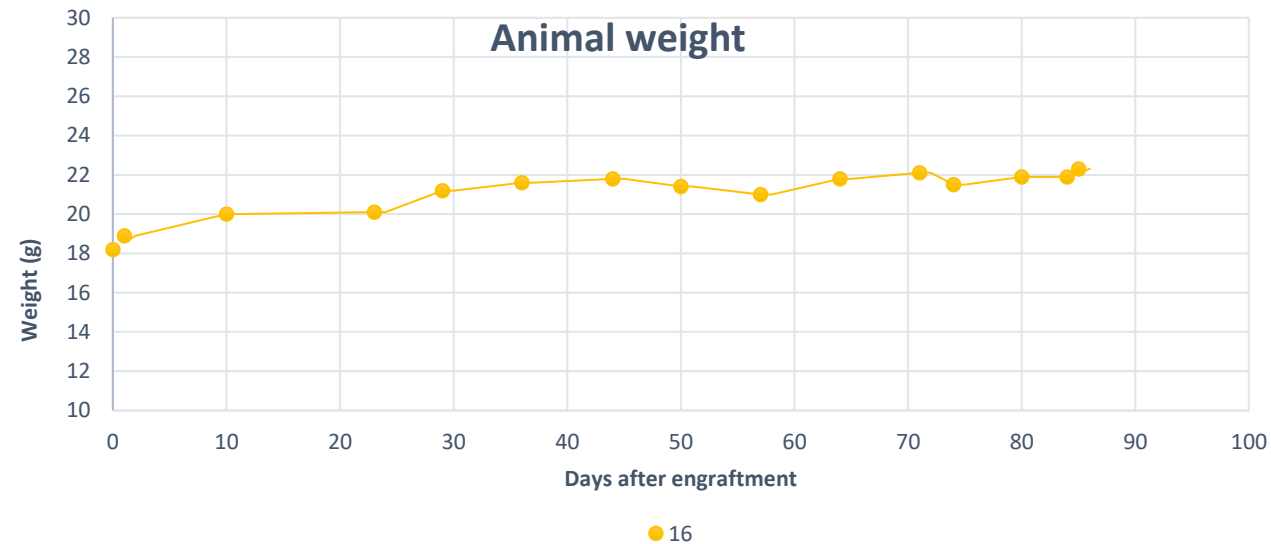
↑ Tuck Cover Here ↑

Name Mus 16 Etterbeh. (P3)
Date 25.6.19 CHP

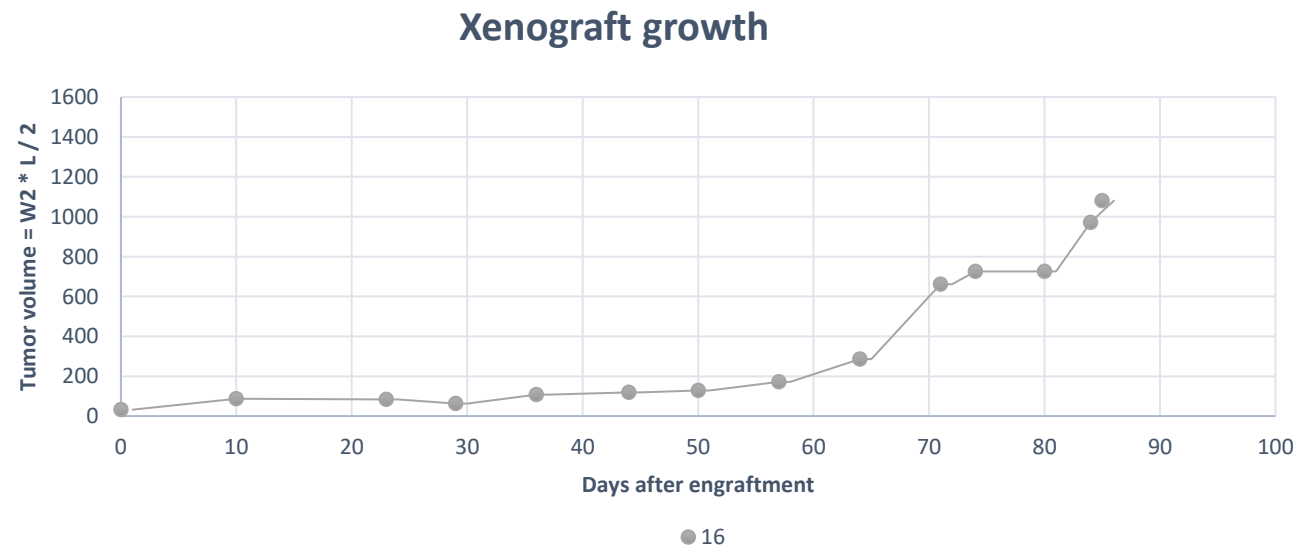
Page 22

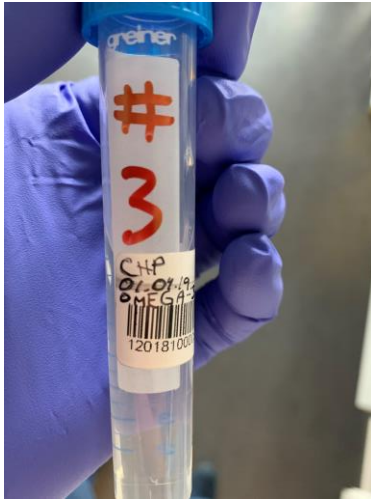
blood my
ends
plasma

Weight curve

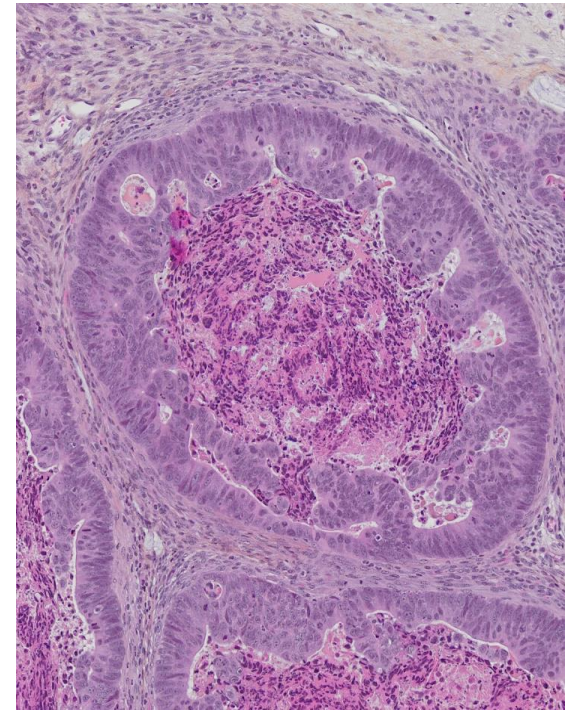
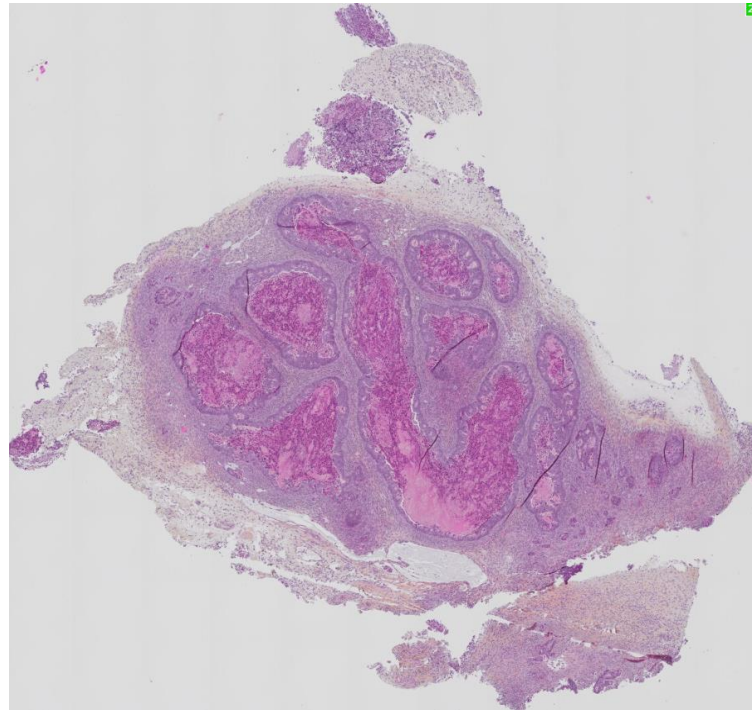


Xenograft growth curve





M16X



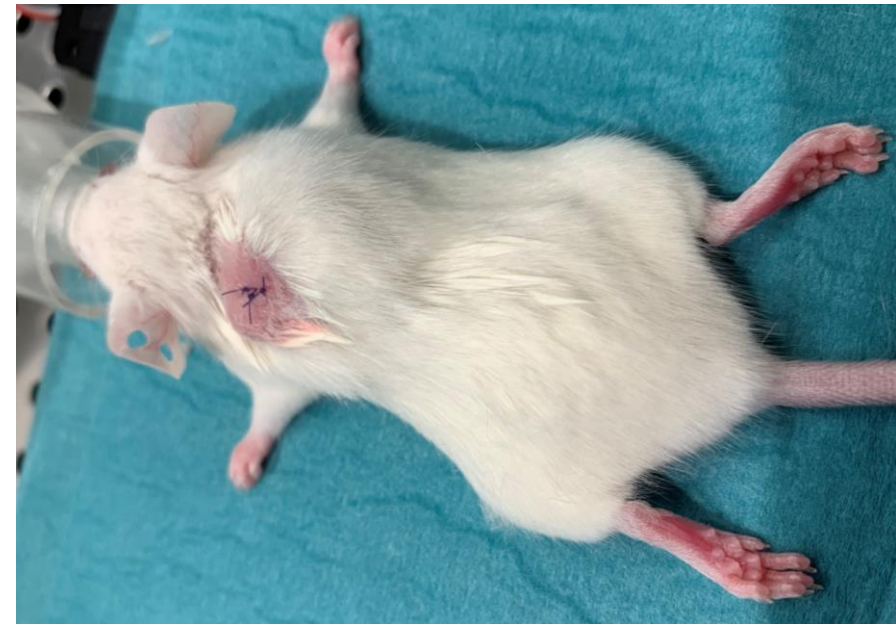
- Typical colorectal adenocarcinoma
- Very similar to the HES staining of patient tumor 3
- Necrotic debris within glandulas

Mouse 17

- Surgery date: 01.04.19
 - Age (weeks) 11
 - Weight (g) 18.4
 - Tumor fragment P3-2B
 - Ear marks 4

MUS			FOTS
Kjønn	♀	Stamme	CIEA NOG
Alder/vekt	6u	Antall	1
Bruker	Caroline H. Pettersen		Ankomst dato
17			25/2-19
1.4.19 satt im xenograft P3-2B - mus nr. 4.			

Supplementary figure 1-17-1.
Pictures from the engraftment day



Supplementary figure 1-17-2. List over weight registrations of the drinking bottle before and after provided to the mice Page 26

Treatment:

- Smartfish with fishoil (OMEGA-3) ; started 04.07.19.
 - Xenograft 7.5 x 7.5 mm
 - Mouse 12 was used as social animal together with mouse 17
- Died 12.07.19 during anasthesia
- Xenograft not sampled
- Xenograft not pictured

Mus 12 brukt som sosialt dyr, plassert i cage
bør nær mus 17 døde

01.07.2019							
02.07.2019							
03.07.2019							
04.07.2019	135,5	127,8					
05.07.2019	139,6	128,6					
08.07.2019	138,6	129,5					
09.07.2019	138,8	129,0					
10.07.2019	136,6	127,4					
11.07.2019	136,7	127,6					
12.07.2019	137,9						
15.07.2019							
16.07.2019							

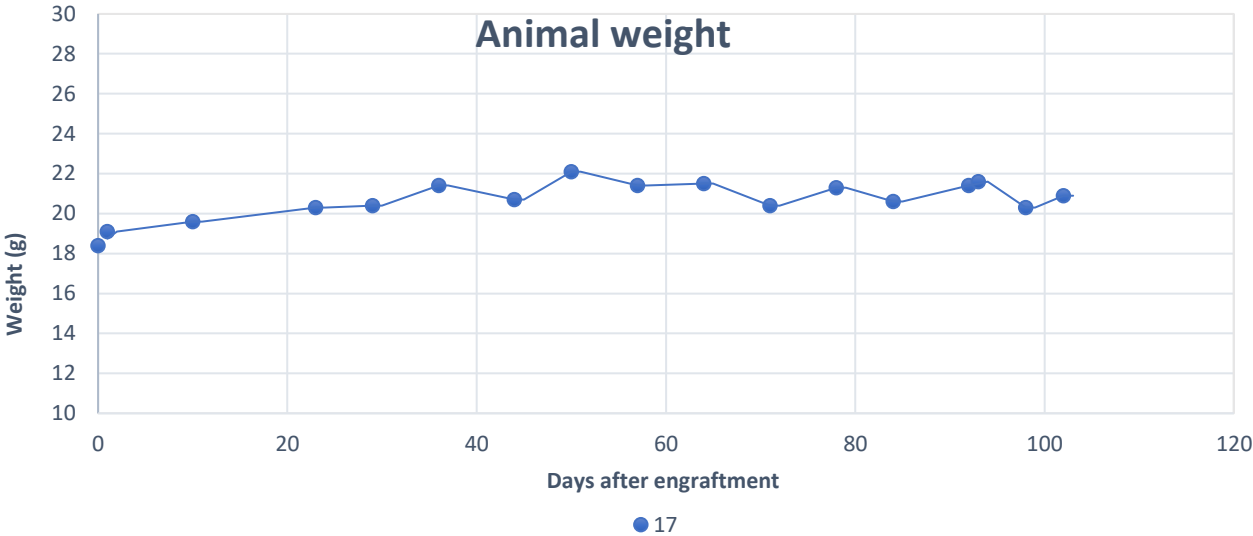
→ Mus 17 døde i maddeskann

Page 27

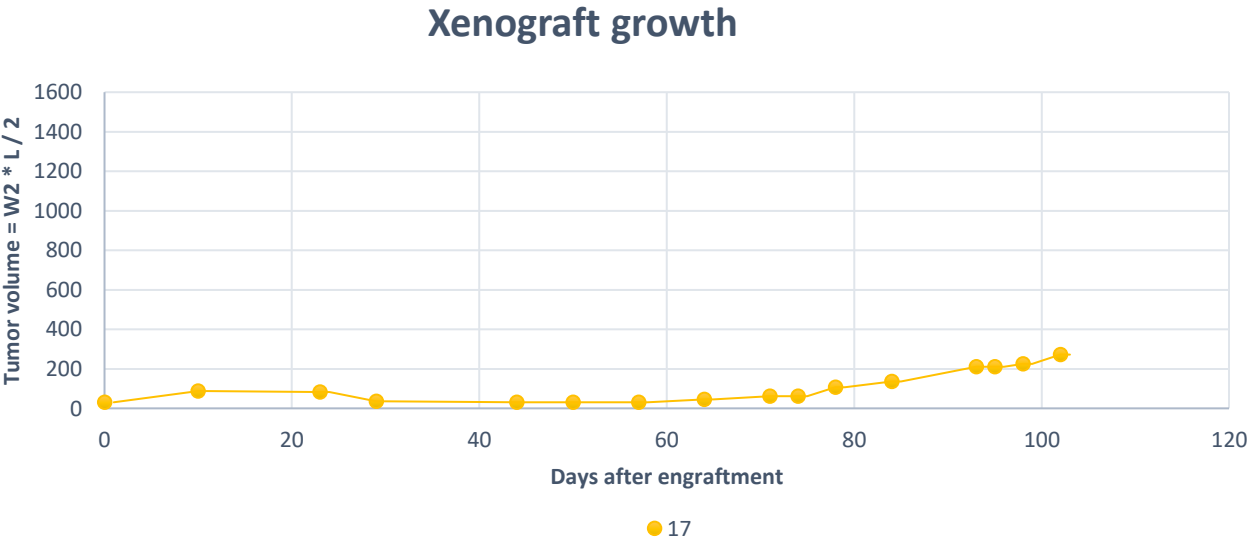
[illegible]

Effect within 3 days, euthanize the animal

Weight curve



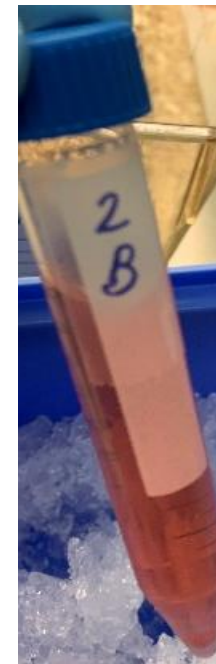
Xenograft growth curve



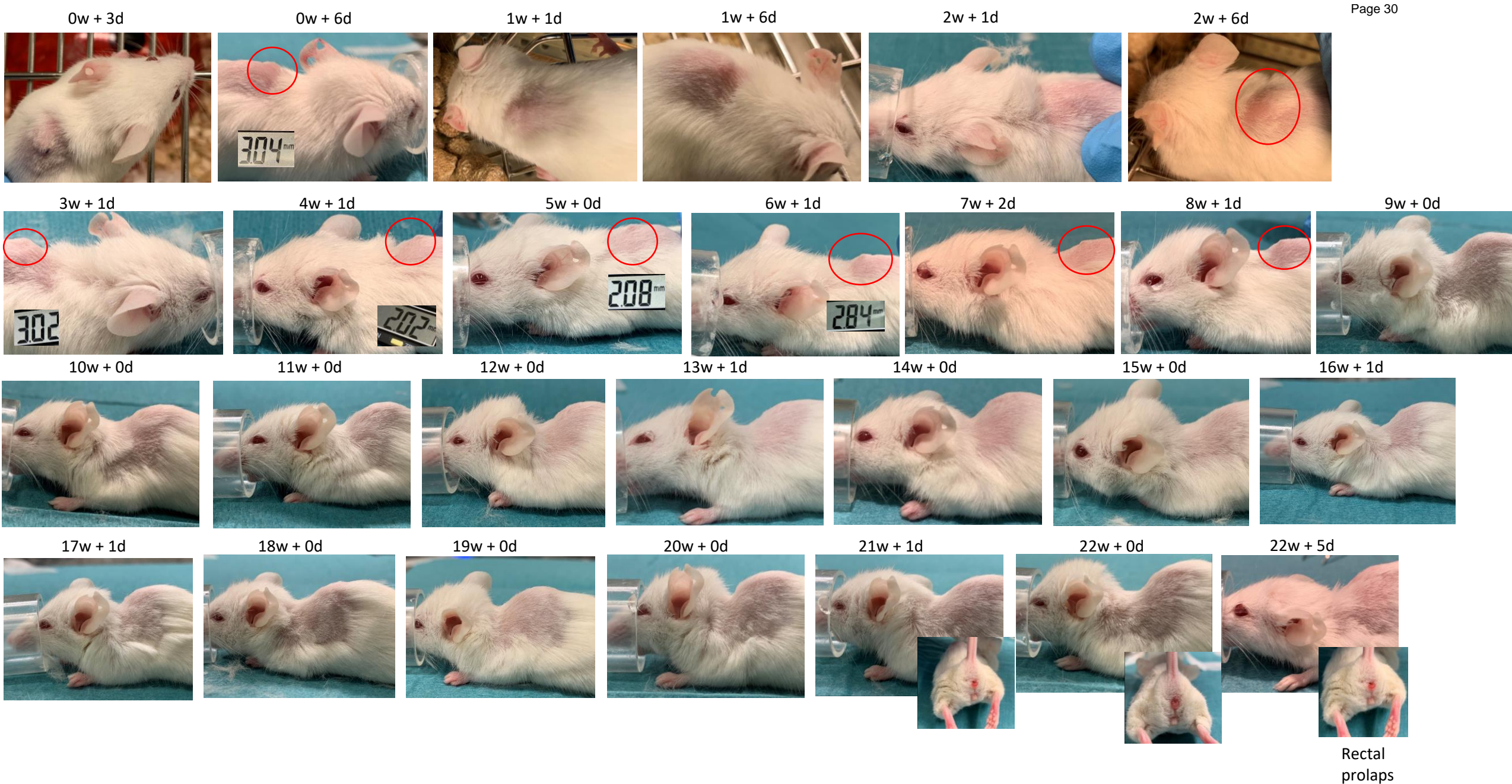
Mouse 18

- Surgery date: 03.09.19
 - Age (weeks) 33
 - Weight (g) 22.1
 - Tumor fragment P19-2b
 - Fragment size 3 x 3 mm
 - Ear marks 4

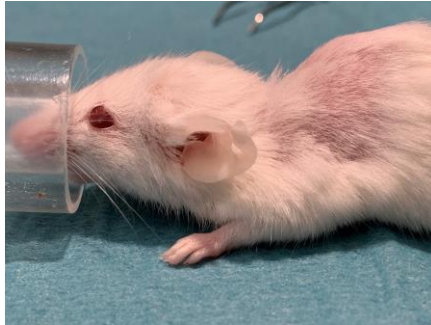
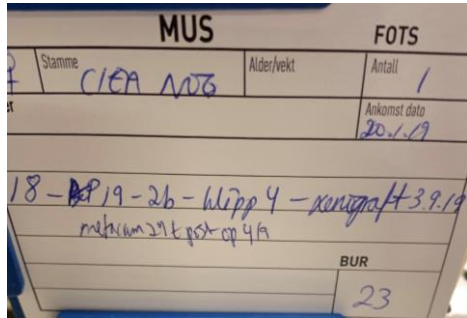
Supplementary figure 1-18-1.
Pictures from the engraftment day



Supplementary figure 1-18-2. Pictures from follow up and tumor size measurement



Supplementary figure 1-18-3. Pictures euthanization (10.02.20)



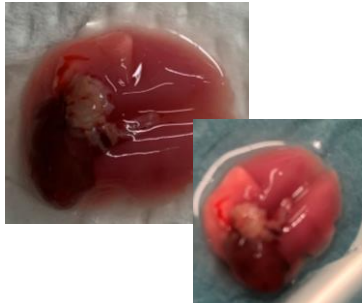
Reduced health, Rectal prolaps; svollen bloody anal opening
Weight slightly reduced.

Before euthanization:

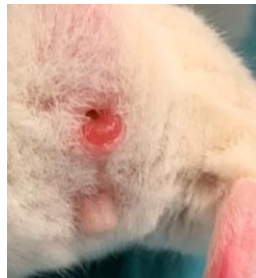
- Reduced health
- Rectal prolaps; red, svollen anus opening
- Reduced Weight 19,8 g
- Not growing xenograft (xenograft almost not visible)
- No treatment given



Large spleen, ca 2,5 cm,
normal colour



Whitish part of one lung



Red, svollen anal opening

After euthanization:

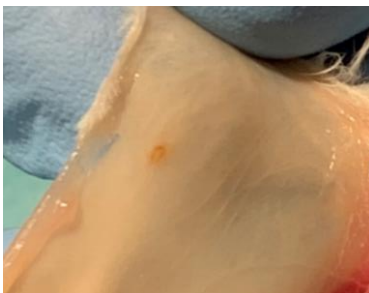
- Enlarged spleen 2,5 cm
- Whitish part of one lung
- Xenograft did not seem to have grown

Histology samples:

- **M32ET** Rectum
- **M32N** Kidneys
- **M32MP** Milt/pancreas
- **M32LH** Lung and Heart
- **M32L** Liver



Bloody anal opening of
rectum



Only a small spot left of the
xenograft

Supplementary figure 1-18-4. Pictures of score sheets

NTNU Score sheet FOTS: Avdeling for komparativ medisin (AKM) Responsible researcher: Pettersen (P19-26) Animal ID: 18 Wipp 4

Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0	3/9	4/9	6/9	9/9	11/9	13/9	16/9	18/9	20/9	23/9	25/9	
	Reduced grooming	1												
	Minor distention of abdomen, rough hair coat	3												
	Hunchback or distended abdomen, inactive	18												
Behaviour (Level of activity)	Normal	0												
	Slightly reduced	1												
	Moderately reduced	3												
	Distressed behaviour due to growing tumour	3												
	Obviously reduced	5												
	Isolated, inactive, lethargic	18												
Body weight (Compared to body weight before experiment)	Body weight:		21.2		21.2	21.4	22.1	21.9	22.5	22.4	21.4	21		
	No loss	0												
	Loss < 5%	1												
	Loss 5-9%	3												
	Loss 10-14%	5												
	Loss > 15%	18												
Clinical signs (Infection, bleeding, discoloration)	Normal	0												
	Minor irritation around surgical wound	1												
	Moderate irritation/infected surgical wound	3												
	Infected/open surgical wound	4*												
	Tumour > 1.0 cm in diameter	10												
	Tumour > 1.5 cm in diameter	18												
Ulcerous tumour	18													

Total: 21

Comments, treatments etc: 0-3: Normal 4-9: Pay attention to health state and consider treatment 10-13: Pay close attention to health state, consider treatment or euthanasia 14-18: Euthanasia *Start treatment with antibiotics. If no effect within 3 days, euthanize the animal

NTNU Score sheet FOTS: Avdeling for komparativ medisin (AKM) Responsible researcher: Pettersen (P19-26) Animal ID: 18 Wipp 4

Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0	25/9	26/9	27/9	28/9	29/9	30/9	1/10	2/10	3/10	4/10	5/10	6/10
	Reduced grooming	1												
	Minor distention of abdomen, rough hair coat	3												
	Hunchback or distended abdomen, inactive	18												
Behaviour (Level of activity)	Normal	0												
	Slightly reduced	1												
	Moderately reduced	3												
	Distressed behaviour due to growing tumour	3												
	Obviously reduced	5												
	Isolated, inactive, lethargic	18												
Body weight (Compared to body weight before experiment)	Body weight:		21	21.3	21.7	21.3	20.9	21.3	21.5	20.5	21.0	21.7		
	No loss	0												
	Loss < 5%	1												
	Loss 5-9%	3												
	Loss 10-14%	5												
	Loss > 15%	18												
Clinical signs (Infection, bleeding, discoloration)	Normal	0												
	Minor irritation around surgical wound	1												
	Moderate irritation/infected surgical wound	3												
	Infected/open surgical wound	4*												
	Tumour > 1.0 cm in diameter	10												
	Tumour > 1.5 cm in diameter	18												
Ulcerous tumour	18													

Total: 21

Comments, treatments etc: 0-3: Normal 4-9: Pay attention to health state and consider treatment 10-13: Pay close attention to health state, consider treatment or euthanasia 14-18: Euthanasia *Start treatment with antibiotics. If no effect within 3 days, euthanize the animal

NTNU Score sheet FOTS: Avdeling for komparativ medisin (AKM) Responsible researcher: Pettersen (P19-26) Animal ID: 18 Wipp 4

Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0	18/11	20/11	22/11	24/11	26/11	28/11	30/11	1/12	3/12	5/12	7/12	9/12
	Reduced grooming	1												
	Minor distention of abdomen, rough hair coat	3												
	Hunchback or distended abdomen, inactive	18												
Behaviour (Level of activity)	Normal	0												
	Slightly reduced	1												
	Moderately reduced	3												
	Distressed behaviour due to growing tumour	3												
	Obviously reduced	5												
	Isolated, inactive, lethargic	18												
Body weight (Compared to body weight before experiment)	Body weight:		21.6	21.5	22.2	21.9	21.1	20.2	20.8	20.6	20.8	20.3		
	No loss	0												
	Loss < 5%	1												
	Loss 5-9%	3												
	Loss 10-14%	5												
	Loss > 15%	18												
Clinical signs (Infection, bleeding, discoloration)	Normal	0												
	Minor irritation around surgical wound	1												
	Moderate irritation/infected surgical wound	3												
	Infected/open surgical wound	4*												
	Tumour > 1.0 cm in diameter	10												
	Tumour > 1.5 cm in diameter	18												
Ulcerous tumour	18													

Total: 21

Comments, treatments etc: 0-3: Normal 4-9: Pay attention to health state and consider treatment 10-13: Pay close attention to health state, consider treatment or euthanasia 14-18: Euthanasia *Start treatment with antibiotics. If no effect within 3 days, euthanize the animal

NTNU Score sheet FOTS: Avdeling for komparativ medisin (AKM) Responsible researcher: Pettersen (P19-26) Animal ID: 18 Wipp 4

Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0	21/10	23/10	25/10	27/10	29/10	31/10	1/11	3/11	5/11	7/11	9/11	11/11
	Reduced grooming	1												
	Minor distention of abdomen, rough hair coat	3												
	Hunchback or distended abdomen, inactive	18												
Behaviour (Level of activity)	Normal	0												
	Slightly reduced	1												
	Moderately reduced	3												
	Distressed behaviour due to growing tumour	3												
	Obviously reduced	5												
	Isolated, inactive, lethargic	18												
Body weight (Compared to body weight before experiment)	Body weight:		21.7	21.6	20.5	20.2	20.5	20.0	21.4	21.8	21.1			
	No loss	0												
	Loss < 5%	1												
	Loss 5-9%	3												
	Loss 10-14%	5												
	Loss > 15%	18												
Clinical signs (Infection, bleeding, discoloration)	Normal	0												
	Minor irritation around surgical wound	1												
	Moderate irritation/infected surgical wound	3												
	Infected/open surgical wound	4*												
	Tumour > 1.0 cm in diameter	10												
	Tumour > 1.5 cm in diameter	18												
Ulcerous tumour	18													

Total: 21

Comments, treatments etc: 0-3: Normal 4-9: Pay attention to health state and consider treatment 10-13: Pay close attention to health state, consider treatment or euthanasia 14-18: Euthanasia *Start treatment with antibiotics. If no effect within 3 days, euthanize the animal

NTNU Score sheet FOTS: Avdeling for komparativ medisin (AKM) Responsible researcher: Pettersen (P19-26) Animal ID: 18 Wipp 4

Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0	18/10	20/10	22/10	24/10	26/10	28/10	30/10	1/11	3/11	5/11	7/11	9/11
	Reduced grooming	1												
	Minor distention of abdomen, rough hair coat	3												
	Hunchback or distended abdomen, inactive	18												
Behaviour (Level of activity)	Normal	0												
	Slightly reduced	1												
	Moderately reduced	3												
	Distressed behaviour due to growing tumour	3												
	Obviously reduced	5												
	Isolated, inactive, lethargic	18												
Body weight (Compared to body weight before experiment)	Body weight:		21	21.3	21.4	21.5	21.4	21.5	21.6	22.6	22.5	22.8	22.2	
	No loss	0												
	Loss < 5%	1												
	Loss 5-9%	3												
	Loss 10-14%	5												
	Loss > 15%	18												
Clinical signs (Infection, bleeding, discoloration)	Normal	0												
	Minor irritation around surgical wound	1												
	Moderate irritation/infected surgical wound	3												
	Infected/open surgical wound	4*												
	Tumour > 1.0 cm in diameter	10												
	Tumour > 1.5 cm in diameter	18												
Ulcerous tumour	18													

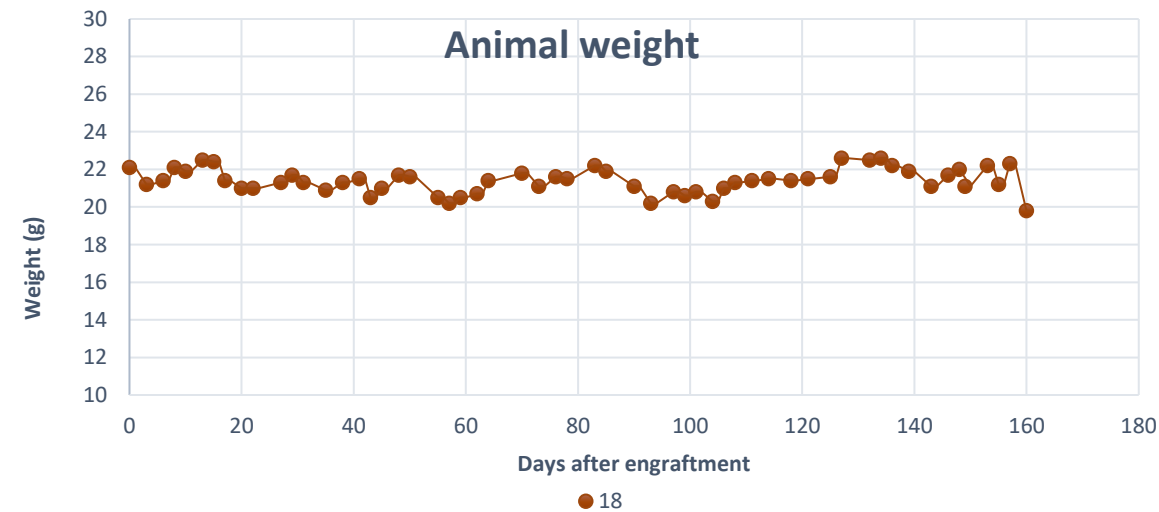
Total: 21

Comments, treatments etc: 0-3: Normal 4-9: Pay attention to health state and consider treatment 10-13: Pay close attention to health state, consider treatment or euthanasia 14-18: Euthanasia *Start treatment with antibiotics. If no effect within 3 days, euthanize the animal

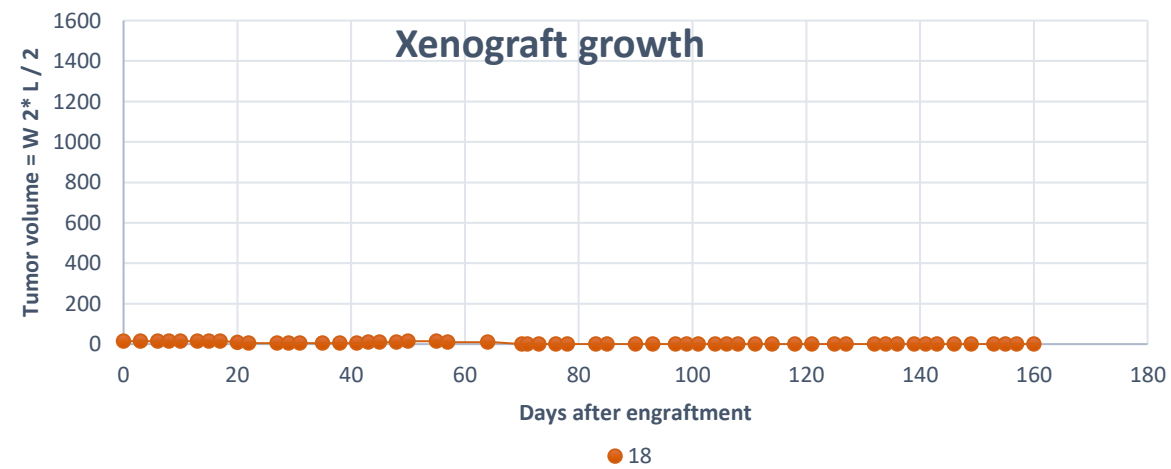
NTNU Score sheet FOTS: Avdeling for komparativ medisin (AKM) Responsible researcher: Pettersen (P19-26) Animal ID: 18 Wipp 4

Parameter	State	Assessment scale	Date	Date
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Weight curve



Xenograft growth curve



Mouse 19

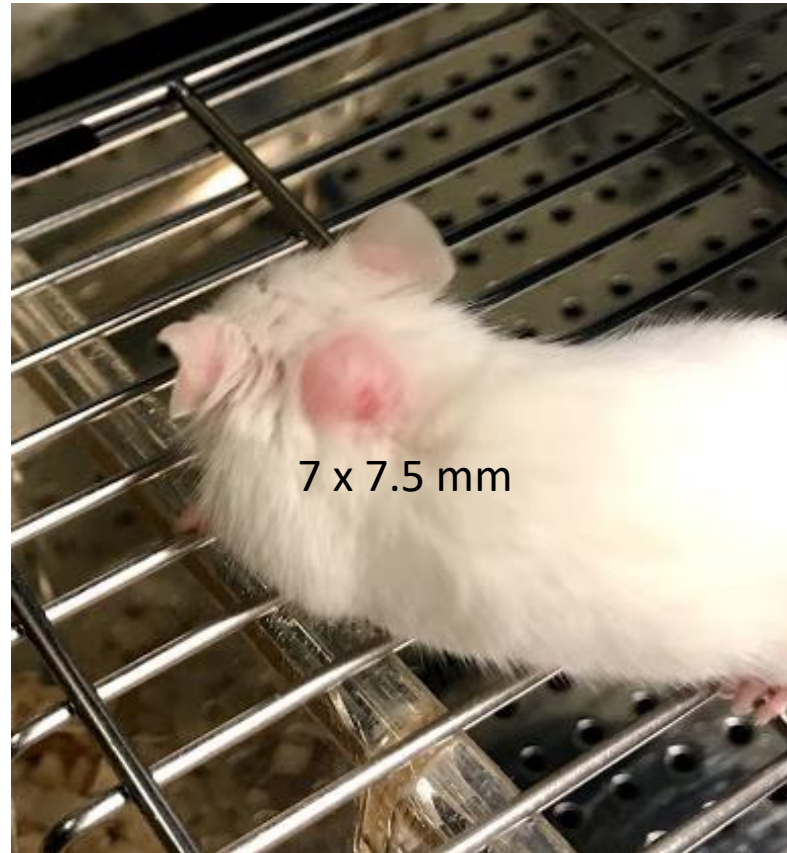
- Surgery date: 14.05.19
 - Age (weeks) 17
 - Weight (g) 20.6
 - Tumor fragment P11-1A
 - Fragment size 4*4 mm
 - Ear marks 1



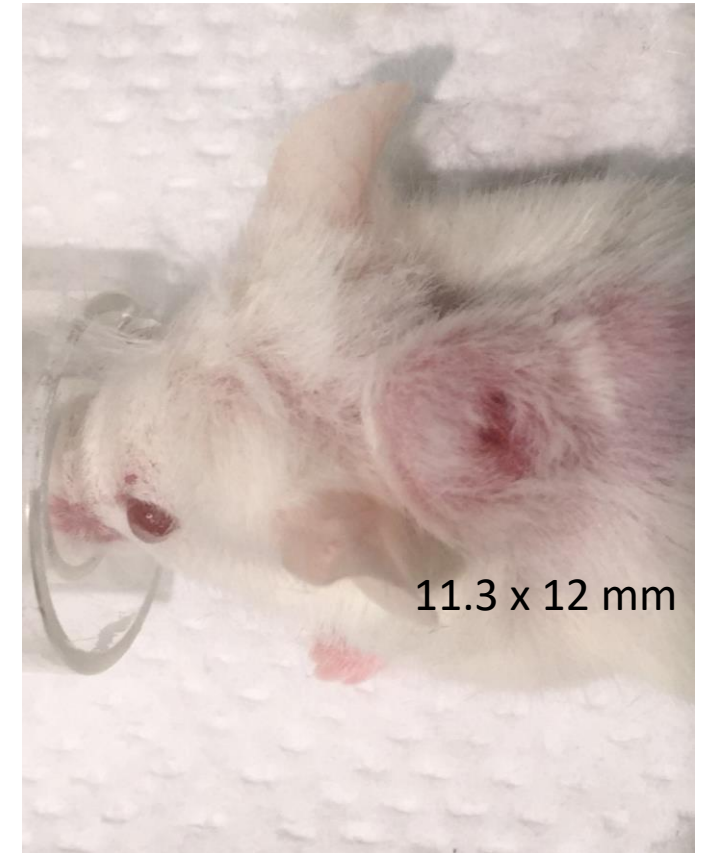
Supplementary figure 1-19-1. Pictures from the engraftment day



Supplementary figure 1-19-2. Pictures from follow up



18.07.2019



30.07.2019

Supplementary figure 1-19-3. List over weight registrations of the drinking bottle
(with Smartfish Remune Peach) before and after provided to the mouse

- Smartfish with fishoil (OMEGA-3)
- 5 days
- Blodsamples were taken before and after treatment

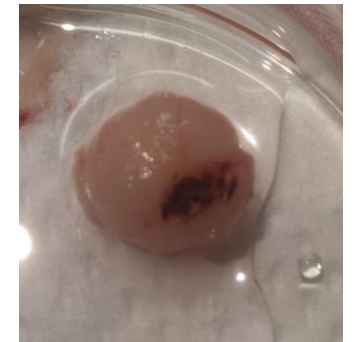
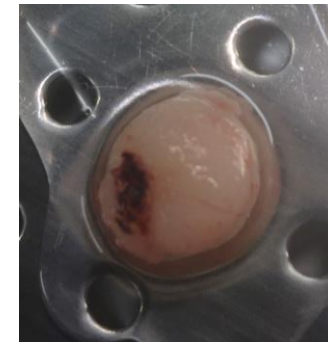
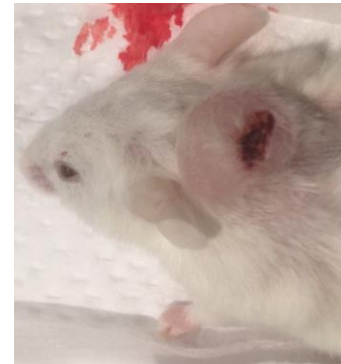
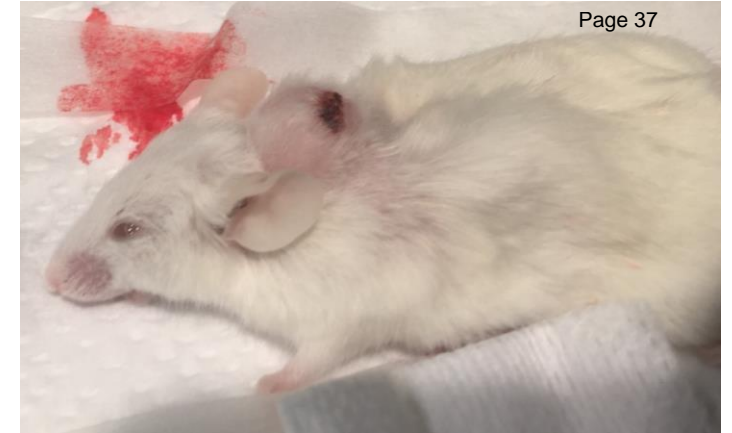
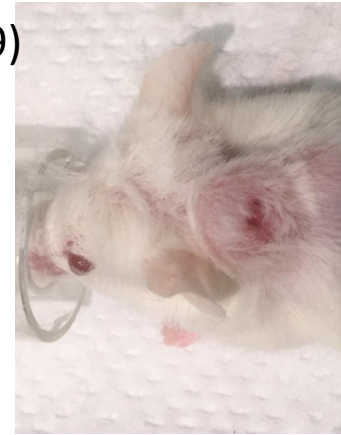
22.07.2019									
23.07.2019									
24.07.2019	130.7	127.0	→ 5 dager	19	OMEGA3				
25.07.2019	138.9	133.8							
26.07.2019	138.8	132.9							
29.07.2019	137.9	126.6							
30.07.2019	140.0								
31.07.									
01.08									
02.09									

in 09⁰⁰


Sår → avviket

Supplementary figure 1-19-4. Pictures from euthanization (30.07.19)

- Xenograft size 11.3 x 12 mm
- Wound on skin over xenograft
- Blood sample (blood card and plasma)
- Tumor tissue for
 - Histology
 - RNA isolation
 - Protein isolation
- Note; stomach contains nutrition drink



Supplementary figure 1-19-5. Pictures of score sheet

 NTNU Score sheet FOTS:
Avdeling for komparativ medisin (AKM)

Responsible researcher: 19

Animal ID: Omega 3
P11-1a

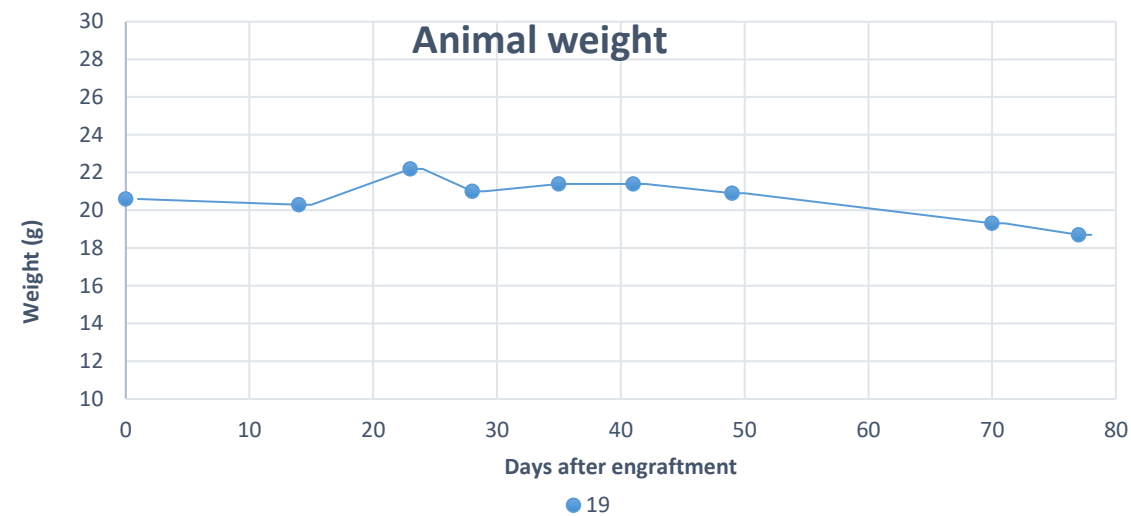
Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0	28/5	6/6/19	11/6-19	14/6	18/6	24/6	02/7	23.7	30.7		
	Reduced grooming	1	6						0	0	0		
	Minor distention of abdomen, rough hair coat	3											
	Hunchback or distended abdomen, inactive	18											
Behaviour (Level of activity)	Normal	0	0										
	Slightly reduced	1							0				
	Moderately reduced	3								0	0		
	Distressed behaviour due to growing tumour	3											
	Obviously reduced	5											
	Isolated, inactive, lethargic	18											
Body weight (Compared to body weight before experiment)	Body weight:		20.3	22.2	21.0		21.4	21.4	20.9	19.3	18.7		
	No loss	0	0										
	Loss < 5%	1											
	Loss 5-9 %	3											
	Loss 10-14%	5											
	Loss ≥ 15%	18											
Clinical signs (Infection, bleeding, discoloration)	Normal	0											
	Minor irritation around surgical wound	1	Ser 1 bla	4ten	4ten	-1-	-1-	-1-	-1-	Bu 7.9	2.07	1.12	
	Moderate irritation/infected surgical wound	3	hilsar	4	4ten								
	Infected/open surgical wound	4 *	ca tube										
	Tumour > 1,0 cm in diameter	10	etter										
	Tumour > 1,5 cm in diameter	18	eprosion										
	Ulcerous tumour	18											
Total:													
Comments, treatments etc:													

0-3: Normal
4-9: Pay attention to health state and consider treatment
10-13: Pay close attention to health state, consider treatment or euthanasia
14-18: Euthanasia *Start treatment with antibiotics. If no effect within 3 days, euthanize the animal

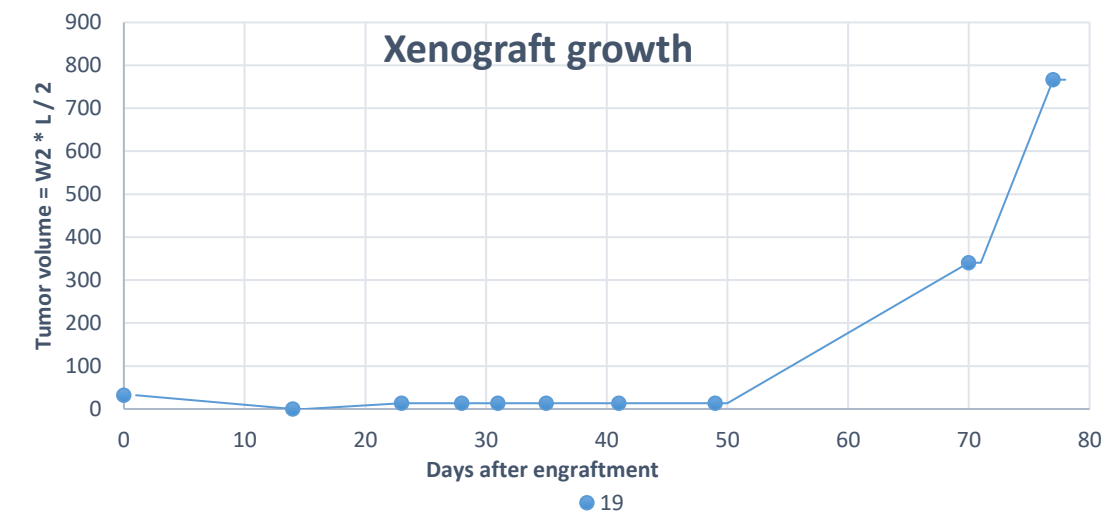
23/7-17 520 p8 luden
der tumoren
sitzen
30/7-19 520 p8 luden
der tumoren
sitzen

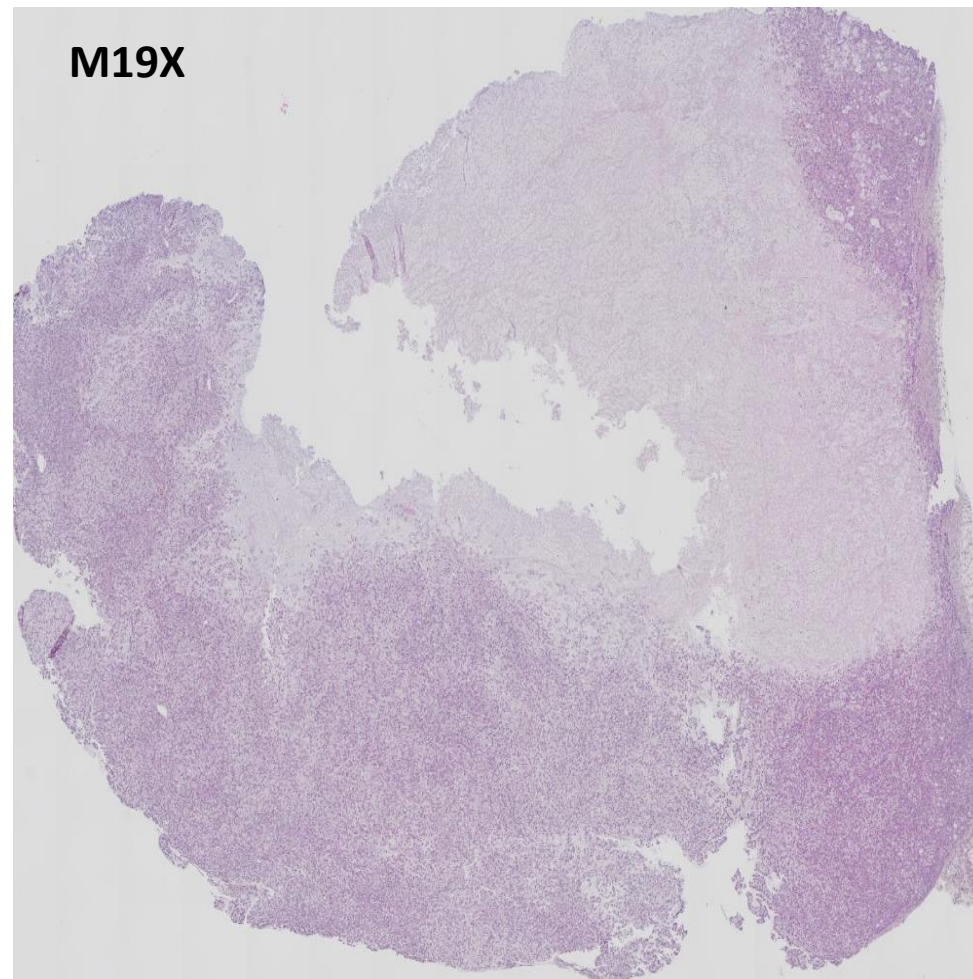
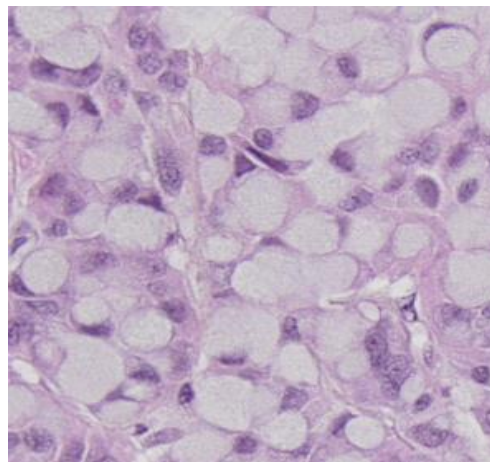
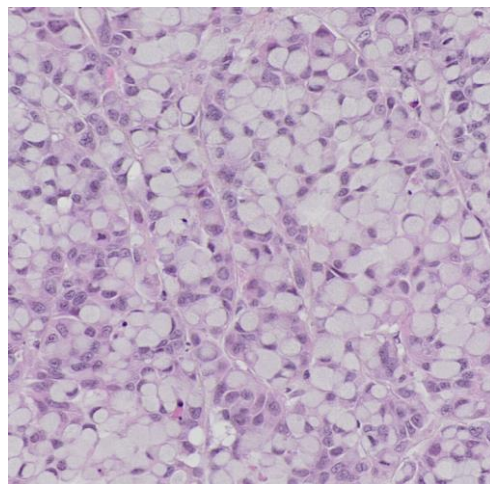
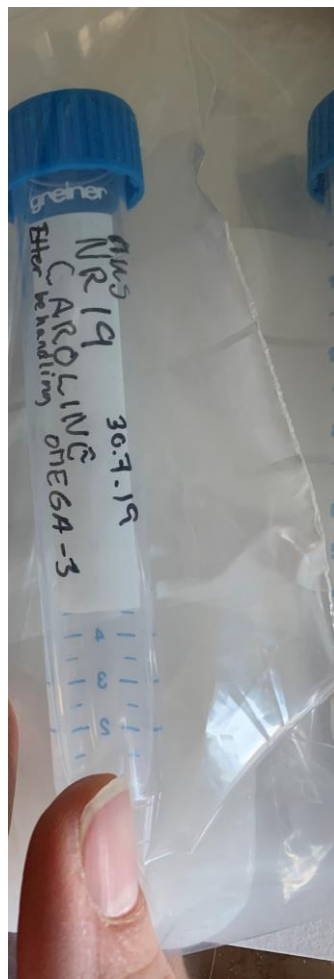
Supplementary figure 1-19-6. Mouse and xenograft growth curves

Weight curve



Xenograft growth curve





- Signet ring cells
- Signet ring cell adenocarcinoma
- Some necrosis

Mouse 20

- Surgery date: 14.5.19
 - Age (weeks) 17
 - Weight (g) 24.0
 - Tumor fragment P11-1B
 - Fragment size 4*4
 - Ear marks 2



Supplementary figure 1-20-1. Pictures from the engraftment day

Supplementary figure 1-20-2. Pictures from follow up (14.06.19)

- the day before treatment start



Blood sample and treatment

- Before: Vena Saphena 11.06.19
 - Hard to get blood sample from
- After: Heart
- Treatment: Placebo

PLACEBO BUR 16

Vekt m/ drikkeløse og tut

Antall gram per flaske før og etter 7 timer

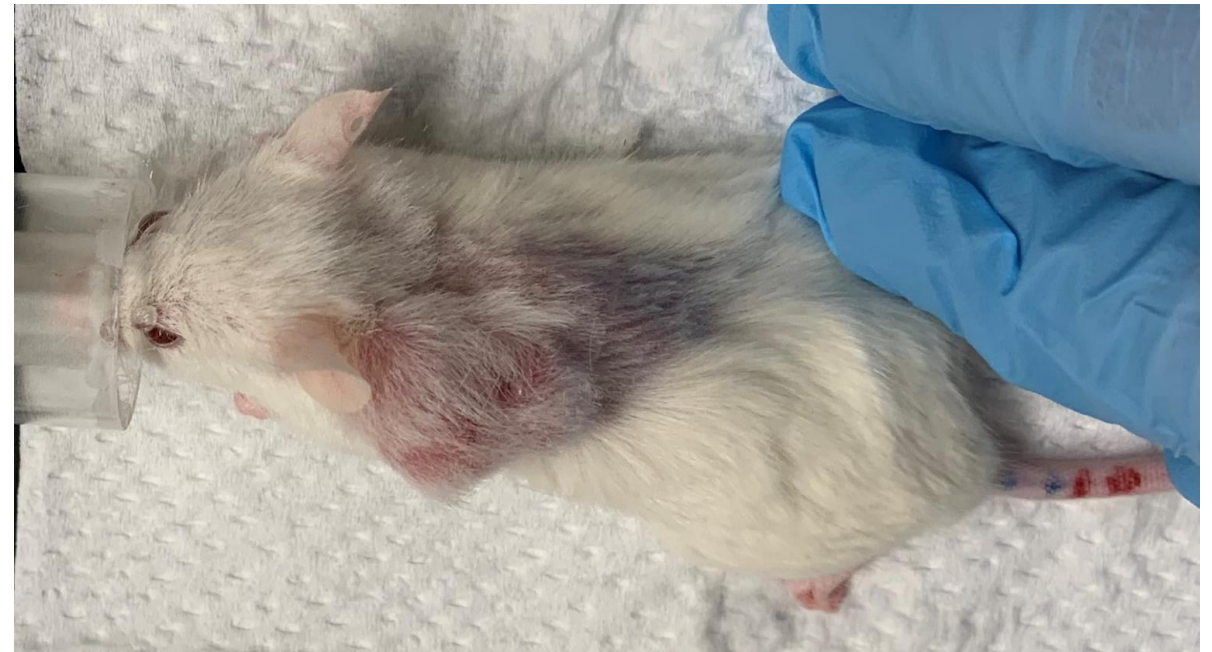
	Weight (g)		ID mus	ID mus	ID mus	ID mus	ID mus	ID mus
	Start	End						
	08.00	15.00						
05.06.2019								
06.06.2019	131,6	126,3	15					
07.06.2019	129,0	122,6						
10.06.2019	—							
11.06.2019	136,4	127,7		20				
12.06.2019	134,3	124,4						
13.06.2019	133,2	121,2						
14.06.2019	132,4	121,0						
17.06.2019	135,1	125,1						
18.06.2019	133,6	125,2						
19.06.2019	135,0	119,2						
20.06.2019	134,2	116,8						
21.06.2019	133,9	121,1						
24.06.2019	133,2	121,6						
25.06.2019	131,1							
26.06.2019								
27.06.2019								
28.06.2019								
01.07.2019								

Start muggsepp i buret!

Supplementary figure 1-20-3. List over weight registrations of the drinking bottle (with Placebo) before and after provided to the mice

Supplementary figure 1-20-4. Pictures from euthanization

- Xenograft size 17 x 11.5
- Blood sample (blood card and plasma)
- Tumor tissue for
 - Histology
 - RNA isolation
 - Protein isolation



903TM Protein Saver Card

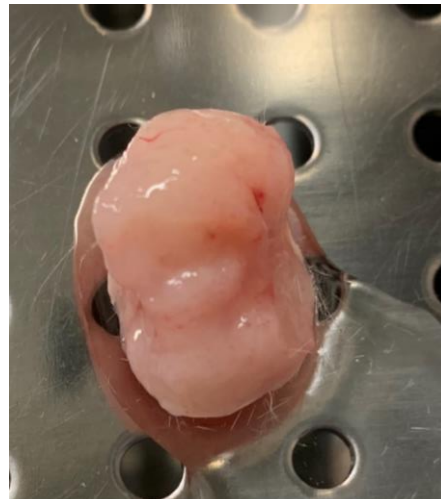
For Research Use Only
Not for use in diagnostic procedures

Tuck Cover Here


Name Mus 20 Etter beh (P11 1B)

Date 25.06.19

CHP



Supplementary figure 1-20-5. Picture of score sheet

 NTNU

Score sheet FOTS:
Avdeling for komparativ medisin (AKM)

Responsible researcher: 99

Animal ID: P11-16
2

0-3: Normal

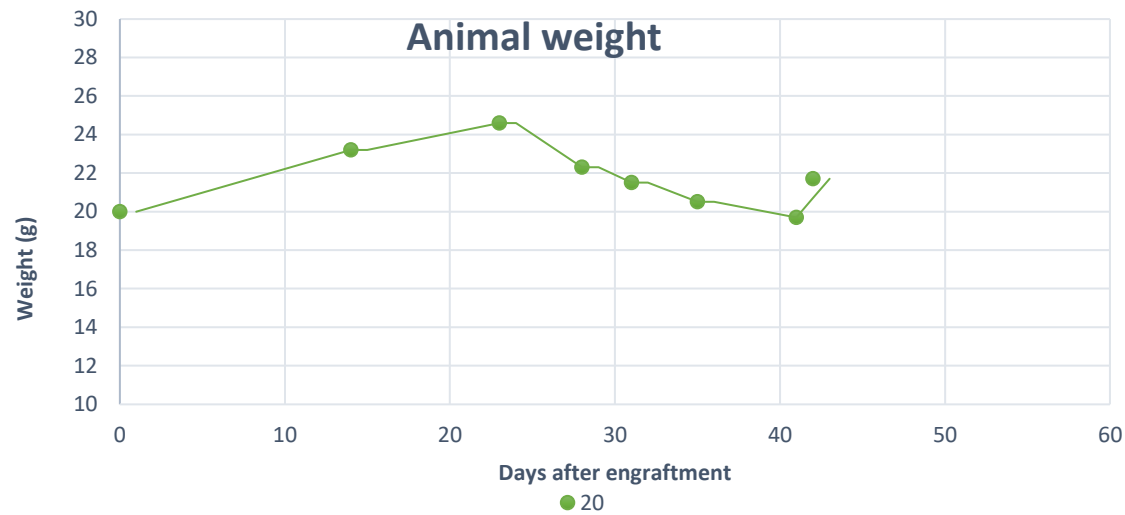
4-9: Pay attention to health state and consider treatment

10-13: Pay close attention to health state, consider treatment or euthanasia

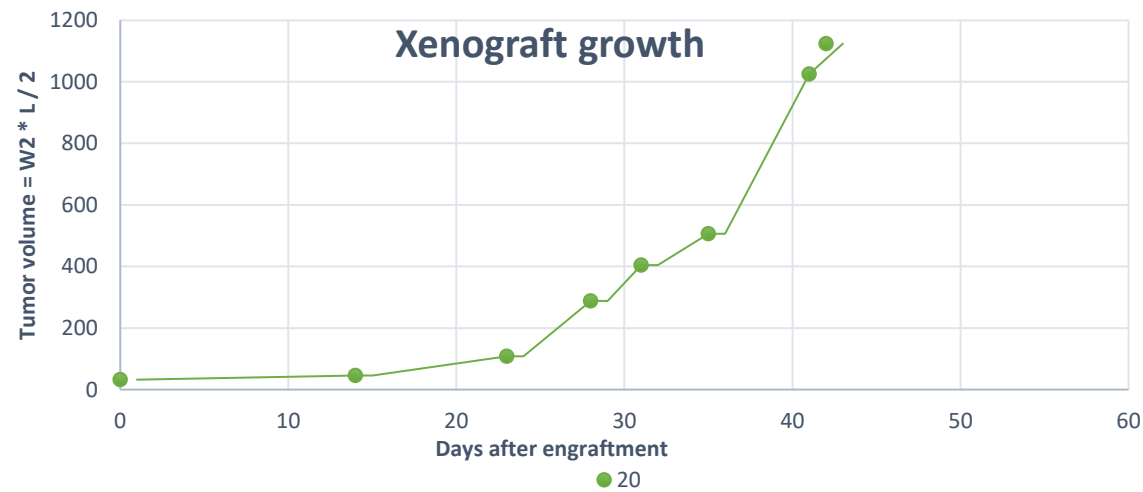
11

Supplementary figure 1-20-6. Mouse and xenograft growth curves

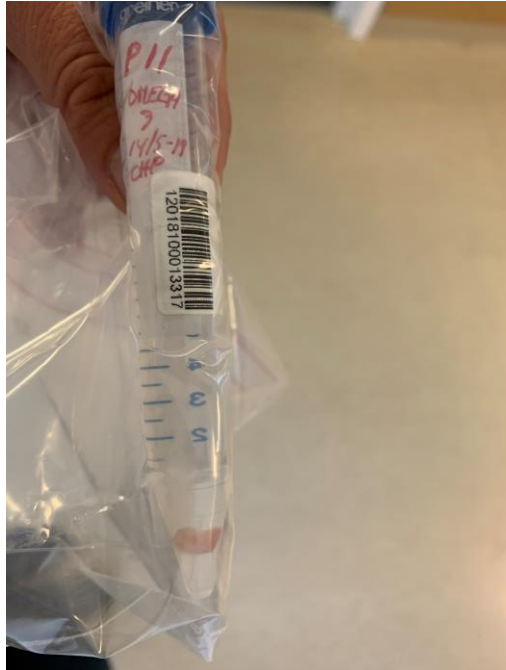
Weight curve



Xenograft growth curve

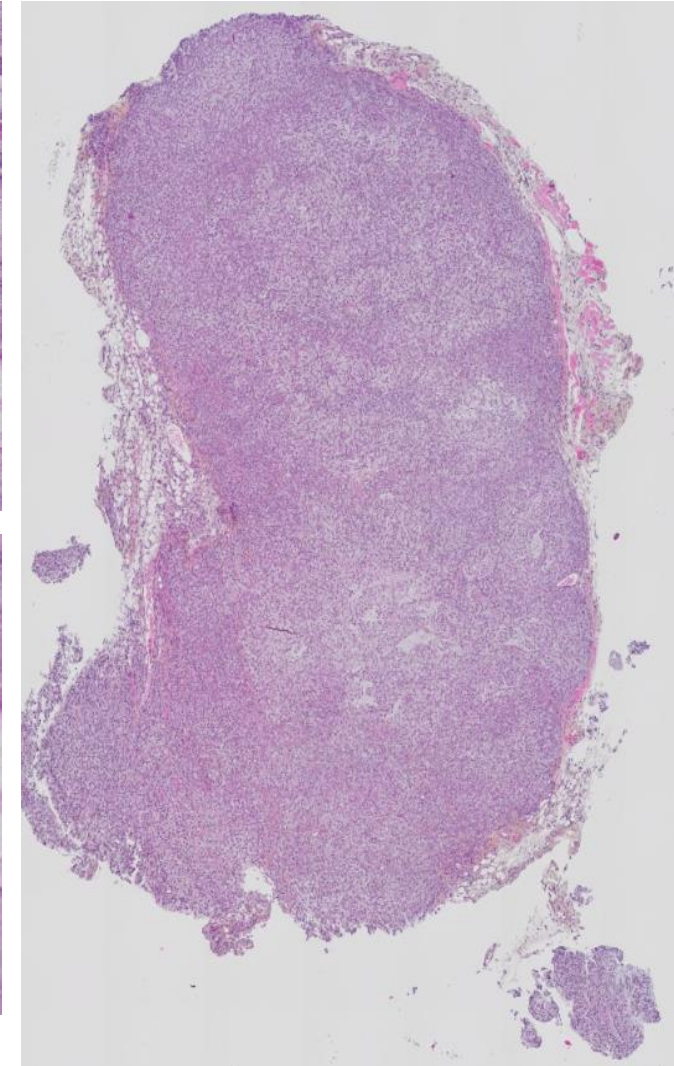
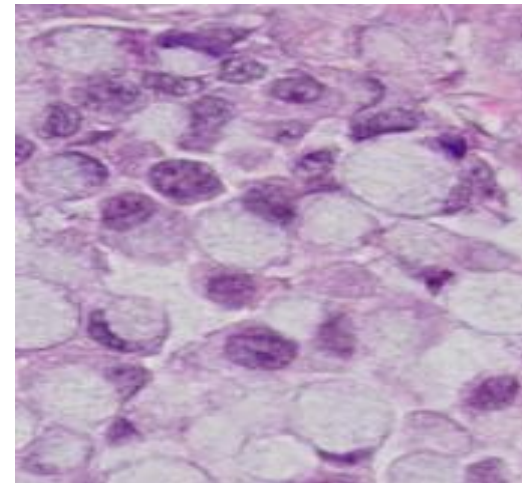
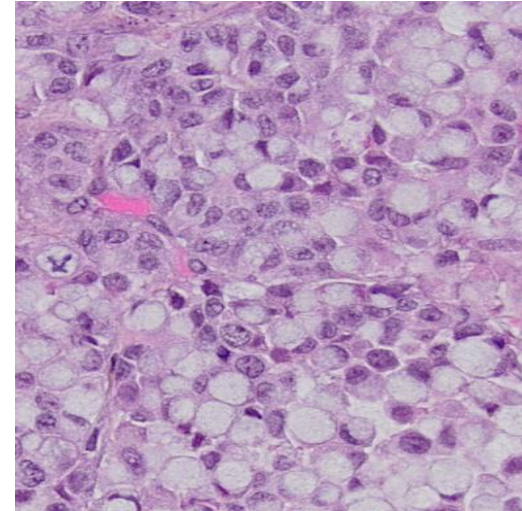


Supplementary figure 1-20-7.
Histology pictures



M20X

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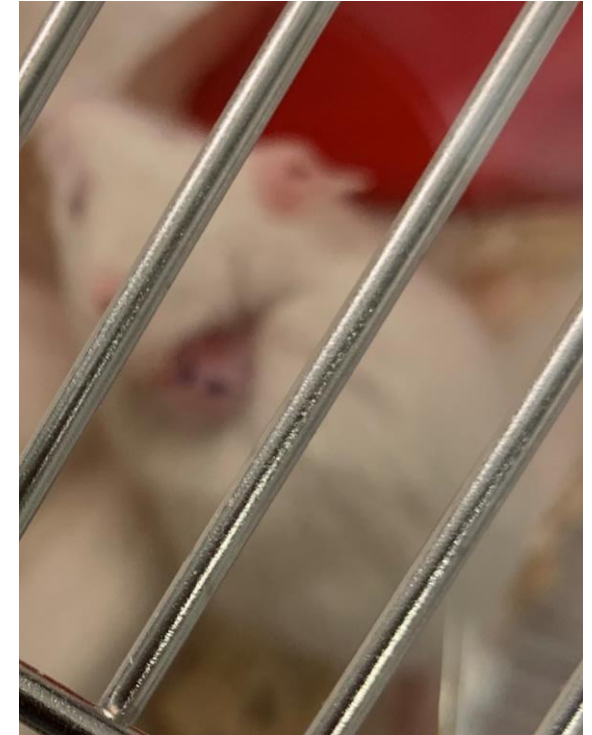


- Origin from signet ring cell adenocarcinoma
- Can see granulocytes in the blood veins getting attached to enter the tissue through the vein wall

Mouse 21

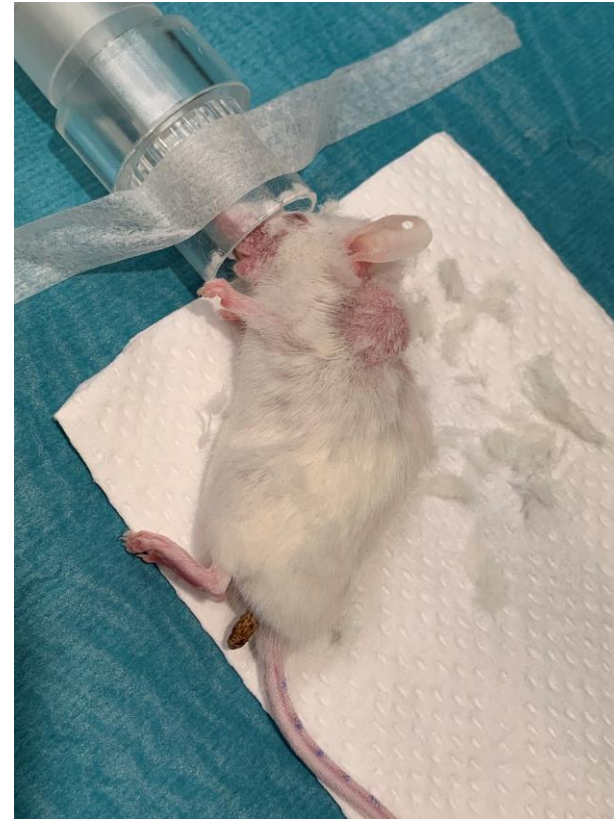
- Surgery date: 14.5.19
 - Age (weeks) 17
 - Weight (g) 20.3
 - Tumor fragment P11-2A
 - Fragment size 4*4
 - Ear marks 3

Supplementary figure 1-21-1. Pictures from the engraftment day



Supplementary figure 1-21-2. Pictures from euthanization (07.08.19)

- Xenograft size 7x9 mm
 - Not registered until 06.08.19
- Reduced health and weight
- Tumor tissue not sampled
- No treatment given
- Low blood volume; could not take blood sample



Normal spleen

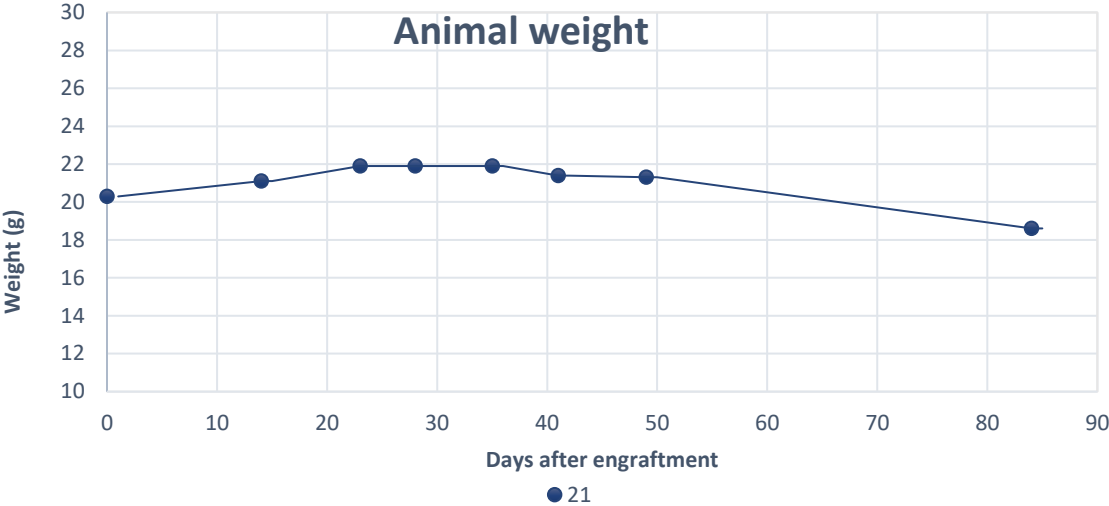
Supplementary figure 1-21-3. Pictures of score sheets

		NTNU		Score sheet FOTS:	Responsible researcher:	(P)	Animal ID:	P 11-2a 3	S pA halen		
Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	
General appearance	Normal	0	28/5	6/6/19	11/6-9	14/8	18/6	24/6	027	6/8	7/8
	Reduced grooming	1	0						0		
	Minor distention of abdomen, rough hair coat	3									
	Hunchback or distended abdomen, inactive	18									
Behaviour <small>(Level of activity)</small>	Normal	0	0								
	Slightly reduced	1								1-2	
	Moderately reduced	3									
	Distressed behaviour due to growing tumour	3							0		
	Obviously reduced	5									
	Isolated, inactive, lethargic	18									
Body weight <small>(Compared to body weight before experiment)</small>	Body weight:		21,1	21,9	21,9		21,9	21,4	21-3	18,6	
	No loss	0	0								
	Loss < 5%	1									
	Loss 5-9 %	3								acute neck velvet	
	Loss 10-14%	5									
	Loss ≥ 15%	18									
Clinical signs <small>(Infection, bleeding, discoloration)</small>	Normal	0	sor ogg	tymk	Lite wal	-1-	-1-	-1-	-1-	disting form	disting form
	Minor irritation around surgical wound	1	npe au	Rud	i sorompa					tumor	Aubret.
	Moderate irritation/infectious surgical wound	3	dekar	i mureld					caxx6	Tumors	
	Infectd/open surgical wound	4 *	porkat	sr ilia	Xenograft				estmet	maling obsemer i morgn	qX 7m
	Tumour > 1,0 cm in diameter	10	, Suret								
	Tumour > 1,5 cm in diameter	18									
	Ulcerous tumour	18									

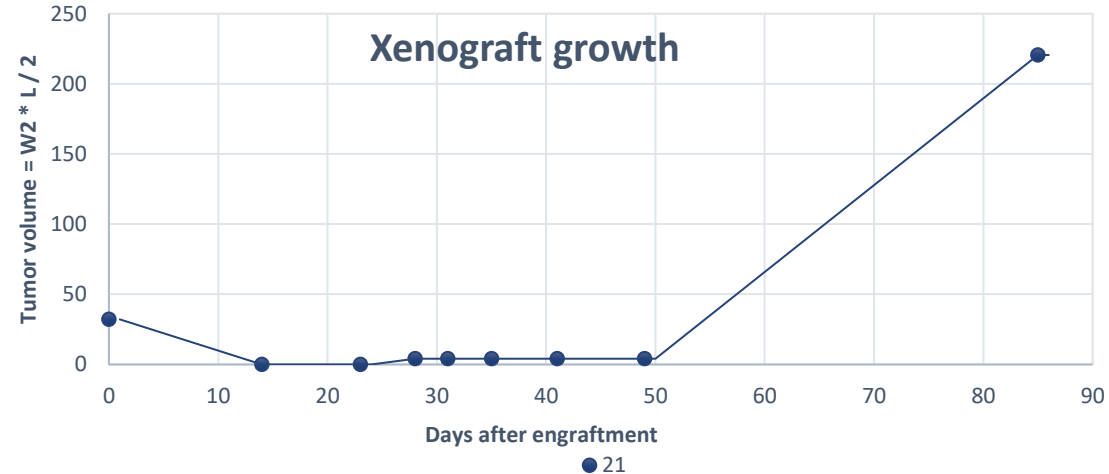
Total: _____
Comments, treatments etc: _____

0-3: Normal

Weight curve



Xenograft growth curve



Mouse 22

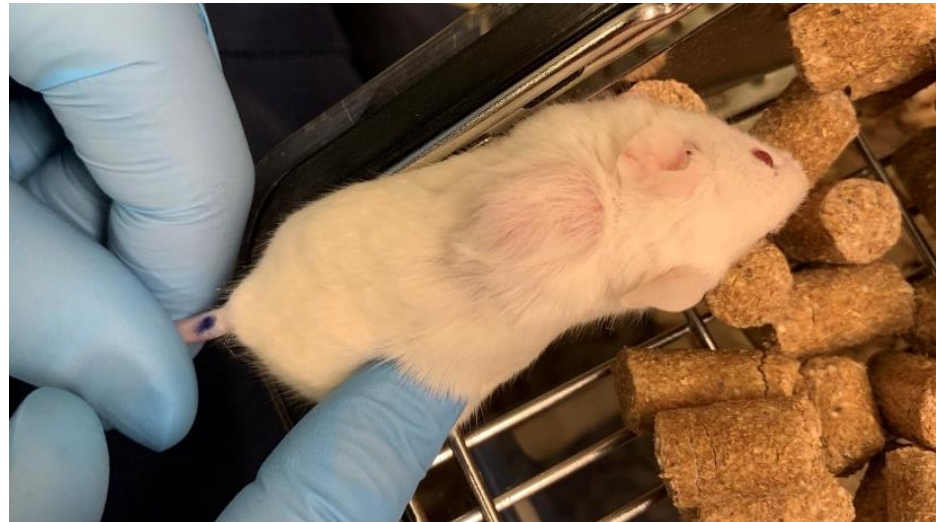
- Surgery date: 14.5.19
 - Age (weeks) 17
 - Weight (g) 21.2
 - Tumor fragment P11-2B
 - Fragment size 4*4
 - Ear marks 4

Supplementary figure 1-22-1. Pictures from the engraftment day



Supplementary figure 1-22-2. Pictures
from follow up (14.06.19)

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Blood sample

- Before: Vena Saphena 11.06.19
 - Hard to get blood sample from
- After treatment: Heart
- Treatment: Smartfish with fishoil (OMEGA-3)

Smartfish - OMEGA3 - BUR 17

Antall gram per flaske før og etter 7 timer Vekt m/drikke og tut

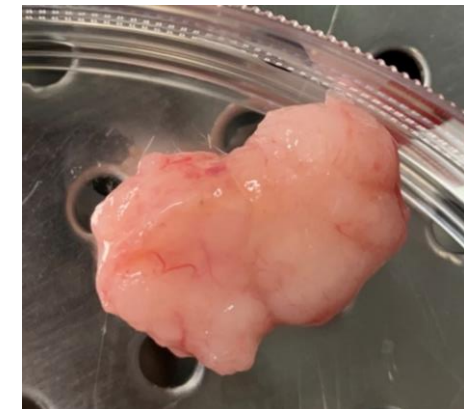
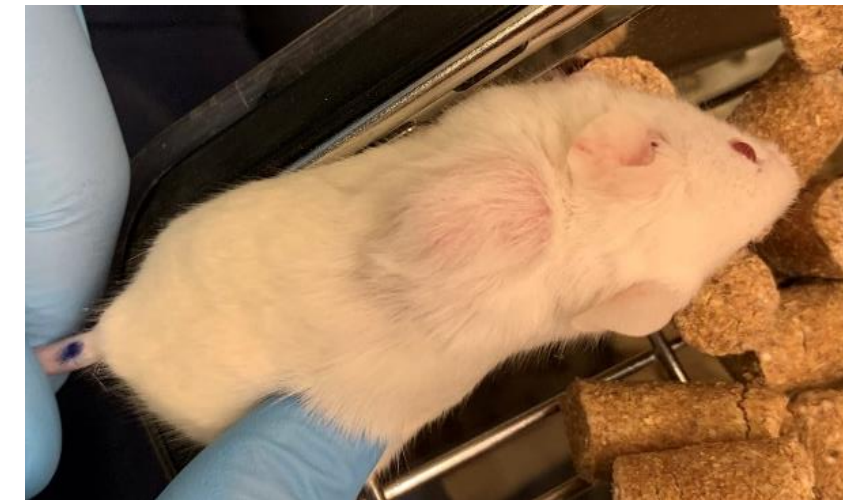
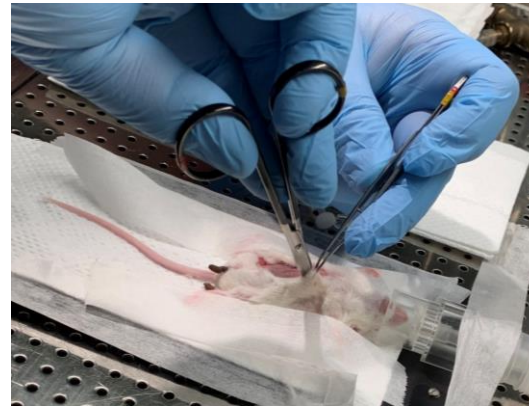
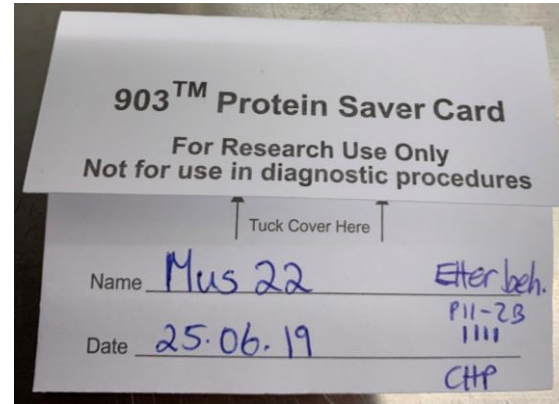
	Weight (g)		ID mus	ID mus	ID mus	ID mus	ID mus	ID mus
	Start	End						
05.06.2019	08.00	15.00						
06.06.2019	134	128,3	16					
07.06.2019	133,7	126,2						
10.06.2019	—	—						
11.06.2019	138,5	130		22				
12.06.2019	138	132,8						
13.06.2019	138,5	131,9						
14.06.2019	142,5	134,6						
17.06.2019	137,8	130,6						
18.06.2019	137,4	129,0						
19.06.2019	139,2	132,3						
20.06.2019	138,8	131,6						
21.06.2019	140,6	134,7						
24.06.2019	139,1	130,5						
25.06.2019	138,2							
26.06.2019								
27.06.2019								
28.06.2019								
01.07.2019								
02.07.2019								
03.07.2019								

← Papiret
kon bort
flaska


Supplementary figure 1-22-3. List over weight registrations of the drinking bottle (with Smartfish Remune Peach) before and after provided to the mice

Supplementary figure 1-22-4. Pictures from euthanization

- Xenograft size 17x11
- Blood sample (blood card and plasma)
- Tumor tissue for
 - Histology
 - RNA isolation
 - Protein isolation



Supplementary figure 1-22-5. Picture of score sheet

 NTNU

Score sheet FOTS:
Avdeling for komparativ medisin (AKM)

Responsible researcher: 22

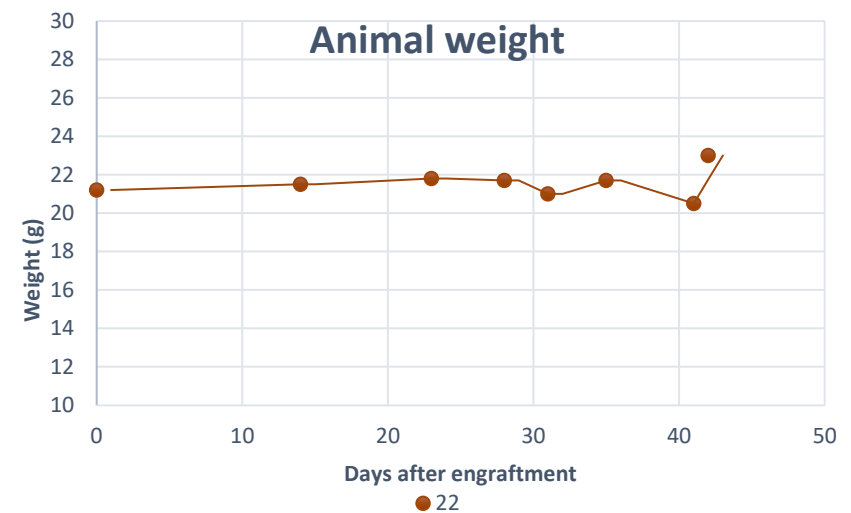
Animal ID: P11-28
4

0-3: Normal
4-9: Pay attention to health state and consider treatment
10-13: Pay close attention to health state, consider treatment or euthanasia

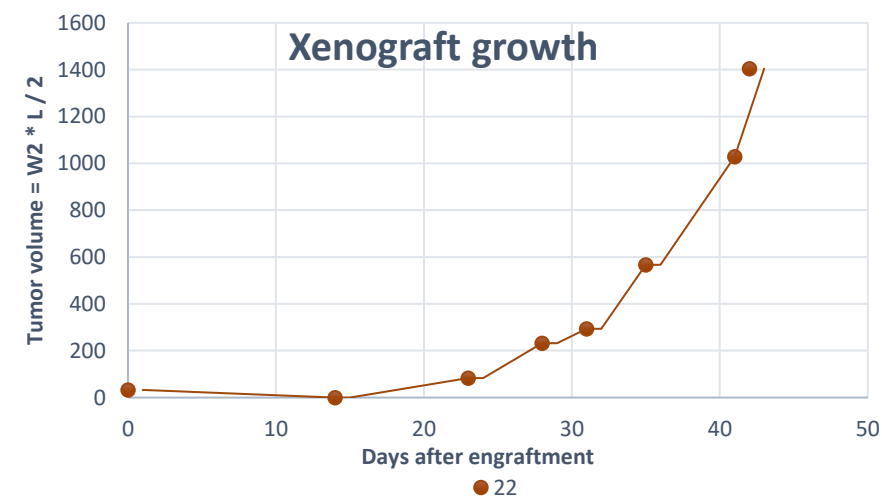
modul 1111

Supplementary figure 1-22-6. Mouse and xenograft growth curves

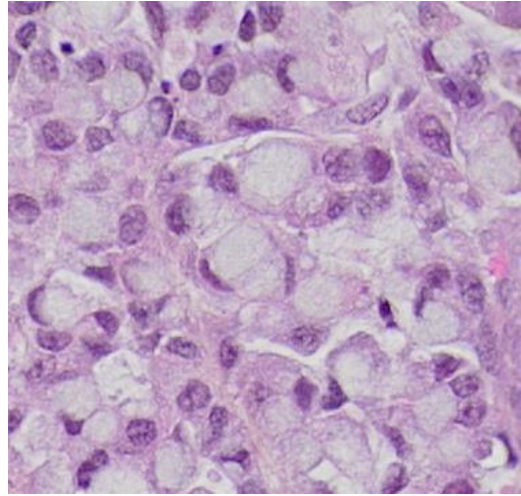
Weight curve



Xenograft growth curve

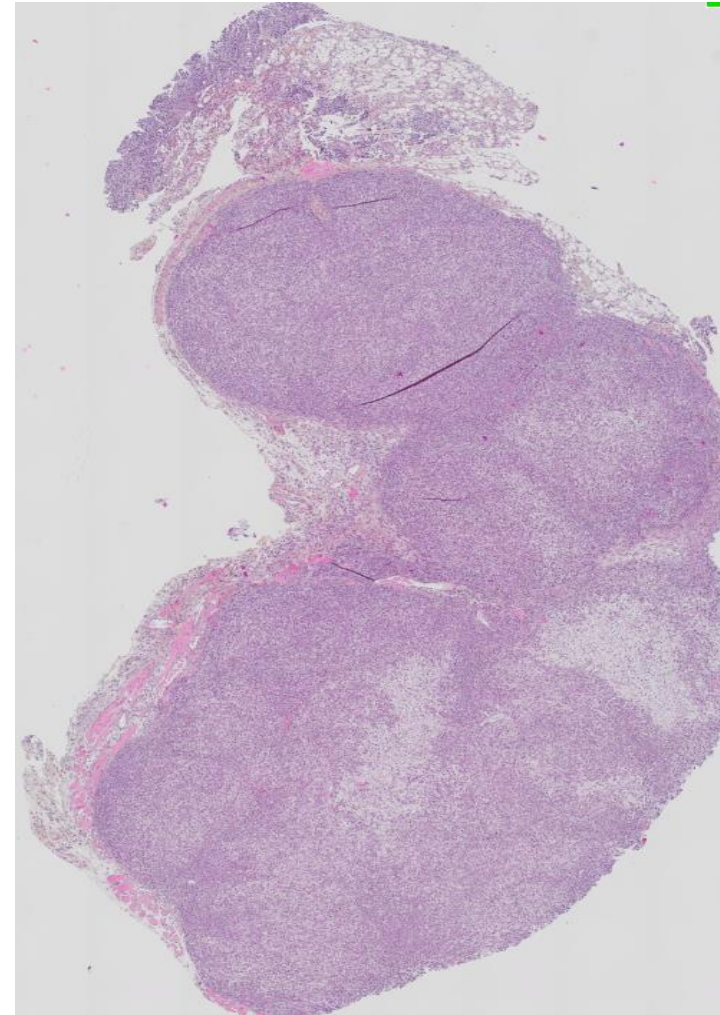


Supplementary figure 1-22-7. Histology pictures



M22X

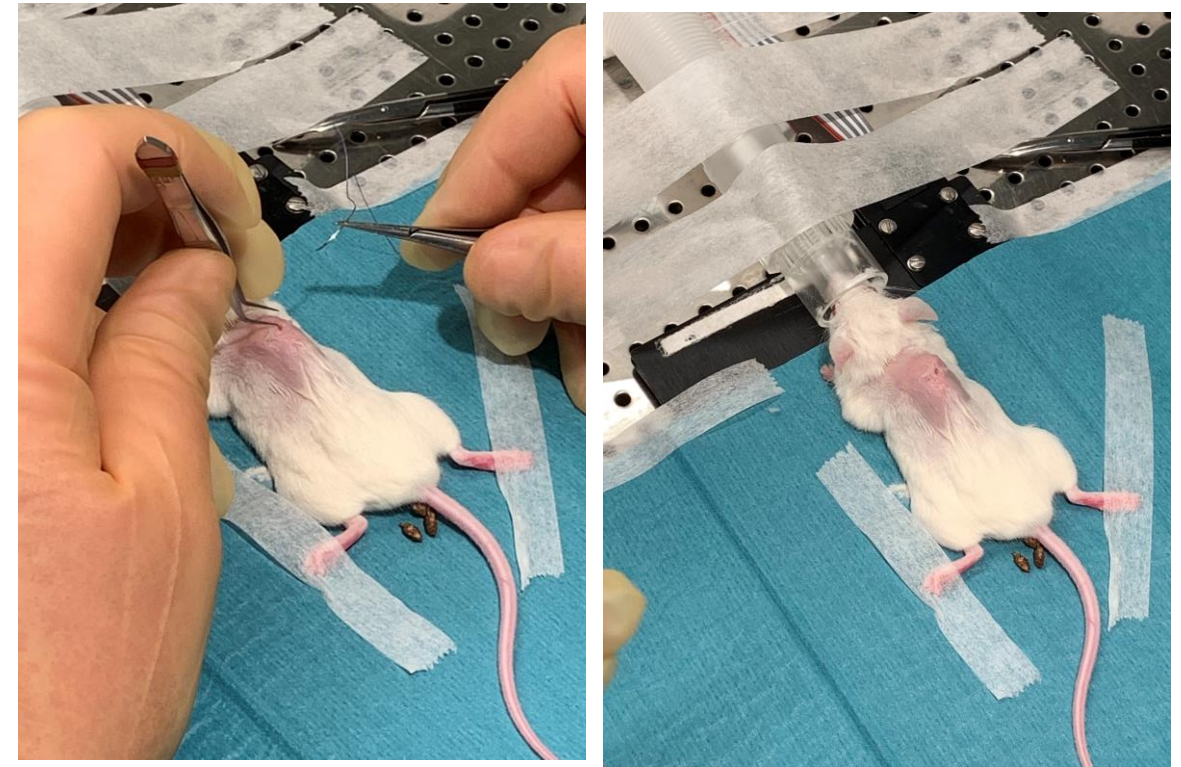
Page 58



- Origin from signet ring cell adenocarcinoma
- Very simial to patient tumor 3
- Can see several mitotic cells, tumor tissue, connective tissue and some blood vains

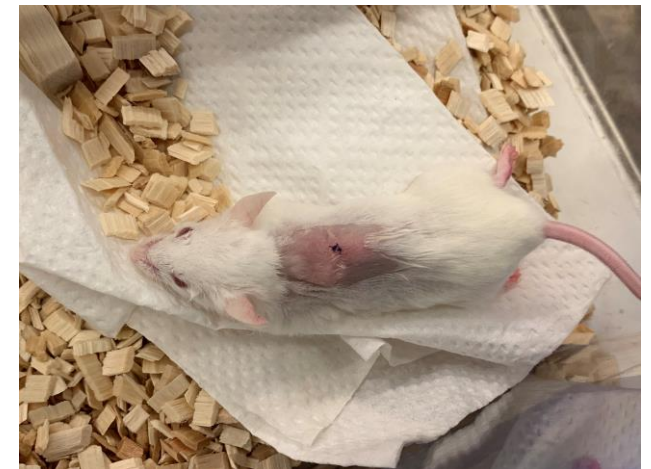
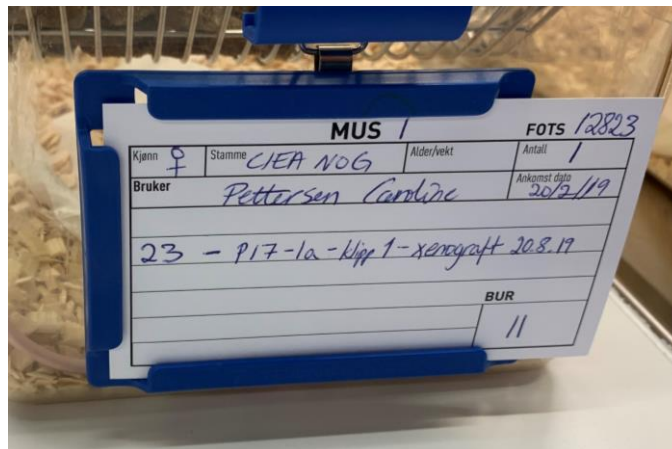
Mouse 23

- Surgery date: 20.08.19
 - Age (weeks) 31
 - Weight (g) 24
 - Tumor fragment P17-1A
 - Fragment size 3 x 3 mm
 - Ear mark 1
- Note; opened 2 stiches after 1 h → restitched

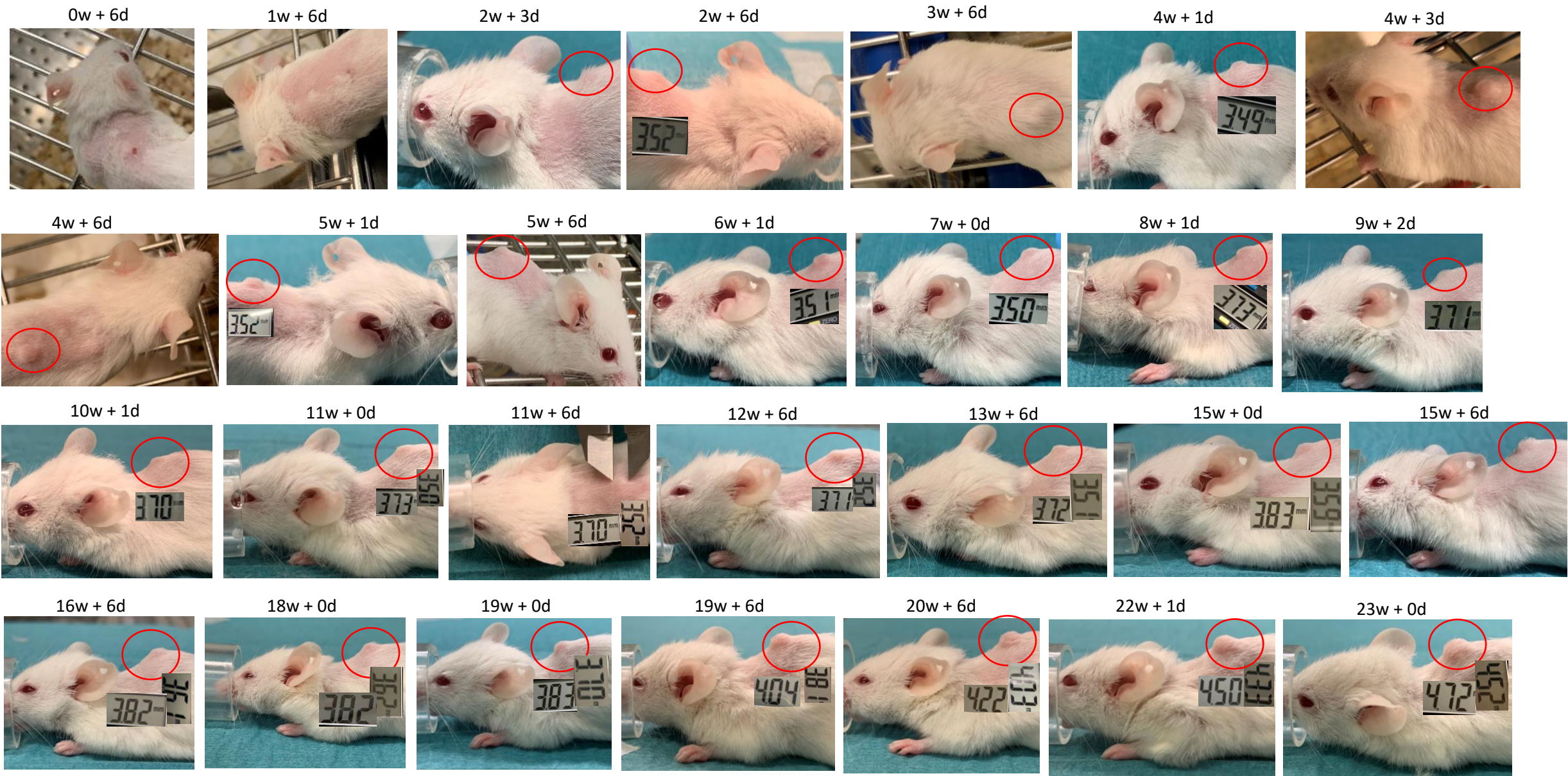


Supplementary figure 1-23-1.

Pictures from the engraftment day



Supplementary figure 1-23-2. Pictures from follow up and tumor size measurement

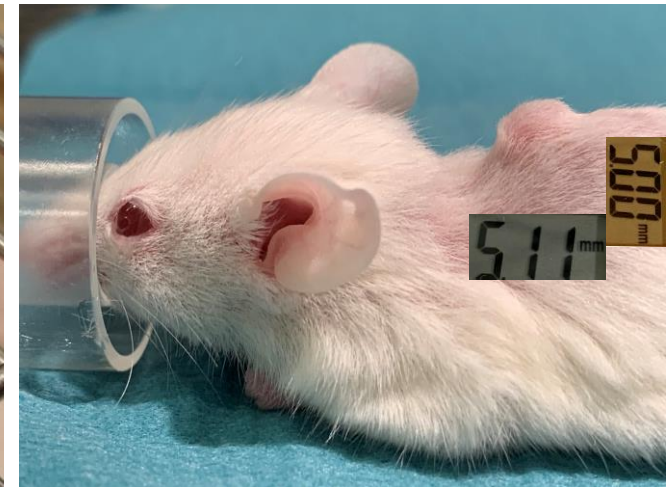


Blood sample (24.02.2020)

- Xenograft 5*5.1 mm
- Stable weight
- Little blood, anemic?, hard to get blood sample.
- Only 40 µl was spotted on blood card instead of 50 µl.
 - Not blood for preparing plasma
- Starting rectal prolaps? Red in the rectum opening.
- Placebo start 25.02.20

MUS 1			FOTS 12823
Kjønn ♀	Stamme CIEA NOG	Alder/vekt	Antall 1
Bruker Pettersen Carline			Ankomst dato 20/2/19
23 - P17-1a-klipp1-xenograft 20.8.19			
24 - P17-1b-klipp2 -11-			
25 - P17-2a-klipp3 -11-			
26 - P17-2b-klipp4 -11-			
			BUR 11

MUS			FOTS 12823
Kjønn ♀	Stamme CIEA NOG	Alder/vekt	Antall 1
Bruker Pettersen Carline			Ankomst dato 20/2/19
23 - P17-1a-klipp1-xenograft 20.8.19			
Start PLACEBO 25.2.19			
			Bur 25



Supplementary figure 1-23-3. Pictures of mouse 23 at treatment startup

Supplementary figure 1-23-4. A) List over weight registrations of drinking bottle (with placebo) before and after provided to the mouse. **B)** Intake of placebo drink

- Placebo
- Treatment for 8 weeks
- Blood samples taken before/after treatment



A)

Antall gram per flaske før og etter 7 timer

— Placebo —

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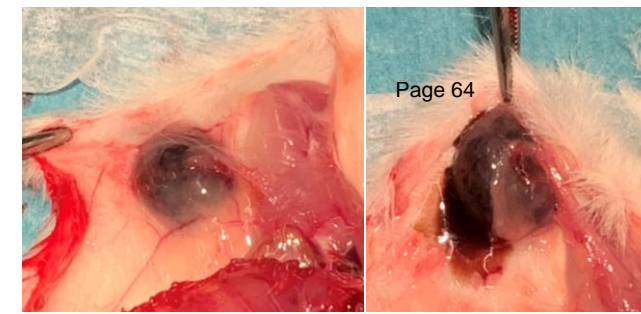
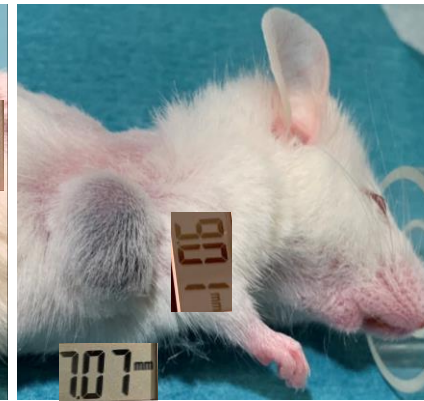
	Weight (g)		ID mus	ID mus	ID mus	ID mus	ID m
	Start	End					
	08.00	15.00					
25.02.2020	147,1	131,3	(23)	mye lukkasje for flasken			
26.02.2020	147,0	128,8					
27.02.2020	143,0	122,5					
28.02.2020	148,6	129,8					
02.03.2020	139,0	123,4					
03.03.2020	144,6	119,7					
04.03.2020	149,5	126,5					
05.03.2020	148,5	125,9					
06.03.2020	150	130,8					
09.03.2020	142,3	126,3					
10.03.2020	146,3	121,9					
11.03.2020	146,9	122,3					
12.03.2020	146,1	112,3	støtt til 12.03.2020				
13.03.2020							
16.03.2020	139,5	120,7					
17.03.2020	148,2	122,2					
18.03.2020	139,6	112,9					
19.03.2020	140,8	118,9	07.00	-14.00			
20.03.2020	142,0	121,8	07.00	-14.00			
23.03.2020	136,6	123,6					
24.03.2020	138,0	114,9	08.00	-15.30			
25.03.2020	139,4	120,0	07.00	-14.00			
26.03.2020	140,7	128,8	07.30	13.30			
27.03.2020	137,6	118,5	07.30	13.30			
30.03.2020	138,1	118,1	07.00	15.00			
31.03.2020	139,9	121,6	08.30	15.30			
01.04.2020	138,1	117,4	08.15	15.30			
02.04.2020	139,0	119,2	08.00	14.30			
03.04.2020	143,3	132,6	08.00	14.15			
06.04.2020	145,0	120,7	08.00	15.00			
07.04.2020	137,0	118	08.00	15.25			
08.04.2020	146,7	131,3	8.00	12.00			
09.04.2020	144,3	136,7	08.15	12.40			
10.04.2020	133,2	128,1	09.15	13.00			
13.04.2020	137,6	130,0	07.30	12.30			
14.04.2020	131,6	122,6	07.00	15.15			
15.04.2020	136,6	131,3	9.20	15.40			
16.04.2020	139,4	120,6	8.00	15.10			
17.04.2020	140,0	127,2	07.00	14.00			
20.04.2020							

FOTS 12823		MUS	
Kjønn	Stamme	Stamme	Stamme
4	C1E7A N06	C1E7A N06	C1E7A N06
Bruker	Bruker	Bruker	Bruker
Pettersen Caroline	Pettersen Caroline	Pettersen Caroline	Pettersen Caroline
23 - P17-1a-lupin1 - x-raygalt 20.8.19		23 - P17-1a-lupin1 - x-raygalt 20.8.19	
Start PLACEBO 25.2.19		Start PLACEBO 25.2.19	
Bur 25		Bur 25	

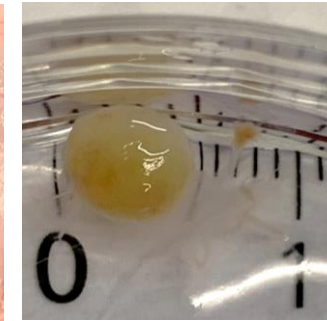
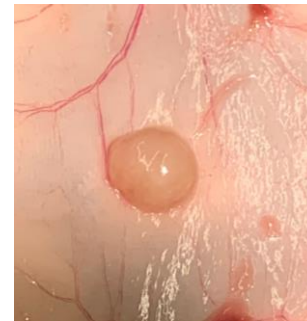
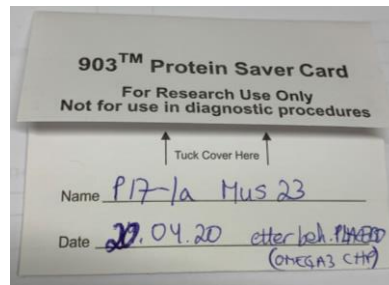
Supplementary figure 1-23-5.

Pictures from euthanization

- Reduced weight
- Necroscopy
 - Xenograft size 5.9 x 5.8 mm
 - Secondary tumor size 7.07 x 9.01 mm
 - Blood sample
 - Tumor tissue for
 - Histology
 - RNA isolation
 - Protein isolation
 - Blood card 40 μ l



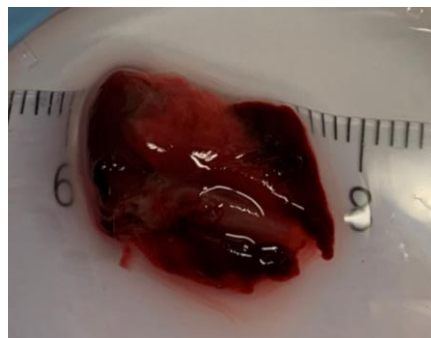
2nd tumor, behind right for leg, dark liquid coming out of it



Xenograft attached to the skin



Stomach clogged, little food in the colon right; clog inspected in microscope (hair and food)



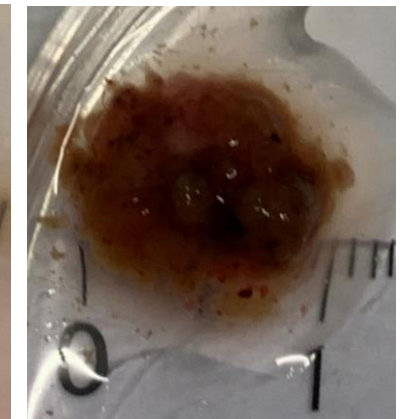
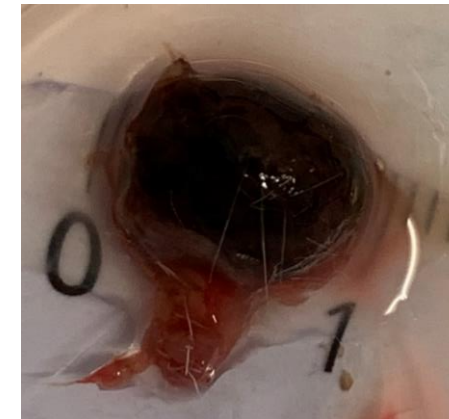
Lungs and heart.
Small lungs?



Spleen, small/normal,
ca 1 cm



Kidneys and thymus



2nd tumor, before and after flushed with NaCl

Supplementary figure 1-23-6. Autopsy card filled out during necroscopy

AUTOPSY CARD

NUMBER 23 – (P17-1a) – ear cut 1	Male Female X	STRAIN CIEA NOG	BIRTH DATE January 2019	EXPERIMENT PDX – Xenograft
AGE AT DEATH	DEATH MODE DATE 20.04.20			GROUP Pettersen, Caroline
CLINICAL SYMPTOMS AT DEATH Secondary tumor right shoulder, xenograft Reduced weight (from 25-20 g in 2 weeks)				
ORGAN WEIGHT		SECTION TAKEN		
ORGAN	WEIGHT	ORGAN	YES	GROSS OBSERVATION
Femur		1) Lung + Heart (LH)	X	small lungs? Filled with formalin
Liver		2) Liver (L)	X	OK
		3) Kidney (N)	X	OK
Spleen		4) Adrenal		
		5) Testis/Ovary		
Kidney		6) Spleen + pancreas (MP)	X	small spleen ca 1cm
		7) Lymph nodes		
Testis/Ovary		8) Bone marrow		
		9) Xenograft (X)	X	light colour
		10) Thymus (T)	X	light colour
		11) 2nd tumor right (TR)	X	7 x 9 mm right shoulder/abdomen, dark colour
		12) 2nd tumor left (TL)		
		13) clump in stomach	X	Inspected in microscope, fur and food clinged together, blocked the stomach, no food in colon.
NB!				
Notes : Blood card ✓ 40 µl, same as before treatment Blood plasma ✓ 1 tube, hard to get blood sampled Pictures ✓				
Prever levert ingunn : TR, MP, X, LH				

Autopsy card modified from: http://www.pathbase.net/Necropsy_of_the_Mouse/

Supplementary figure 1-23-7. Score sheets

NTNU Score sheet FOTS: Avdeling for komparativ medisin (AKM) Responsible researcher: Pettersen Animal ID: (P17-1a) (23) Wipp 1

Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0	20/8	24/8	29/8	29/8	24/9	6/9	8/9	11/9	13/9	18/9
	Reduced grooming	1										
	Minor distention of abdomen, rough hair coat	3										
	Hunchback or distended abdomen, inactive	18										
Behaviour (Level of activity)	Normal	0										
	Slightly reduced	1										
	Moderately reduced	3										
	Distressed behaviour due to growing tumour	3										
	Obviously reduced	5										
Body weight (Compared to body weight before experiment)	Isolated, inactive, lethargic	18										
	Body weight:		23,6g	24,5	24,1	24,1	24,1	24,1	24,1	24,1	24,1	24,1
	No loss	0										
	Loss < 5%	1										
	Loss 5-9%	3										
Clinical signs (Infection, bleeding, discoloration)	Loss 10-14%	5										
	Loss > 15%	18										
	Normal	0										
	Minor irritation around surgical wound	1										
	Moderate irritation/infected surgical wound	3										
Total:	Infected/open surgical wound	4*										
	Tumour > 1,0 cm in diameter	10										
	Tumour > 1,5 cm in diameter	18										
	Ulcerous tumour	18										
	Comments, treatments etc:											

0-3: Normal
4-9: Pay attention to health state and consider treatment
10-13: Pay close attention to health state, consider treatment or euthanasia
14-18: Euthanasia *Start treatment with antibiotics. If no effect within 3 days, euthanize the animal

NTNU Score sheet FOTS: Avdeling for komparativ medisin (AKM) Responsible researcher: Pettersen Animal ID: (P17-1a) (23) Wipp 1

Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0	20/9	23/9	25/9	30/9	2/10	4/10	8/10	11/10	14/10	16/10
	Reduced grooming	1										
	Minor distention of abdomen, rough hair coat	3										
	Hunchback or distended abdomen, inactive	18										
Behaviour (Level of activity)	Normal	0										
	Slightly reduced	1										
	Moderately reduced	3										
	Distressed behaviour due to growing tumour	3										
	Obviously reduced	5										
Body weight (Compared to body weight before experiment)	Isolated, inactive, lethargic	18										
	Body weight:		24,0	23,8	22,8	23,6	23,8	23,1	23,1	24,1	23,5	22,9
	No loss	0										
	Loss < 5%	1										
	Loss 5-9%	3										
Clinical signs (Infection, bleeding, discoloration)	Loss 10-14%	5										
	Loss > 15%	18										
	Normal	0										
	Minor irritation around surgical wound	1										
	Moderate irritation/infected surgical wound	3										
Total:	Infected/open surgical wound	4*										
	Tumour > 1,0 cm in diameter	10										
	Tumour > 1,5 cm in diameter	18										
	Ulcerous tumour	18										
	Comments, treatments etc:											

0-3: Normal
4-9: Pay attention to health state and consider treatment
10-13: Pay close attention to health state, consider treatment or euthanasia
14-18: Euthanasia *Start treatment with antibiotics. If no effect within 3 days, euthanize the animal

NTNU Score sheet FOTS: Avdeling for komparativ medisin (AKM) Responsible researcher: Pettersen Animal ID: (P17-1a) (23) Wipp 1

Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0	16/10	18/10	20/10	23/10	28/10	30/10	1/11	4/11	8/11	12/11
	Reduced grooming	1										
	Minor distention of abdomen, rough hair coat	3										
	Hunchback or distended abdomen, inactive	18										
Behaviour (Level of activity)	Normal	0										
	Slightly reduced	1										
	Moderately reduced	3										
	Distressed behaviour due to growing tumour	3										
	Obviously reduced	5										
Body weight (Compared to body weight before experiment)	Isolated, inactive, lethargic	18										
	Body weight:		22,9	23,4	23,2	23,5	24,4	26,0	23,4	24,1	25,2	24,1
	No loss	0										
	Loss < 5%	1										
	Loss 5-9%	3										
Clinical signs (Infection, bleeding, discoloration)	Loss 10-14%	5										
	Loss > 15%	18										
	Normal	0										
	Minor irritation around surgical wound	1										
	Moderate irritation/infected surgical wound	3										
Total:	Infected/open surgical wound	4*										
	Tumour > 1,0 cm in diameter	10										
	Tumour > 1,5 cm in diameter	18										
	Ulcerous tumour	18										
	Comments, treatments etc:											

0-3: Normal
4-9: Pay attention to health state and consider treatment
10-13: Pay close attention to health state, consider treatment or euthanasia
14-18: Euthanasia *Start treatment with antibiotics. If no effect within 3 days, euthanize the animal

NTNU Score sheet FOTS: Avdeling for komparativ medisin (AKM) Responsible researcher: Pettersen Animal ID: (P17-1a) (23) Wipp 1

Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0	15/11	18/11	20/11	25/11	30/11	2/12	5/12	9/12	11/12	14/12
	Reduced grooming	1										
	Minor distention of abdomen, rough hair coat	3										
	Hunchback or distended abdomen, inactive	18										
Behaviour (Level of activity)	Normal	0										
	Slightly reduced	1										
	Moderately reduced	3										
	Distressed behaviour due to growing tumour	3										
	Obviously reduced	5										
Body weight (Compared to body weight before experiment)	Isolated, inactive, lethargic	18										
	Body weight:		22,2	24,3	23,4	23,7	23	23,4	23,5	23,4	24,6	24,2
	No loss	0										
	Loss < 5%	1										
	Loss 5-9%	3										
Clinical signs (Infection, bleeding, discoloration)	Loss 10-14%	5										
	Loss > 15%	18										
	Normal	0										
	Minor irritation around surgical wound	1										
	Moderate irritation/infected surgical wound	3										
Total:	Infected/open surgical wound	4*										
	Tumour > 1,0 cm in diameter	10										
	Tumour > 1,5 cm in diameter	18										
	Ulcerous tumour	18										
	Comments, treatments etc:											

0-3: Normal
4-9: Pay attention to health state and consider treatment
10-13: Pay close attention to health state, consider treatment or euthanasia
14-18: Euthanasia *Start treatment with antibiotics. If no effect within 3 days, euthanize the animal

NTNU Score sheet FOTS: Avdeling for komparativ medisin (AKM) Responsible researcher: Pettersen Animal ID: (P17-1a) (23) Wipp 1

Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0	8/12	20/12	23/12	24/12	27/12	31/12	4/1	8/1	13/1	15/1
	Reduced grooming	1										
	Minor distention of abdomen, rough hair coat	3										
	Hunchback or distended abdomen, inactive	18										
Behaviour (Level of activity)	Normal	0										
	Slightly reduced	1										
	Moderately reduced	3										
	Distressed behaviour due to growing tumour	3										
	Obviously reduced	5										
Body weight (Compared to body weight before experiment)	Isolated, inactive, lethargic	18										
	Body weight:		23,3	23	24,2	24,6	22,8	23,5	23,6	24,3	23	24,2
	No loss	0										
	Loss < 5%	1										
	Loss 5-9%	3										
Clinical signs (Infection, bleeding, discoloration)	Loss 10-14%	5										
	Loss > 15%	18										
	Normal	0										
	Minor irritation around surgical wound	1										
	Moderate irritation/infected surgical wound	3										
Total:	Infected/open surgical wound	4*										
	Tumour > 1,0 cm in diameter	10										
	Tumour > 1,5 cm in diameter	18										
	Ulcerous tumour	18										
	Comments, treatments etc:											

0-3: Normal
4-9: Pay attention to health state and consider treatment
10-13: Pay close attention to health state, consider treatment or euthanasia
14-18: Euthanasia *Start treatment with antibiotics. If no effect within 3 days, euthanize the animal

NTNU Score sheet FOTS: Avdeling for komparativ medisin (AKM) Responsible researcher: Pettersen Animal ID: (P17-1a) (23) Wipp 1

Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0	20/1	22/1	24/1	27/1	29/1	30/1	3/2	5/2	7/2	11/2
	Reduced grooming	1										
	Minor distention of abdomen, rough hair coat	3										
	Hunchback or distended abdomen, inactive	18										
Behaviour (Level of activity)	Normal	0										
	Slightly reduced	1										
	Moderately reduced	3										
	Distressed behaviour due to growing tumour	3										
	Obviously reduced	5										
Body weight (Compared to body weight before experiment)	Isolated, inactive, lethargic	18										
	Body weight:		21,2	24,2	22,2	24,4	24,8	24,5	25,6	22,2	25	24
	No loss	0										
	Loss < 5%	1										
	Loss 5-9%	3										
Clinical signs (Infection, bleeding, discoloration)	Loss 10-14%	5										
	Loss > 15%	18										
	Normal	0										
	Minor irritation around surgical wound	1										
	Moderate irritation/infected surgical wound	3										
Total:	Infected/open surgical wound	4*										
	Tumour > 1,0 cm in diameter	10										
	Tumour > 1,5 cm in diameter	18										
	Ulcerous tumour	18										
	Comments, treatments etc:											

0-3: Normal
4-9: Pay attention to health state and consider treatment
10-13: Pay close attention to health state, consider treatment or euthanasia
14-18: Euthanasia *Start treatment with antibiotics. If no effect within 3 days, euthanize the animal

Supplementary figure 1-23-7. Score sheets

NTNU Score sheet FOTS: Avdeling for komparativ medisin (AKM) Responsible researcher: Pettersen (P17-1a) Animal ID: 23 klipp 1

Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0	11/2	12/2	14/2	17/2	19/2	21/2	24/2	25/2	26/2	28/2	29/2
	Reduced grooming	1											
	Minor distention of abdomen, rough hair coat	3											
	Hunchback or distended abdomen, inactive	18											
Behaviour (Level of activity)	Normal	0											
	Slightly reduced	1											
	Moderately reduced	3											
	Distressed behaviour due to growing tumour	3											
	Obviously reduced	5											
Body weight (Compared to body weight before experiment)	Isolated, inactive, lethargic	18											
	Body weight:		24	23	22,9	22,4	23,1	22,1	23,1	23,1	23,1	23,1	23,7
	No loss	0											
	Loss < 5%	1											
	Loss 5-9%	3											
Clinical signs (Infection, bleeding, discoloration)	Loss 10-14%	5											
	Loss ≥ 15%	18											
	Normal	0	4,9	4,9	4,9	4,9	4,9	5	5	5,1	5,2	5,2	5,2
	Minor irritation around surgical wound	1											
	Moderate irritation/infected surgical wound	3											

Comments, treatments etc: 22-25g PLACEBO

apemic, little blood below a stripe each day but never visible for at least 3 days

NTNU Score sheet FOTS: Avdeling for komparativ medisin (AKM) Responsible researcher: Pettersen (P17-1a) Animal ID: 23 klipp 1

Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0	4/3	6/3	9/3	11/3	16/3	20/3	23/3	27/3	30/3	3/4	10/4
	Reduced grooming	1											
	Minor distention of abdomen, rough hair coat	3											
	Hunchback or distended abdomen, inactive	18											
Behaviour (Level of activity)	Normal	0											
	Slightly reduced	1											
	Moderately reduced	3											
	Distressed behaviour due to growing tumour	3											
	Obviously reduced	5											
Body weight (Compared to body weight before experiment)	Isolated, inactive, lethargic	18											
	Body weight:		23,2	23,6	23,1	24,5	22,5	24,6	22,7	24,3	25,0	24,8	25,5
	No loss	0											
	Loss < 5%	1											
	Loss 5-9%	3											
Clinical signs (Infection, bleeding, discoloration)	Loss 10-14%	5											
	Loss ≥ 15%	18											
	Normal	0	5,3	5,4	5,6	5,6	5,6	5,7	5,8	5,8	5,8	5,8	5,8
	Minor irritation around surgical wound	1											
	Moderate irritation/infected surgical wound	3											

Comments, treatments etc: PLACEBO

apemic, little blood below a stripe each day but never visible for at least 3 days

NTNU Score sheet FOTS: Avdeling for komparativ medisin (AKM) Responsible researcher: Pettersen (P17-1a) Animal ID: 23 klipp 1

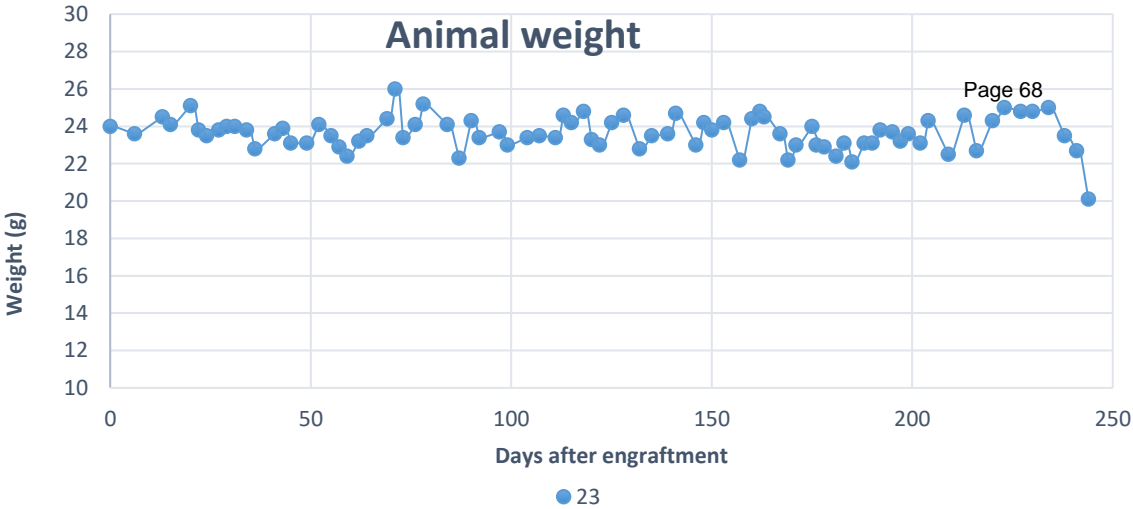
Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0	10/4	14/4	17/4	20/4							
	Reduced grooming	1											
	Minor distention of abdomen, rough hair coat	3											
	Hunchback or distended abdomen, inactive	18											
Behaviour (Level of activity)	Normal	0											
	Slightly reduced	1											
	Moderately reduced	3											
	Distressed behaviour due to growing tumour	3											
	Obviously reduced	5											
Body weight (Compared to body weight before experiment)	Isolated, inactive, lethargic	18											
	Body weight:		25	23,5	22,7	20,1							
	No loss	0											
	Loss < 5%	1											
	Loss 5-9%	3											
Clinical signs (Infection, bleeding, discoloration)	Loss 10-14%	5											
	Loss ≥ 15%	18											
	Normal	0	5,9	5,9	5,9	5,9	5,9	5,9	5,9	5,9	5,9	5,9	5,9
	Minor irritation around surgical wound	1											
	Moderate irritation/infected surgical wound	3											

Comments, treatments etc: PLACEBO

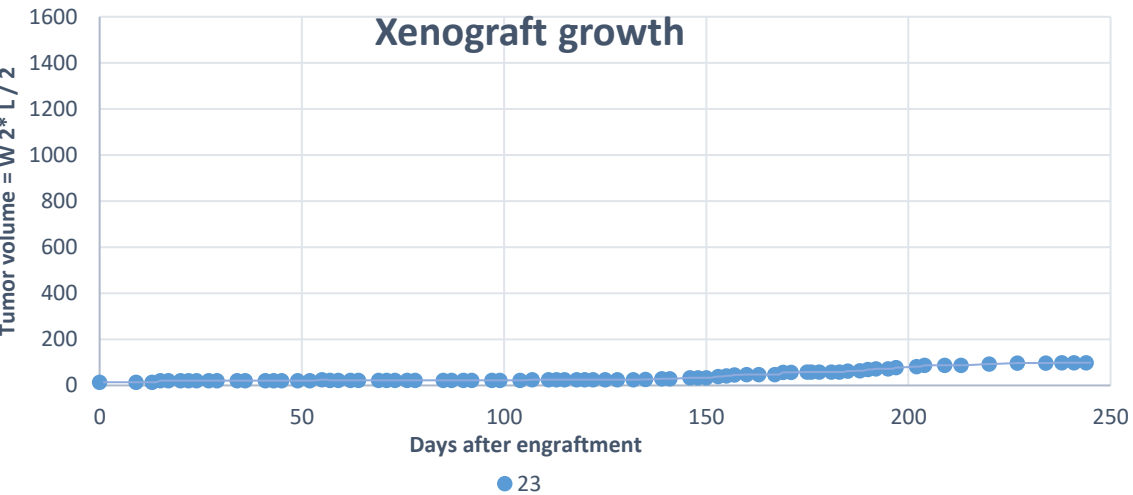
apemic, little blood below a stripe each day but never visible for at least 3 days

Supplementary figure 1-23-8.
Mouse, xenograft and secondary
tumor growth curves

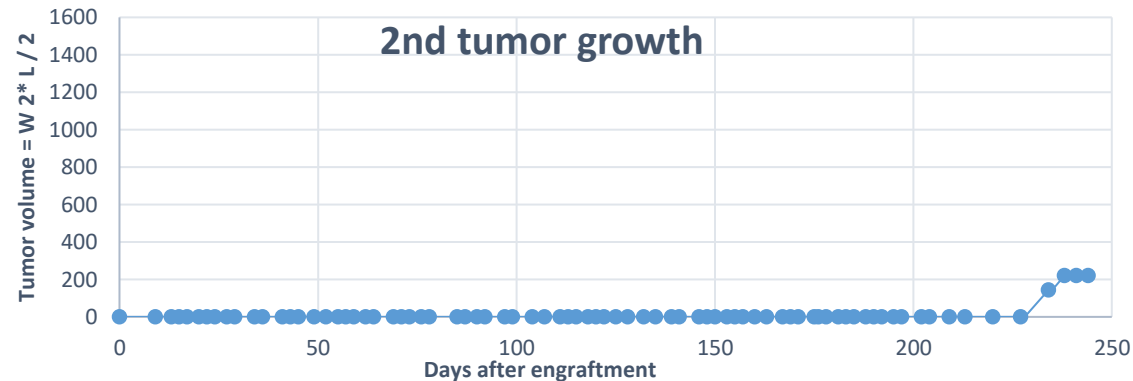
Weight curve



Xenograft growth curve



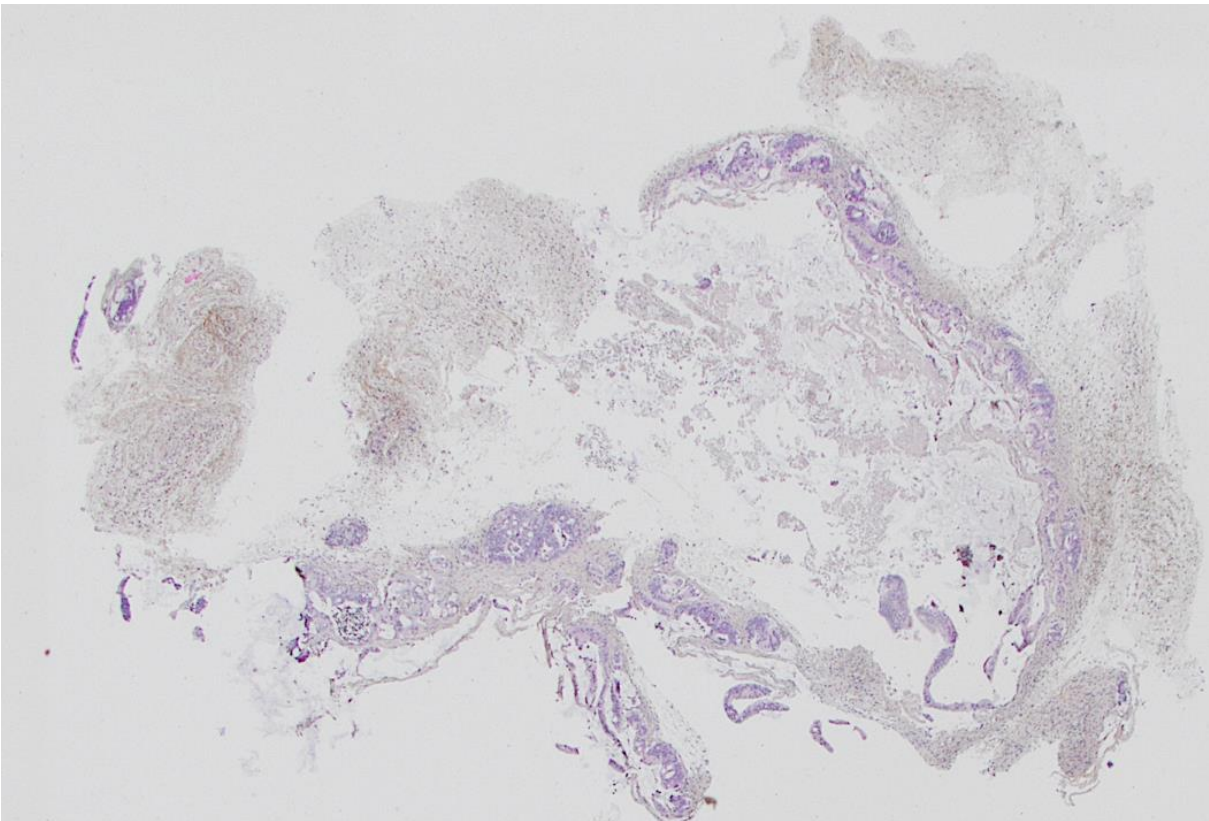
Secondary tumor growth curve



Supplementary figure 1-23-9. Histology pictures

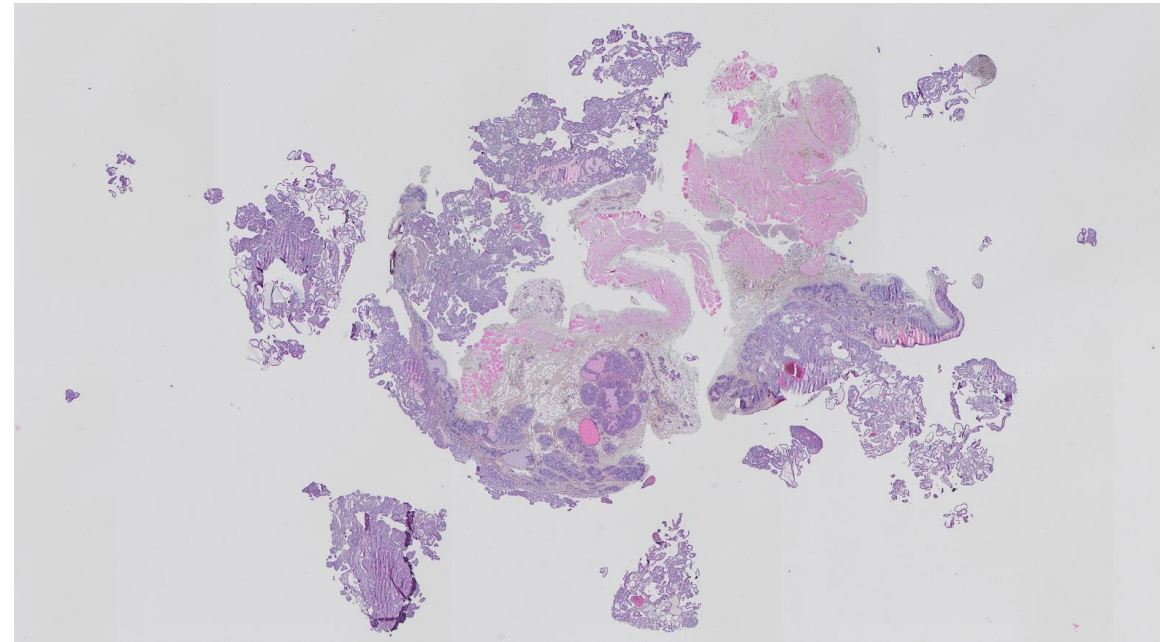
X – xenograft

- CRC Tumor glandulas with necrotic debris in the lumen
- No lymphoma cells
- Mucus
- Necrotic tissue
- Connective tissue



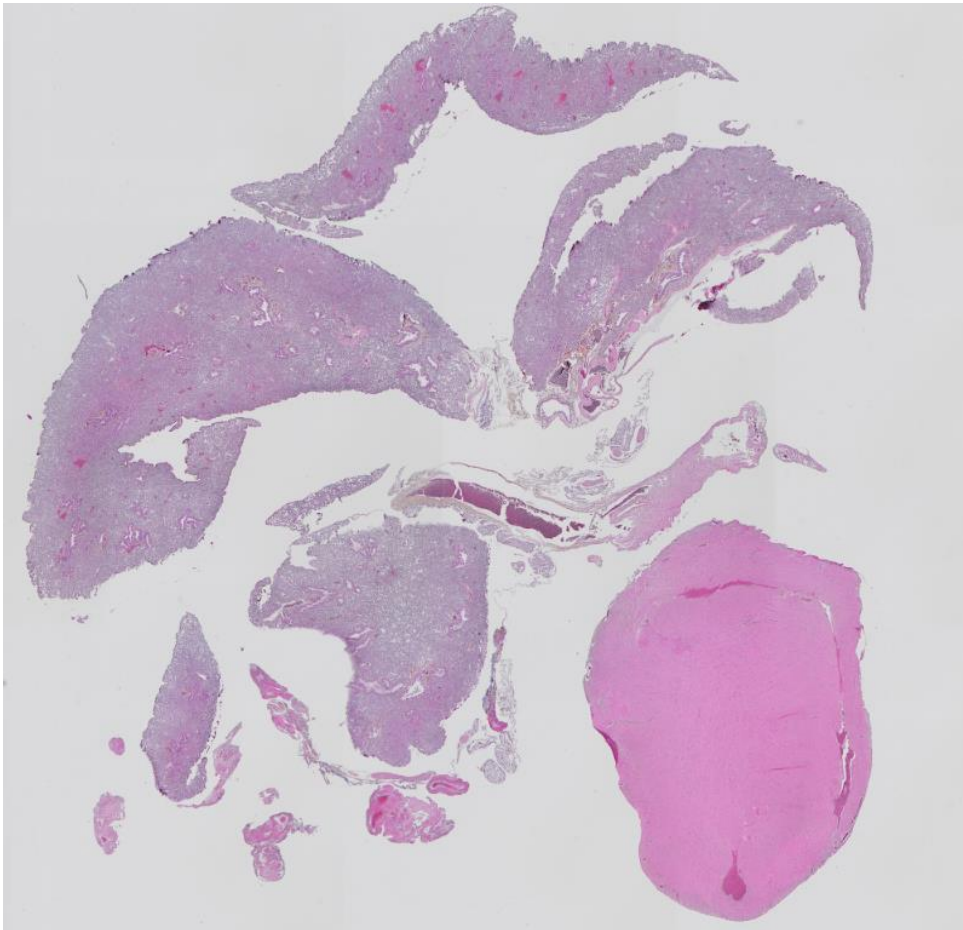
TR – tumor right side (dark bladder with liquid)

- Possible some kind of cyst
- Liquid filled structures
- Does not look malign
- Regularly epithelia



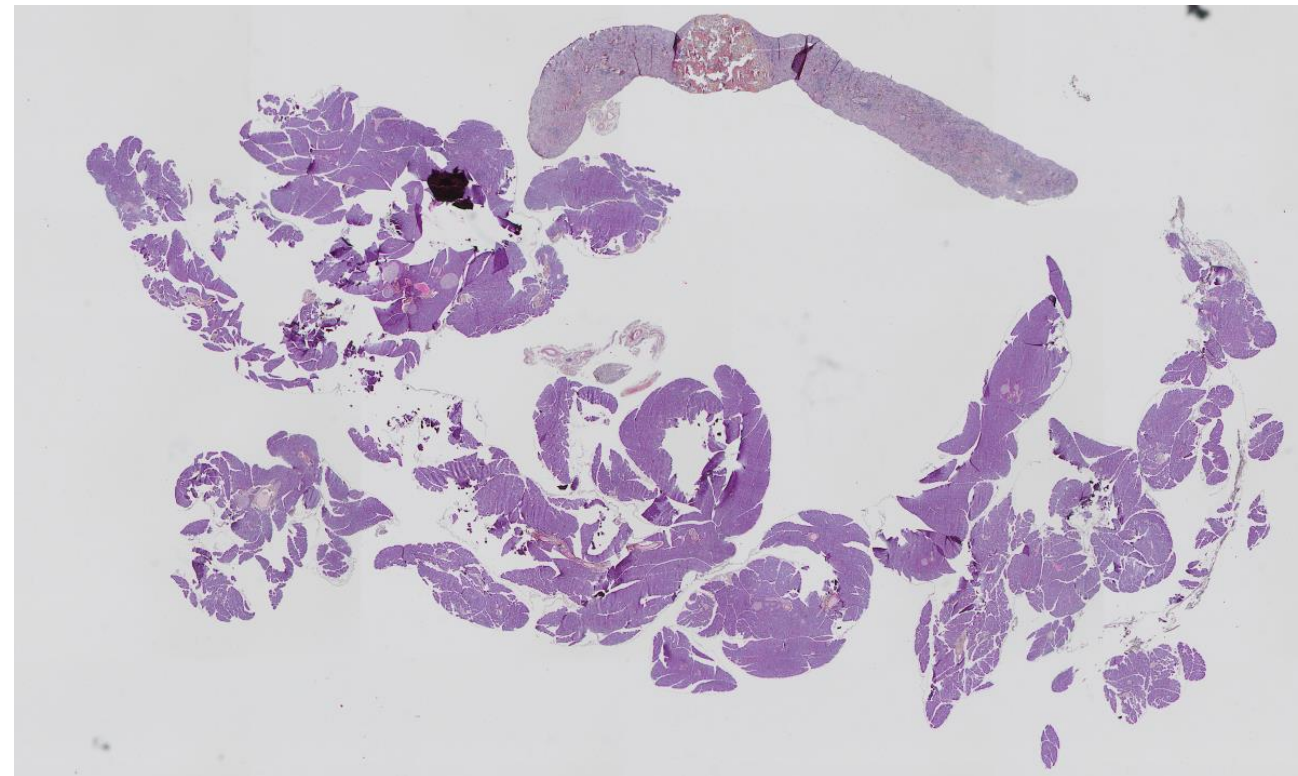
Lungs and heart

- Look normal, however a bit compact lungs
- Possibly macrophages in the lungs



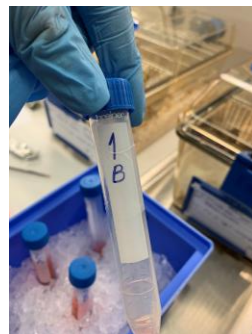
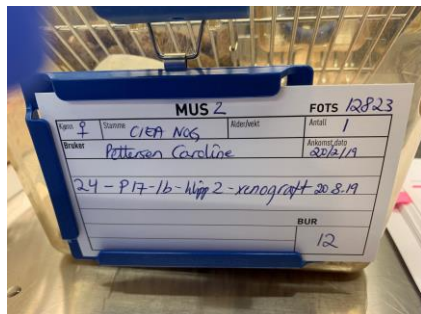
Spleen and pancreas

- pancreas looks normal
- no lymphoid cancer cells
- fibrotic field in the middle of the spleen



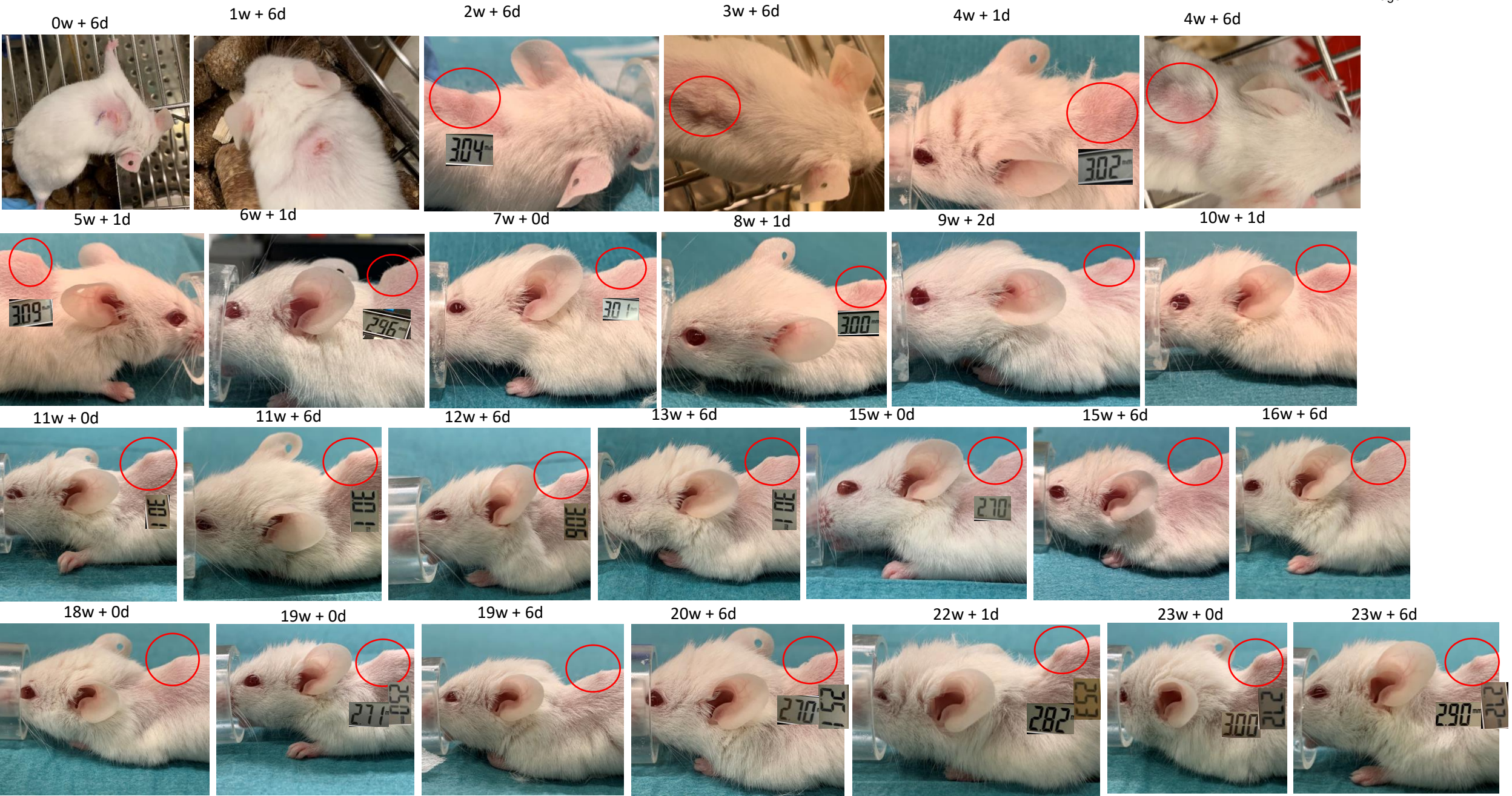
Mouse 24

- Surgery date: 20.08.19
 - Age (weeks) 31
 - Weight (g) 23.6
 - Tumor fragment P17-1B
 - Fragment size 3 x 3 mm
 - Ear mark 2

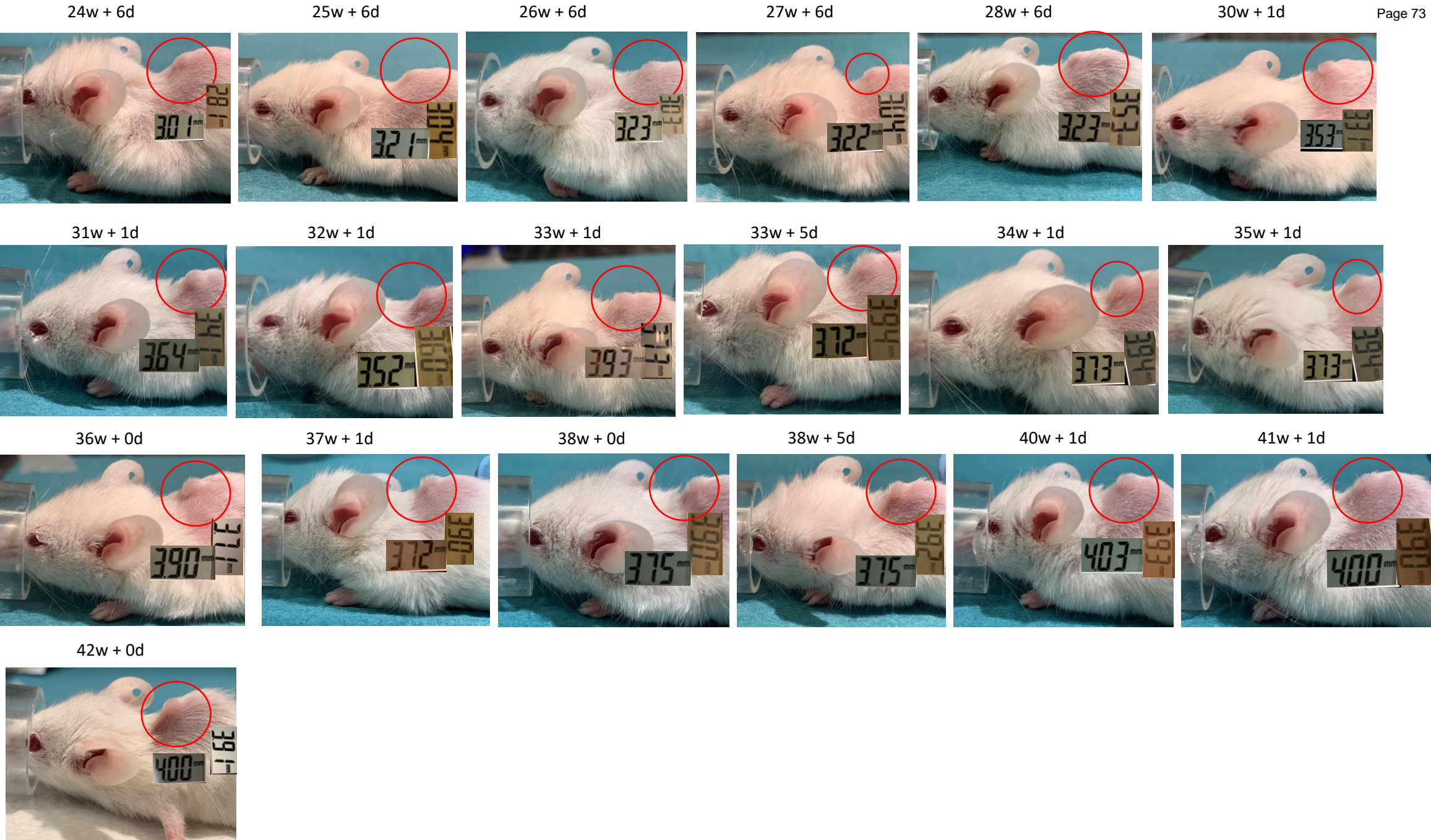


Supplementary figure 1-24-1. Pictures from the engraftment day

Supplementary figure 1-24-2. Pictures from follow up and tumor size measurement



Supplementary figure 1-24-2. Pictures from follow up and tumor size measurement



Supplementary figure 1-24-3. Pictures from euthanization

- No treatment given; Did not pass tumor size indicating treatment start
- Necroscopy
 - Xenograft size
 - Blood sample
 - Blood card and plasma
 - Tumor tissue for
 - Histology (only for histology due to small xenograft size)

Prosedyre for avlivning og påfølgende prøvetaking av CIA NOG mus

Human endepunkter:

- 8 ukers behandling med Smartfish eller Placebo
- Tumor volum ~1500 mm³ eller 10 % tap av kroppsvekt

Prosedyre:

- Vel musen og noter vekten 21.4g
- Legg mus i anestesibur med isofluran 2%
- Legg musen på varmeteppe med operasjonsduk og anestesimaske
- Barber og vask tumorområdet
- Mål tumorstørrelse
- Vask og barber området for inngrep
- Åpne abdomen/brysthulen
- Blod (50 µL) samles i pipettespiss og settes direkte på blodkort.
 - Merk blodkort med navn på mus og dato
- Tapp blod fra hjertet i EDTA rør
- Kutt aorta
- Sett på troppe på EDTA rør og bland innholdet
- Sentrifuger røret på 4C, 3000 rpm, 10 min
- Bruk skalpell til å skjære ut tumoren
 - Fjern nekrotisk vev/bindevev
 - Ta ut 3 biter
 - 4x4x4 mm til IHC i rør med 4% formalin (sentrifugerør m/blå topp, oppbevares på romtemperatur i skap inntil levering til kjernefasiliteten)
 - 4x4x4 mm til RNA-sekvensering i cryorør (rør med 5 x volum RNA later, kjøleskap 4°C over natt, ta av RNA later, legg i nytt cryorør og frys på -80°C)
 - 4x4x4 til proteinisolering i cryorør (snapfreez N₂, deretter frys på -80°C)
- Resten av tumoren fryses ned i cryorør (1-3 avhengig av størrelse, (snapfreez N₂, deretter frys på -80°C)
- Pipetter av plasmaet som er øverst i røret, uten å få med blodceller
- Fordel plasma i 2 x 500 µl eppendorfrør
- Merk plasmarøret godt (mus nr, plasma, dato, initialer, og frys det på -80C (egen boks merket Caroline Pettersen «plasma etter behandling»)
- La blodkortet tørke i romtemp i 2 timer
- La blodkort i zip-plastpose på -80°C (press ut luft)
- Frys blodkort i zip-plastpose på -80°C (press ut luft)


EDTA plasma

Blodkort

Protein

Immunohistochemistry

RNA sequencing



AUTOPSY CARD

NUMBER 24 - (P17-1b) - ear cut 2	Male Female X	STRAIN CIA NOG	BIRTH DATE January 2019	EXPERIMENT PDX - Xenograft
AGE AT DEATH	DEATH MODE DATE 11.06.20	GROUP Pettersen, Caroline		
CLINICAL SYMPTOMS AT DEATH xenograft not growing reduced weight				
ORGAN WEIGHT		SECTION TAKEN		
ORGAN	WEIGHT	ORGAN	YES	GROSS OBSERVATION
Femur		1) Lung + Heart (LH)	✓	lungs filled with formalin
Liver		2) Liver (L)	✓	
		3) Kidney (N)	✓	
		4) Adrenal		
Spleen		5) Testis/Ovary		Pass i livmor
		6) Spleen + pancreas (MP)	✓	Small spleen < 1cm
Kidney		7) Lymph nodes		
		8) Bone marrow		
Testis/Ovary		9) Xenograft (X)	✓	Small ~3mm, only sampled for histology
		10) Thymus (T)	✓	
		11) 2nd tumor right (TR)		
		12) 2nd tumor left (TL)		
		13)		

Notes: Blood card ✓
Blood plasma ✓
Pictures ✓
Weight: 21.4g
Tumor size 39/4.0

MUS 1				FOTS 12823
Kjønn ♀	Stamme CIA NOG	Alder/vekt	Antall 1	
Bruker Pettersen Caroline				Ankomst dato 20/2/19
23 - P17-1a - klipp 1 - xenograft 20.8.19				
24 - P17-1b - klipp 2 - 11 - BUR				
25 - P17-2a - klipp 3 - 11 -				
26 - P17-2b - klipp 4 - 11 -				
				11

Autopsy card modified from: http://www.pathbase.net/Necropsy_of_the_Mouse/

Supplementary figure 1-24-3. Pictures from euthanization (11.06.20)

- *Xenograft slow growth
- *3 months since animals with not growing xenografts were euthanized

MUS 1		FOTS 12823	
Kjønn ♀	Stamme CIEA NOG	Alder/vekt	Antall 1 2 3
Bruker Pettersen Caroline		Ankomst dato 20/2/19	
23 - P17-1a - klipp 1 - xenograft 20.8.17			
24 - P17-1b - klipp 2 - 11-			
25 - P17-2a - klipp 3 - 11-			
26 - P17-2b - klipp 4 - 11-			
		BUR	11



Xenograft (3.9 * 4.0 mm)



Blood draining

503™ Protein Saver Card
Not for use in diagnostic procedures

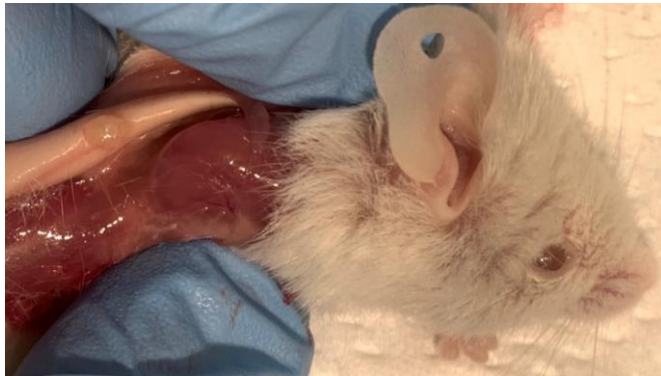
↑ Tuck Cover Here ↑

Name Mus 24 (P17-1b)

Date 11.06.20

onSAS CHP

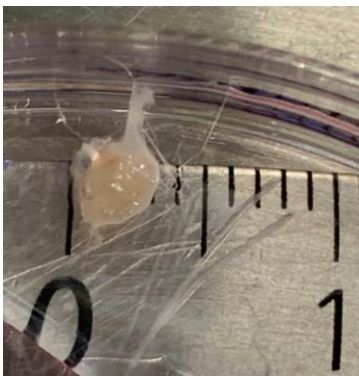
Bloodcard



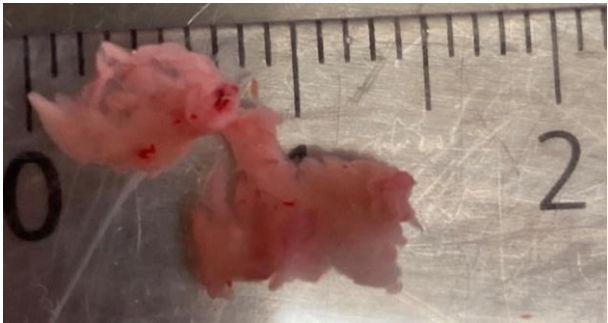
Xenograft



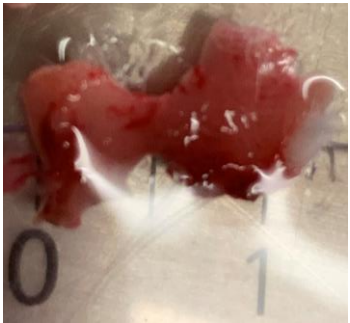
Xenograft



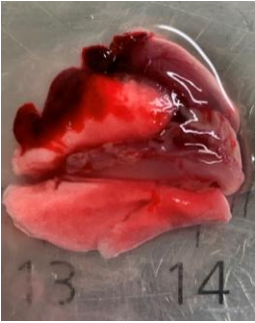
Xenograft



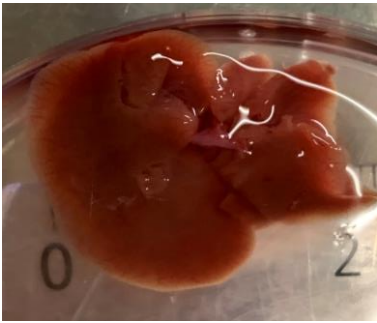
Pancreas



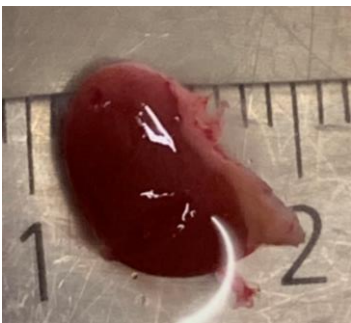
Thymus



Lungs and heart



Liver



Kidney



Spleen

Supplementary figure 1-24-4. Score sheets

NTNU Score sheet FOTS: Avdeling for komparativ medisin (AKM) Responsible researcher: Pettersen Animal ID: (P17-16) (24) Wipf (2)

Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0	20/9	24/9	27/9	29/9	4/10	6/10	9/10	11/10	13/10	16/10
	Reduced grooming	1										
	Minor distention of abdomen, rough hair coat	3										
	Hunchback or distended abdomen, inactive	18										
Behaviour (Level of activity)	Normal	0										
	Slightly reduced	1										
	Moderately reduced	3										
	Distressed behaviour due to growing tumour	3										
	Obviously reduced	5										
	Isolated, inactive, lethargic	18										
Body weight (Compared to body weight before experiment)	Body weight:		23,8	22,7	22,7	5	23,6	22,9	20,5	22	22,1	
	No loss	0										
	Loss < 5%	1										
	Loss 5-9%	3										
	Loss 10-14%	5										
	Loss > 15%	18										
Clinical signs (Infection, bleeding, discoloration)	Normal	0										
	Minor irritation around surgical wound	1										
	Moderate irritation/infected surgical wound	3										
	Infected/open surgical wound	4*										
	Tumour > 1,0 cm in diameter	10										
	Tumour > 1,5 cm in diameter	18										
Ulcerous tumour	18											

Total: 22,1

Comments, treatments etc:

0-3: Normal
4-9: Pay attention to health state and consider treatment
10-13: Pay close attention to health state, consider treatment or euthanasia
14-18: Euthanasia *Start treatment with antibiotics. If no effect within 3 days, euthanize the animal

NTNU Score sheet FOTS: Avdeling for komparativ medisin (AKM) Responsible researcher: Pettersen Animal ID: (P17-16) (24) Wipf (2)

Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0	20/9	23/9	25/9	30/9	2/10	4/10	8/10	10/10	14/10	18/10
	Reduced grooming	1										
	Minor distention of abdomen, rough hair coat	3										
	Hunchback or distended abdomen, inactive	18										
Behaviour (Level of activity)	Normal	0										
	Slightly reduced	1										
	Moderately reduced	3										
	Distressed behaviour due to growing tumour	3										
	Obviously reduced	5										
	Isolated, inactive, lethargic	18										
Body weight (Compared to body weight before experiment)	Body weight:		23,1	23,5	22,5	23,0	22,7	22,3	21,2	21,7	21,3	
	No loss	0										
	Loss < 5%	1										
	Loss 5-9%	3										
	Loss 10-14%	5										
	Loss > 15%	18										
Clinical signs (Infection, bleeding, discoloration)	Normal	0										
	Minor irritation around surgical wound	1										
	Moderate irritation/infected surgical wound	3										
	Infected/open surgical wound	4*										
	Tumour > 1,0 cm in diameter	10										
	Tumour > 1,5 cm in diameter	18										
Ulcerous tumour	18											

Total: 21,3

Comments, treatments etc:

0-3: Normal
4-9: Pay attention to health state and consider treatment
10-13: Pay close attention to health state, consider treatment or euthanasia
14-18: Euthanasia *Start treatment with antibiotics. If no effect within 3 days, euthanize the animal

NTNU Score sheet FOTS: Avdeling for komparativ medisin (AKM) Responsible researcher: Pettersen Animal ID: (P17-16) (24) Wipf (2)

Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0	16/10	18/10	21/10	23/10	26/10	29/10	1/11	4/11	6/11	13/11
	Reduced grooming	1										
	Minor distention of abdomen, rough hair coat	3										
	Hunchback or distended abdomen, inactive	18										
Behaviour (Level of activity)	Normal	0										
	Slightly reduced	1										
	Moderately reduced	3										
	Distressed behaviour due to growing tumour	3										
	Obviously reduced	5										
	Isolated, inactive, lethargic	18										
Body weight (Compared to body weight before experiment)	Body weight:		21,3	22,2	21,7	23	23,9	28,4	22	20,5	22,8	22,6
	No loss	0										
	Loss < 5%	1										
	Loss 5-9%	3										
	Loss 10-14%	5										
	Loss > 15%	18										
Clinical signs (Infection, bleeding, discoloration)	Normal	0										
	Minor irritation around surgical wound	1										
	Moderate irritation/infected surgical wound	3										
	Infected/open surgical wound	4*										
	Tumour > 1,0 cm in diameter	10										
	Tumour > 1,5 cm in diameter	18										
Ulcerous tumour	18											

Total: 22,6

Comments, treatments etc:

0-3: Normal
4-9: Pay attention to health state and consider treatment
10-13: Pay close attention to health state, consider treatment or euthanasia
14-18: Euthanasia *Start treatment with antibiotics. If no effect within 3 days, euthanize the animal

NTNU Score sheet FOTS: Avdeling for komparativ medisin (AKM) Responsible researcher: Pettersen Animal ID: (P17-16) (24) Wipf (2)

Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0	15/11	18/11	20/11	25/11	27/11	29/11	2/12	5/12	9/12	11/12
	Reduced grooming	1										
	Minor distention of abdomen, rough hair coat	3										
	Hunchback or distended abdomen, inactive	18										
Behaviour (Level of activity)	Normal	0										
	Slightly reduced	1										
	Moderately reduced	3										
	Distressed behaviour due to growing tumour	3										
	Obviously reduced	5										
	Isolated, inactive, lethargic	18										
Body weight (Compared to body weight before experiment)	Body weight:		22,6	23,6	22,5	23,0	23,2	23,7	21,3	21,1	23,1	23,5
	No loss	0										
	Loss < 5%	1										
	Loss 5-9%	3										
	Loss 10-14%	5										
	Loss > 15%	18										
Clinical signs (Infection, bleeding, discoloration)	Normal	0										
	Minor irritation around surgical wound	1										
	Moderate irritation/infected surgical wound	3										
	Infected/open surgical wound	4*										
	Tumour > 1,0 cm in diameter	10										
	Tumour > 1,5 cm in diameter	18										
Ulcerous tumour	18											

Total: 23,5

Comments, treatments etc:

0-3: Normal
4-9: Pay attention to health state and consider treatment
10-13: Pay close attention to health state, consider treatment or euthanasia
14-18: Euthanasia *Start treatment with antibiotics. If no effect within 3 days, euthanize the animal

NTNU Score sheet FOTS: Avdeling for komparativ medisin (AKM) Responsible researcher: Pettersen Animal ID: (P17-16) (24) Wipf (2)

Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0	18/12	20/12	23/12	26/12	30/12	31/12	2/1/13	6/1/13	8/1/13	13/1
	Reduced grooming	1										
	Minor distention of abdomen, rough hair coat	3										
	Hunchback or distended abdomen, inactive	18										
Behaviour (Level of activity)	Normal	0										
	Slightly reduced	1										
	Moderately reduced	3										
	Distressed behaviour due to growing tumour	3										
	Obviously reduced	5										
	Isolated, inactive, lethargic	18										
Body weight (Compared to body weight before experiment)	Body weight:		23,7	22,4	22,4	23,9	23,7	22,7	22,4	22,2	21,9	24
	No loss	0										
	Loss < 5%	1										
	Loss 5-9%	3										
	Loss 10-14%	5										
	Loss > 15%	18										
Clinical signs (Infection, bleeding, discoloration)	Normal	0										
	Minor irritation around surgical wound	1										
	Moderate irritation/infected surgical wound	3										
	Infected/open surgical wound	4*										
	Tumour > 1,0 cm in diameter	10										
	Tumour > 1,5 cm in diameter	18										
Ulcerous tumour	18											

Total: 24

Comments, treatments etc:

0-3: Normal
4-9: Pay attention to health state and consider treatment
10-13: Pay close attention to health state, consider treatment or euthanasia
14-18: Euthanasia *Start treatment with antibiotics. If no effect within 3 days, euthanize the animal

NTNU Score sheet FOTS: Avdeling for komparativ medisin (AKM) Responsible researcher: Pettersen Animal ID: (P17-16) (24) Wipf (2)

Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0	20/1	22/1	24/1	27/1	29/1	30/1	3/2	5/2	7/2	11/2
	Reduced grooming	1										
	Minor distention of abdomen, rough hair coat	3										
	Hunchback or distended abdomen, inactive	18										
Behaviour (Level of activity)	Normal	0										
	Slightly reduced	1										
	Moderately reduced	3										
	Distressed behaviour due to growing tumour	3										
	Obviously reduced	5										
	Isolated, inactive, lethargic	18										
Body weight (Compared to body weight before experiment)	Body weight:		22,8	23,7	23,8	24	23,5	22,3	21,5	22	22,5	
	No loss	0										
	Loss < 5%	1										
	Loss 5-9%	3										
	Loss 10-14%	5										
	Loss > 15%	18										
Clinical signs (Infection, bleeding, discoloration)	Normal	0										
	Minor irritation around surgical wound	1										
	Moderate irritation/infected surgical wound	3										
	Infected/open surgical wound	4*										
	Tumour > 1,0 cm in diameter	10										
	Tumour > 1,5 cm in diameter	18										
Ulcerous tumour	18											

Total: 22,5

Comments, treatments etc:

0-3: Normal
4-9: Pay attention to health state and consider treatment
10-13: Pay close attention to health state, consider treatment or euthanasia
14-18: Euthanasia *Start treatment with antibiotics. If no effect within 3 days, euthanize the animal

Supplementary figure 1-24-4. Score sheets

NTNU

Score sheet FOTS:
Avdeling for komparativ medisin (AKM)

Responsible researcher:
Pettersen

Animal ID:
(24)

Wipp
(2)

Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0	1/12	12/12	14/12	17/12	19/12	21/12	24/12	26/12	28/12	30/12	31/12
	Reduced grooming	1											
	Minor distention of abdomen, rough hair coat	3											
	Hunchback or distended abdomen, inactive	18											
Behaviour (Level of activity)	Normal	0											
	Slightly reduced	1											
	Moderately reduced	3											
	Distressed behaviour due to growing tumour	3											
	Obviously reduced	5											
	Isolated, inactive, lethargic	18											
Body weight (Compared to body weight before experiment)	Body weight:		22,5	22,7	21,7	23	24,2	23,3	22,5	22,4	22,7	22,4	22,5
	No loss	0											
	Loss < 5%	1											
	Loss 5-9%	3											
	Loss 10-14%	5											
Clinical signs (Infection, bleeding, discoloration)	Loss > 15%	18											
	Normal	0	2,7	2,8									
	Minor irritation around surgical wound	1											
	Moderate irritation/infected surgical wound	3											
	Infected/open surgical wound	4*	2,9	3,1	11	3,2	3,4	3,2	3,2	3,2	3,1	3,4	3,2
	Tumour > 1,0 cm in diameter	10											
	Tumour > 1,5 cm in diameter	18											
	Ulcerous tumour	18											
Total:													
Comments, treatments etc:													
0-3: Normal 4-9: Pay attention to health state and consider treatment 10-13: Pay close attention to health state, consider treatment or euthanasia 14-18: Euthanasia *Start treatment with antibiotics. If no effect within 3 days, euthanize the animal													

NTNU

Score sheet FOTS:
Avdeling for komparativ medisin (AKM)

Responsible researcher:
Pettersen

Animal ID:
(24)

Wipp
(2)

Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0	14/4	17/4	20/4	24/4	27/4	30/4	4/5	8/5	11/5	14/5	22/5
	Reduced grooming	1											
	Minor distention of abdomen, rough hair coat	3											
	Hunchback or distended abdomen, inactive	18											
Behaviour (Level of activity)	Normal	0											
	Slightly reduced	1	Fin	Fin	Fin	Fin		Fin	Fin	Fin	Fin	Fin	11
	Moderately reduced	3	form	form	form	form		form	form	form	form	form	
	Distressed behaviour due to growing tumour	3											
	Obviously reduced	5											
	Isolated, inactive, lethargic	18											
Body weight (Compared to body weight before experiment)	Body weight:		22,5	22,4	22,7	22,3	22,5	22,4	22,4	21,9	22,3		21,3
	No loss	0											
	Loss < 5%	1											
	Loss 5-9%	3											
	Loss 10-14%	5											
Clinical signs (Infection, bleeding, discoloration)	Loss > 15%	18											
	Normal	0	3,7	3,7	3,7	3,7		3,7		3,7		3,7	
	Minor irritation around surgical wound	1											
	Moderate irritation/infected surgical wound	3											
	Infected/open surgical wound	4*	3,9	3,9	3,9	3,9		3,9		3,9		3,9	
	Tumour > 1,0 cm in diameter	10											
	Tumour > 1,5 cm in diameter	18											
	Ulcerous tumour	18											
Total:													
Comments, treatments etc:													
0-3: Normal 4-9: Pay attention to health state and consider treatment 10-13: Pay close attention to health state, consider treatment or euthanasia 14-18: Euthanasia *Start treatment with antibiotics. If no effect within 3 days, euthanize the animal													

NTNU

Score sheet FOTS:
Avdeling for komparativ medisin (AKM)

Responsible researcher:
Pettersen

Animal ID:
(24)

Wipp
(2)

Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0	1/3	16/3	20/3	23/3	27/3	27/3	31/4	6/4	10/4	14/4	
	Reduced grooming	1											
	Minor distention of abdomen, rough hair coat	3											
	Hunchback or distended abdomen, inactive	18											
Behaviour (Level of activity)	Normal	0											
	Slightly reduced	1											
	Moderately reduced	3											
	Distressed behaviour due to growing tumour	3											
	Obviously reduced	5											
	Isolated, inactive, lethargic	18											
Body weight (Compared to body weight before experiment)	Body weight:		22,6	21,7	22,2	22,7	22,7	23,1	22,6	22,5	23,5	22,5	
	No loss	0											
	Loss < 5%	1											
	Loss 5-9%	3											
	Loss 10-14%	5											
Clinical signs (Infection, bleeding, discoloration)	Loss > 15%	18											
	Normal	0	3,2	3,2	3,3		3,4		3,6		3,7	3,7	
	Minor irritation around surgical wound	1											
	Moderate irritation/infected surgical wound	3											
	Infected/open surgical wound	4*	3,2	3,4	3,5		3,6		3,5		3,9	3,9	
	Tumour > 1,0 cm in diameter	10											
	Tumour > 1,5 cm in diameter	18											
	Ulcerous tumour	18											
Total:													
Comments, treatments etc:													
0-3: Normal 4-9: Pay attention to health state and consider treatment 10-13: Pay close attention to health state, consider treatment or euthanasia 14-18: Euthanasia *Start treatment with antibiotics. If no effect within 3 days, euthanize the animal													

NTNU

Score sheet FOTS:
Avdeling for komparativ medisin (AKM)

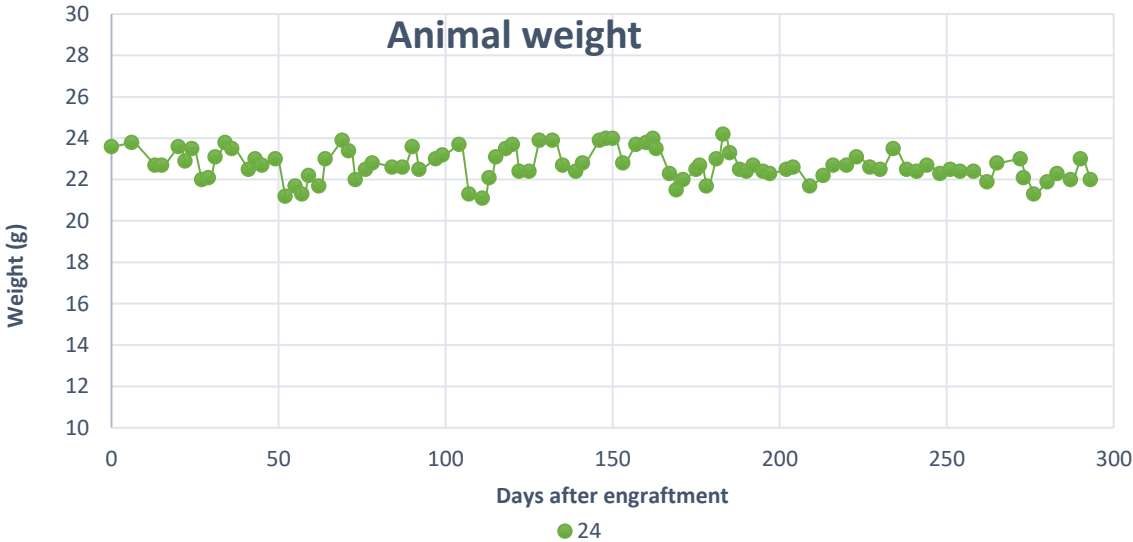
Responsible researcher:
Pettersen

Animal ID:
(24)

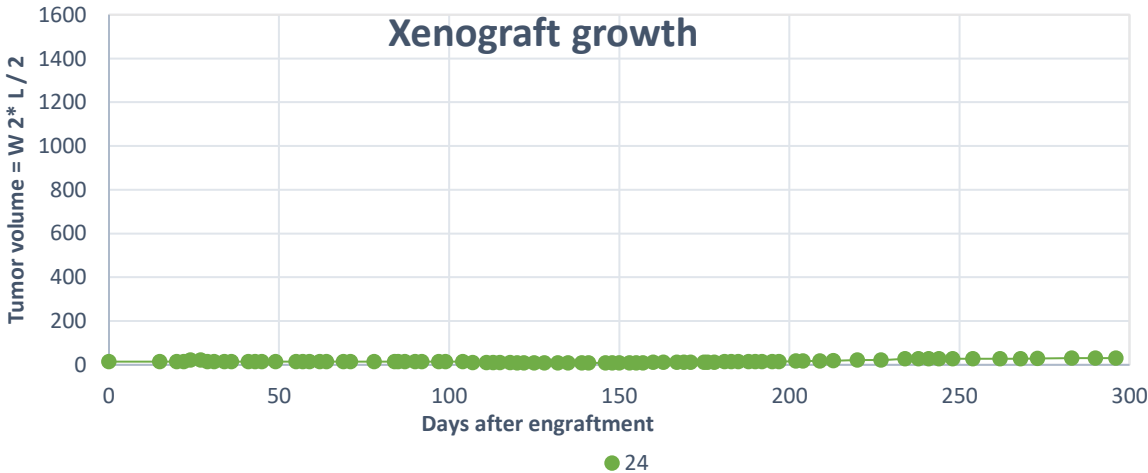
Wipp
(2)

Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0	14/5	18/5	19/5	22/5	26/5	29/5	2/6	5/6	8/6	11/6	
	Reduced grooming	1											
	Minor distention of abdomen, rough hair coat	3											
	Hunchback or distended abdomen, inactive	18											
Behaviour (Level of activity)	Normal	0											
	Slightly reduced	1											
	Moderately reduced	3	Fin		Fin				Fin				
	Distressed behaviour due to growing tumour	3	form		form				form				
	Obviously reduced	5											
	Isolated, inactive, lethargic	18											
Body weight (Compared to body weight before experiment)	Body weight:		23,0	22,1	21,3	21,9	22,3	22,0	23,0	22,0	21,4		
	No loss	0											
	Loss < 5%	1											
	Loss 5-9%	3											
	Loss 10-14%	5											
Clinical signs (Infection, bleeding, discoloration)	Loss > 15%	18											
	Normal	0											
	Minor irritation around surgical wound	1											
	Moderate irritation/infected surgical wound	3											
	Infected/open surgical wound	4*	3,9		3,9				3,9		3,9		3,9
	Tumour > 1,0 cm in diameter	10											
	Tumour > 1,5 cm in diameter	18											
	Ulcerous tumour	18											
Total:													
Comments, treatments etc:													
0-3: Normal 4-9: Pay attention to health state and consider treatment 10-13: Pay close attention to health state, consider treatment or euthanasia 14-18: Euthanasia *Start treatment with antibiotics. If no effect within 3 days, euthanize the animal													

Weight curve



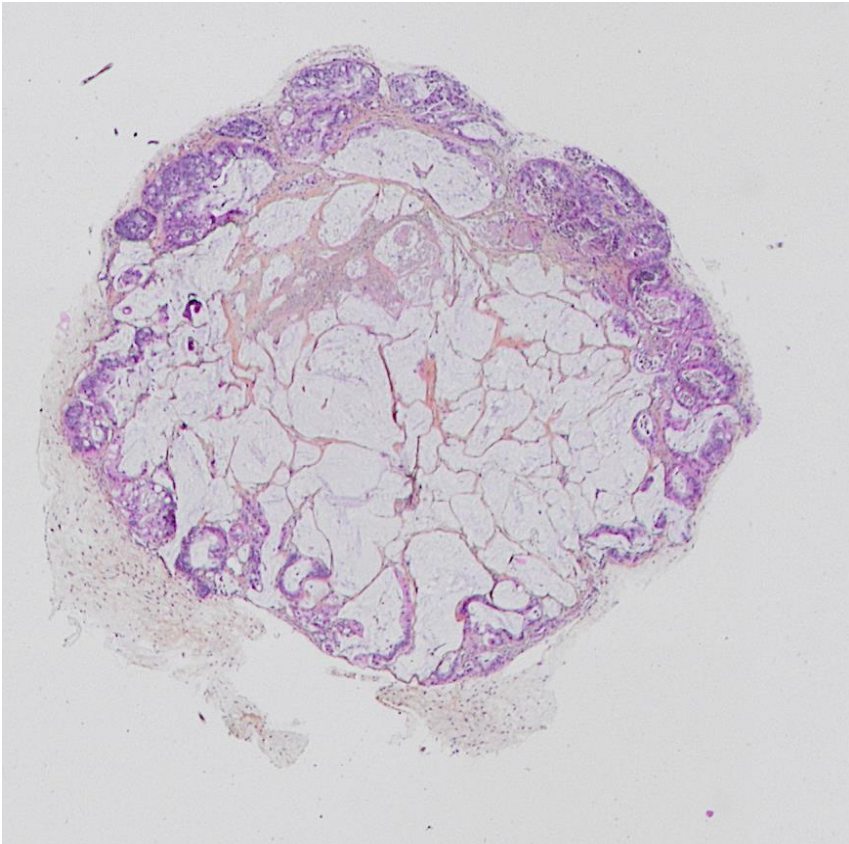
Xenograft growth curve



Supplementary figure 1-24-6. Histology pictures

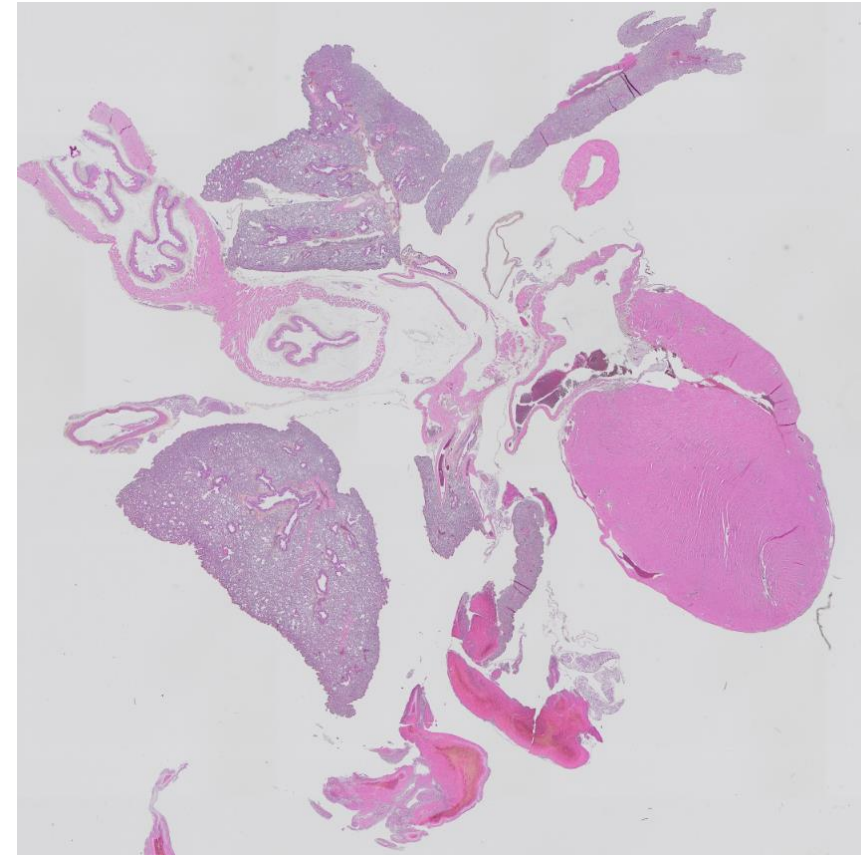
M24X – Xenograft

- Typical colorectal adenocarcinoma
- Glandulas with necrotic debris in lumen
- Mucus producing adenocarcinoma
- Necrotic tissue in the middle



M24LH – Lungs and heart

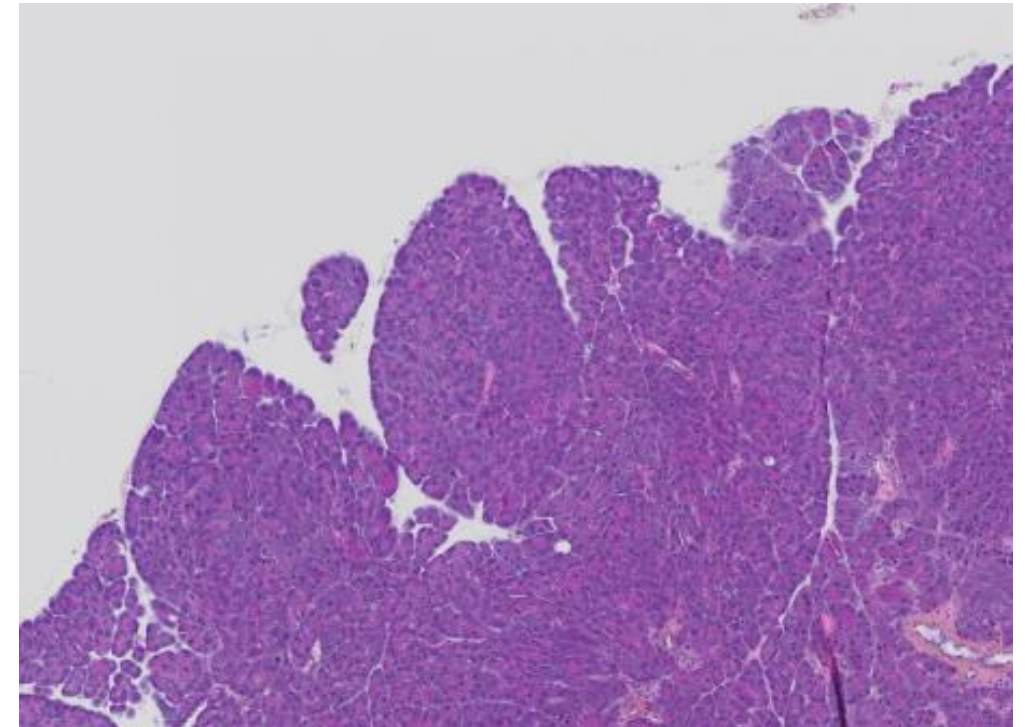
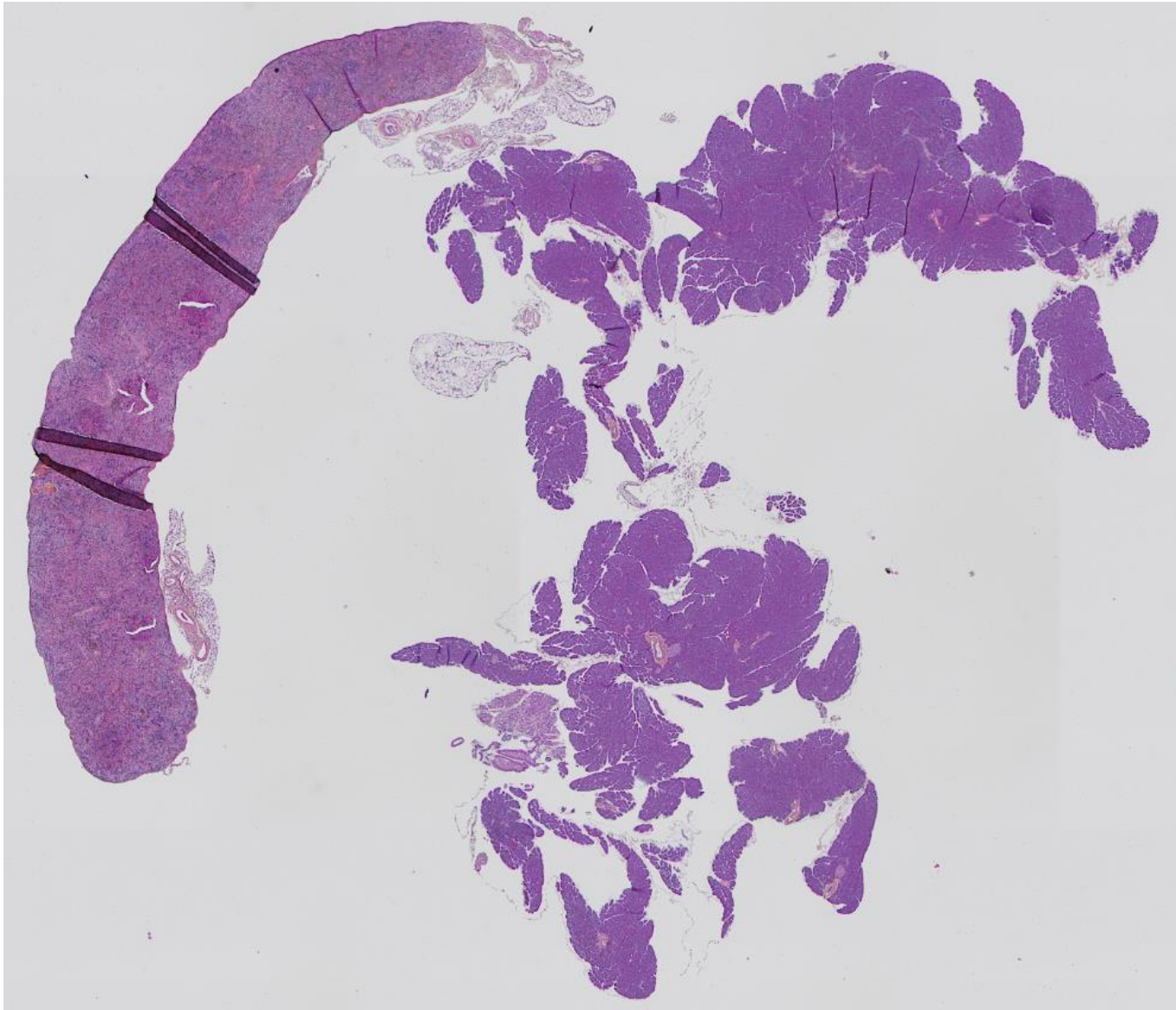
- Looks normal



Supplementary figure 1-24-6. Histology pictures

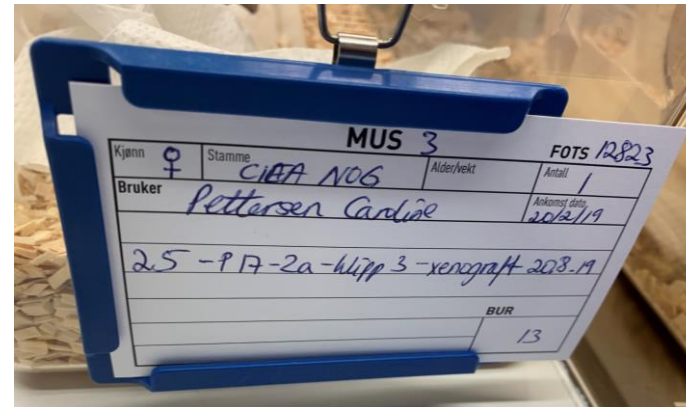
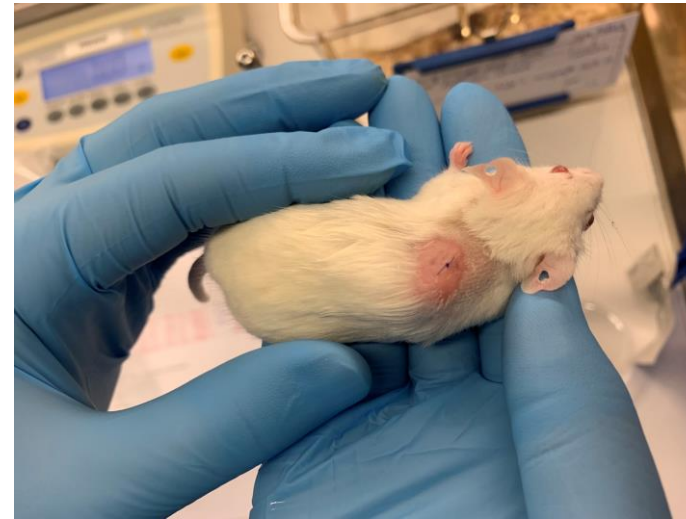
M24MP – Spleen and pancreas

- Spleen looks normal
- Pancreas looks normal



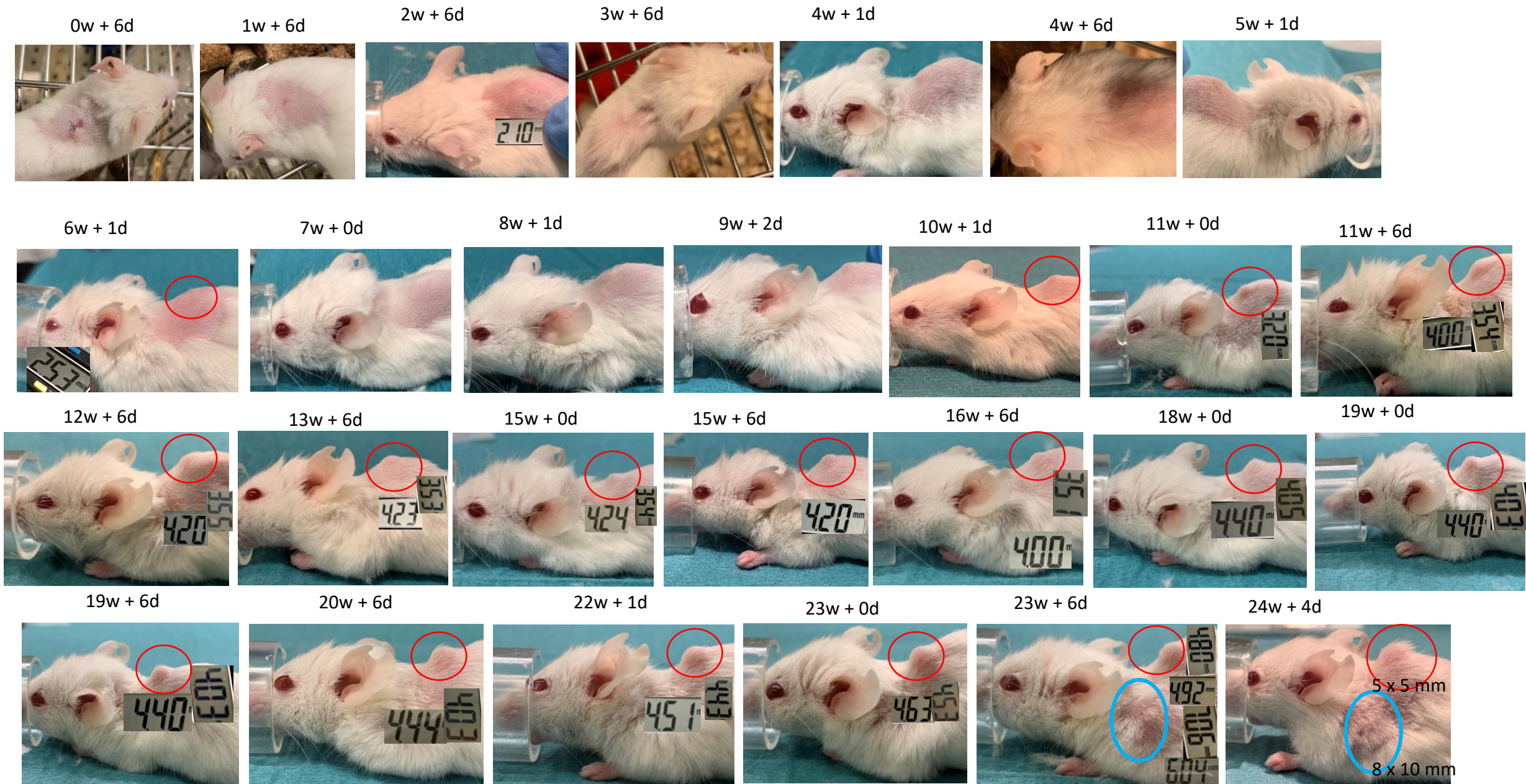
Mouse 25

- Surgery date: 20.08.19
 - Age (weeks) 31
 - Weight (g) 24.6
 - Tumor fragment P17-2A
 - Fragment size 3 x 3 mm
 - Ear mark 3



Supplementary figure 1-25-1.
Pictures from the engraftment day

Supplementary figure 1-25-2. Pictures from follow up and xenograft size measurement



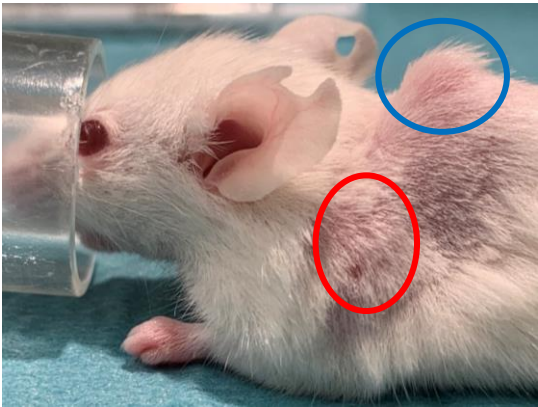
Supplementary figure 1-25-3. Picture from follow up

- Thick skin and a wound on the right shoulder at day 82, 11w + 5d (12.11.19)
- Looked better 15.11.19
- Shaving machine checked for any defaults



Supplementary figure 1-25-3. Pictures from euthanization 10.02.20

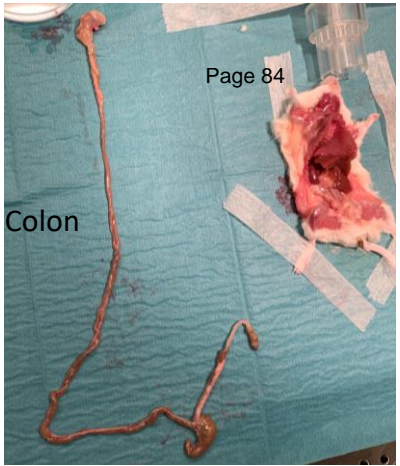
- Reduced general health
- Rapidly growing secondary tumor on the left shoulder
- Necroscopy
 - Xenograft size; 5 x 5 mm
 - Treatment not started due to reduced health
 - Secondary tumor at left shoulder 10 x 8 mm
 - Colon taken out and washed with sterile NaCl
 - To be used for testing antibodies for IHC
 - Blood sample
 - Tumor tissue for
 - Histology



Blue; xenograft
Red; secondary tumor

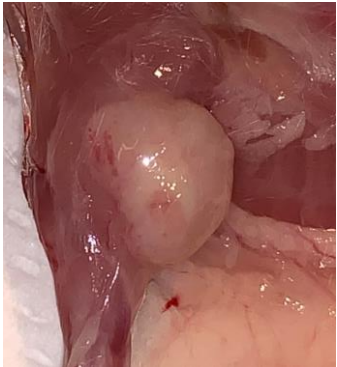
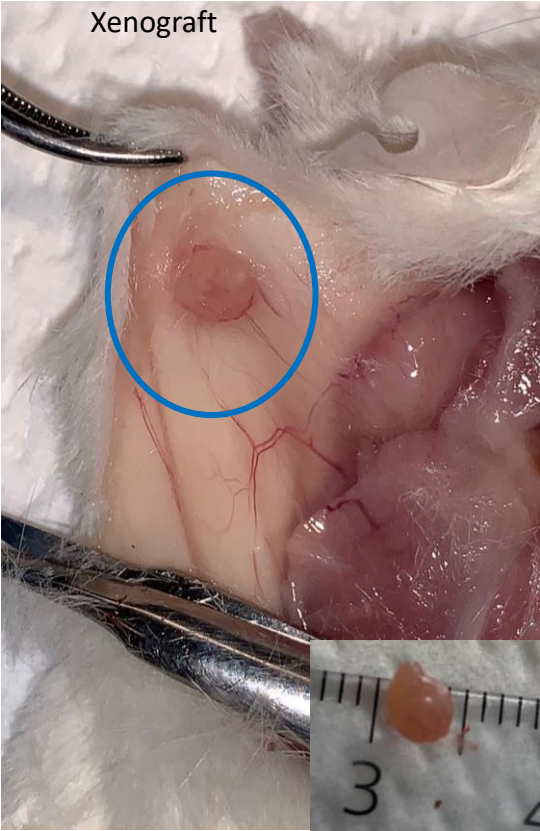


Whiteish colour on the lungs

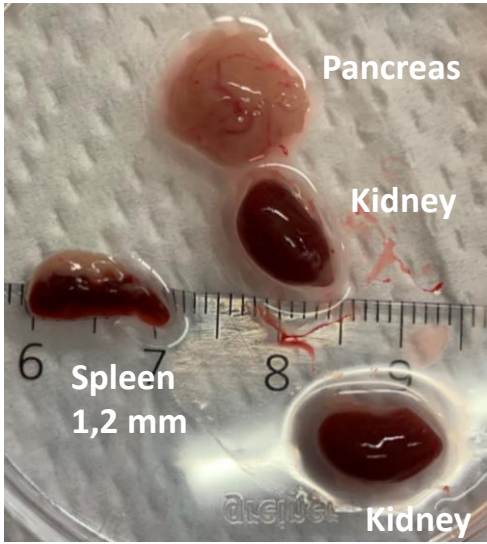
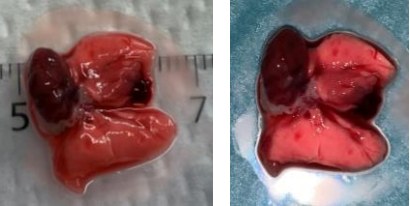


Colon taken out to use for antibody testing for IHC. Flushed with sterile NaCl.

MUS 1			
Stamme	CIEA NOG	Alider/vekt	As
trucker	Petterson Caroline		
#3 har fått ekstra luf pi vensire skulder Tumor left shoulder			
23	- P17-1a-Klipp 1-xenograft		
24	- P17-1b-Klipp 2 -11-	BU	
25	- P17-2a-Klipp 3 -11-		
26	- P17-2b-Klipp 4 -11-		




Tumor left shoulder



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<div> <div>NTNU</div> <div>Score sheet FOTS:</div> </div> <div> <div>Adveling for komparativt medisn (AKM)</div> <div>Petterson</div> </div> <div> <div>Responsible researcher:</div> <div>(P17-2a)</div> </div> <div> <div>Animal ID:</div> <div>(25)</div> </div>													
Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0	14/10	18/10	21/10	23/10	26/10	29/10	31/11	3/11	6/11	12/11	13/3
	Reduced grooming	1											
	Minor distention of abdomen, rough hair coat	3											
	Hunched back or distended abdomen, inactive	18											
Behaviour (Level of activity)	Normal	0											
	Slightly reduced	1											
	Moderately reduced	3											
	Distressed behaviour due to growing tumour	3											
	Obviously reduced	5											
	Isolated, inactive, lethargic	18											
Body weight (Compared to body weight before experiment)	Body weight:		23.0	23.4	25.4	23.8	24.6	28.7	23.0	24.1	25.1	23.8	
	No loss	0											
	Loss < 5 %	1											
	Loss 5-9 %	3											
	Loss 10-14 %	5											
	Loss > 15 %	18											
Clinical signs (Infection, bleeding, discoloration)	Normal	0	2.5	2.5	-11	3	-11	3	-11	3.2	3.2	3.5	3.5
	Minor irritation around surgical wound	1											
	Moderate irritation/infected surgical wound	3											
	Infected/open surgical wound	4+											
	Tumour > 1.0 cm in diameter	10											
	Tumour > 1.5 cm in diameter	18											
	Ulcerous tumour	18											
Total:													
Comments, treatments etc:													

0-3: Normal
 4-9: Pay attention to health state and consider treatment
 10-13: Pay close attention to health state, consider treatment or euthanasia
 14-18: Euthanasia *Start treatment with antibiotics. If no effect within 3 days, euthanize the animal

<div>  NTNU Score sheet FOTS: Avdeling for komparativ medisin (AKM) </div>		<div> Responsible researchers: Petersen </div>		<div> Animal ID: 23 </div>		<div> Weight </div>						
Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0	20/1	22/1	24/1	27/1	29/1	30/1	3/2	4/2	5/2	7/2
	Reduced grooming	1										
	Minor distention of abdomen, rough hair coat	3										
	Hunched or distended abdomen, inactive	18										
Behaviour (Level of activity)	Normal	0										
	Slightly reduced	1										
	Moderately reduced	3										
	Distressed behaviour due to growing tumour	3										
	Obviously reduced	5										
Body weight (Compared to body weight before experiment)	Isolated, inactive, lethargic	18										
	Body weight		24.2	24.4	24.2	23.8	22.8	23.5	23	24.4	24.5	
	No loss	0										
	Loss < 5%	1										
	Loss 5-9%	3										
Clinical signs (Coughing, bleeding, discoloration)	Loss 10-14%	5										
	Loss > 15%	18										
	Normal	0										
	Minor irritation around surgical wound	1	9.4	9.4	4.5	4.5	4.5	4.8	4.8	4.8	4.8	5
	Moderate irritation/infected surgical wound	3	4.4	4.5	4.5	4.6	4.6	4.7	4.7	4.7	4.7	5.1
	Indefinite ripened surgical wound	4*										
	Tumour > 1.0 cm in diameter	10										
	Tumour > 1.5 cm in diameter	18										
	Ulcerous tumour	18										

Comments, treatments etc:

22-15g

3-5: Pay attention to health state and consider treatment

10-13: Pay close attention to health state, consider treatment or euthanasia

14-18: Euthanasia *Start treatment with antibiotics. If no effect within 3 days, euthanize the animal

Total:

--	--	--	--	--	--	--	--	--	--	--	--	--

Weight:

5

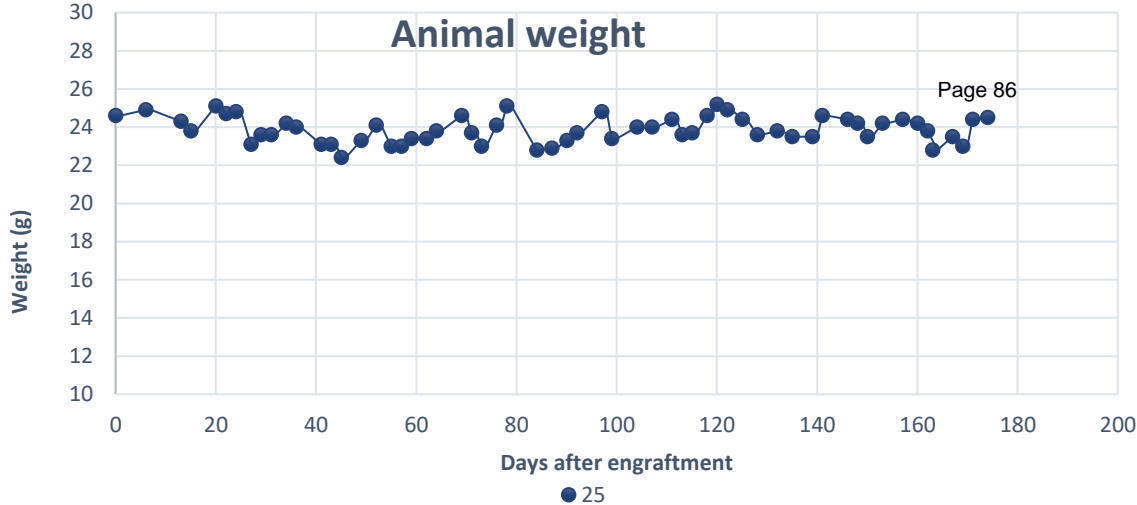
5.1

10

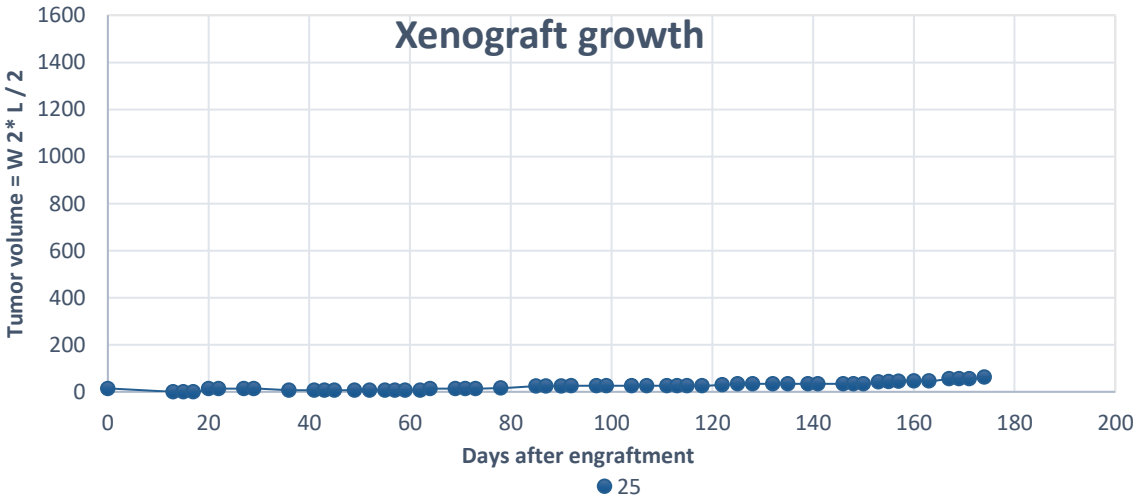
10.1

Supplementary figure 1-25-5.
Mouse, xenograft and
secondary tumor growth
curves

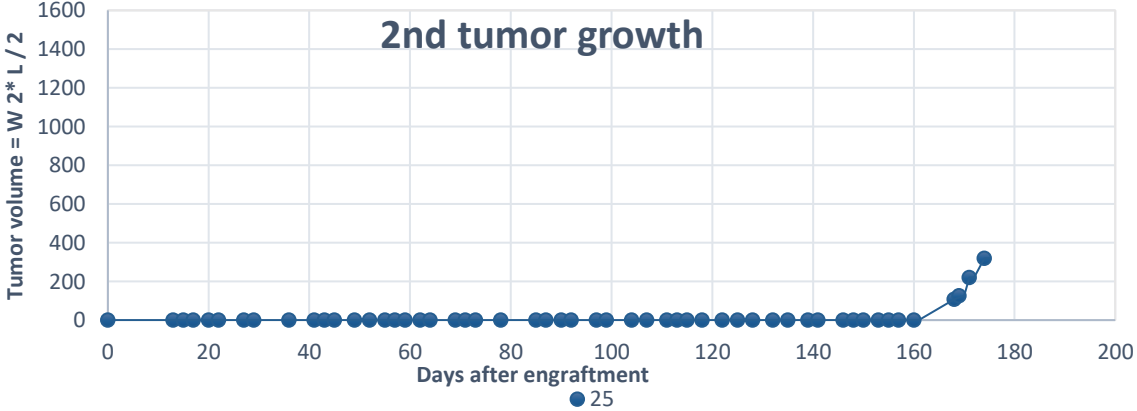
Weight curve



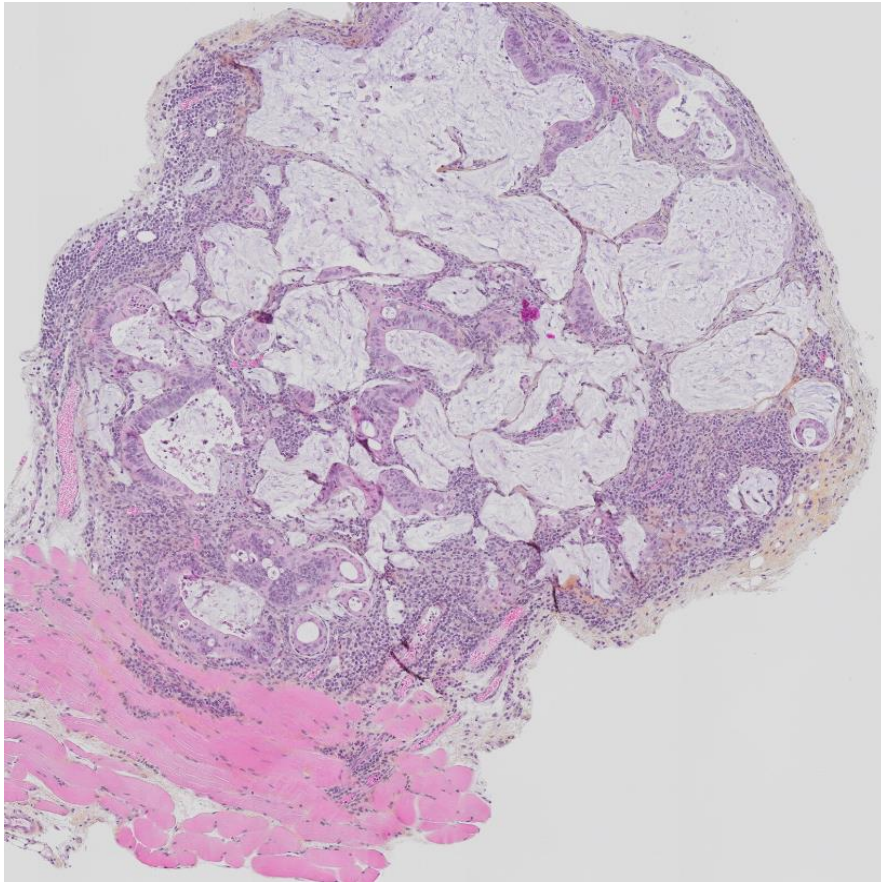
Xenograft growth curve



Secondary tumor growth curve

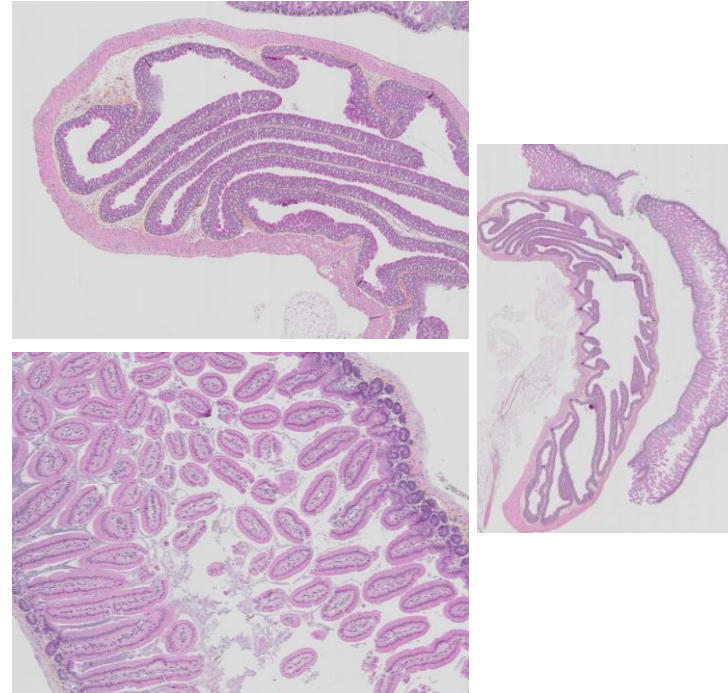


M25X



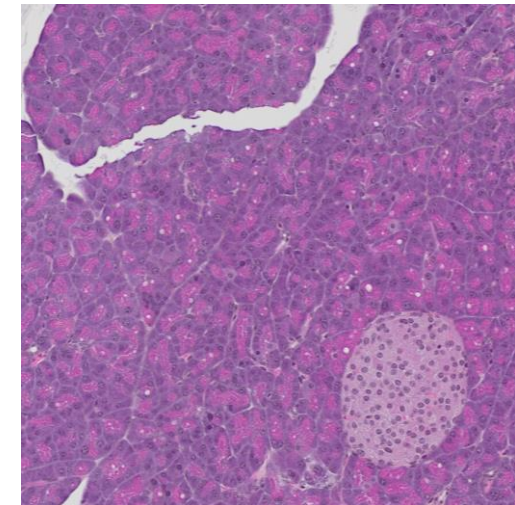
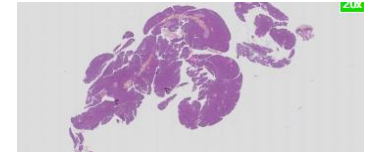
- Typical colorectal cancer tissue
- Areas with glandulas
- Lymphoid cells at the border of the xenograft
- Mucus producing adenocarcinoma
- Unregular nuclear membranes might indicate stressed cells
 - Could be that the lymphoid cells are about taking over the xenograft

M25T



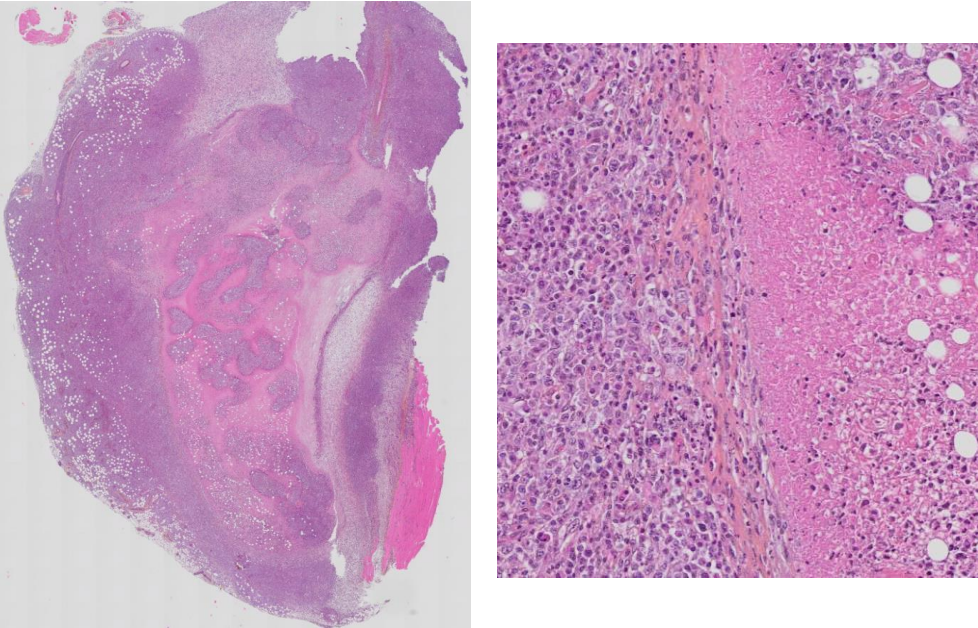
- Colon tissue; looks healthy
 - To be used for antibody testing

M25P



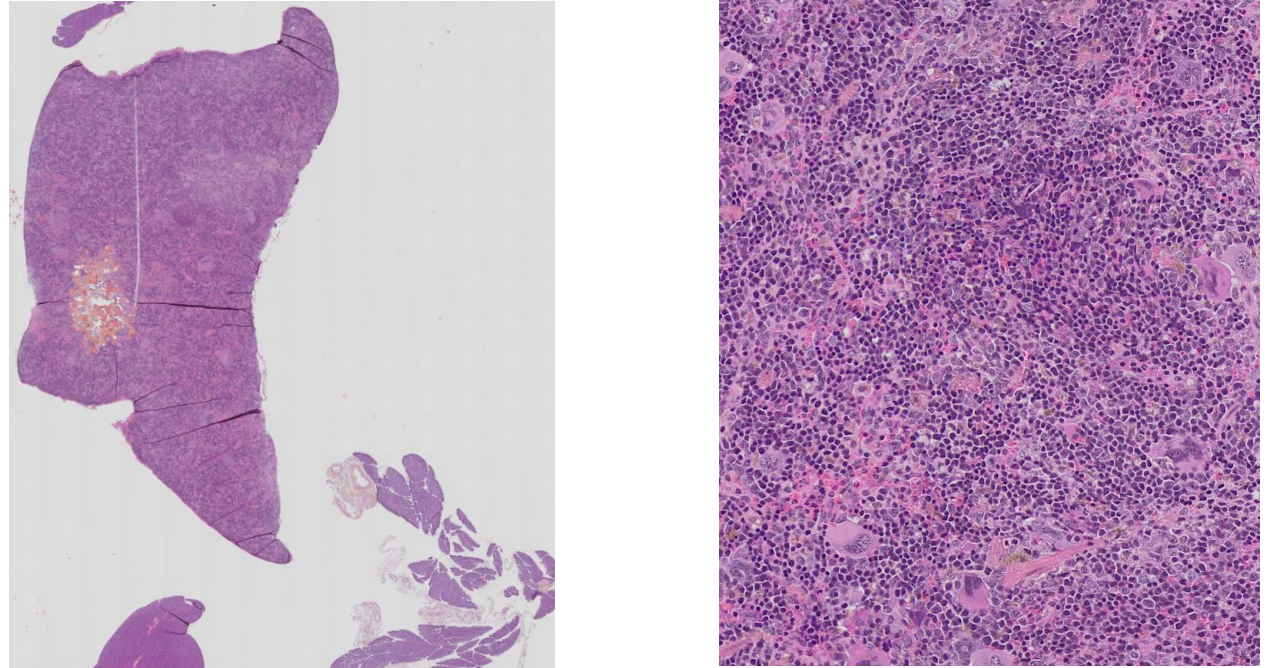
- Pancreas

M25TV (tumor left shoulder)

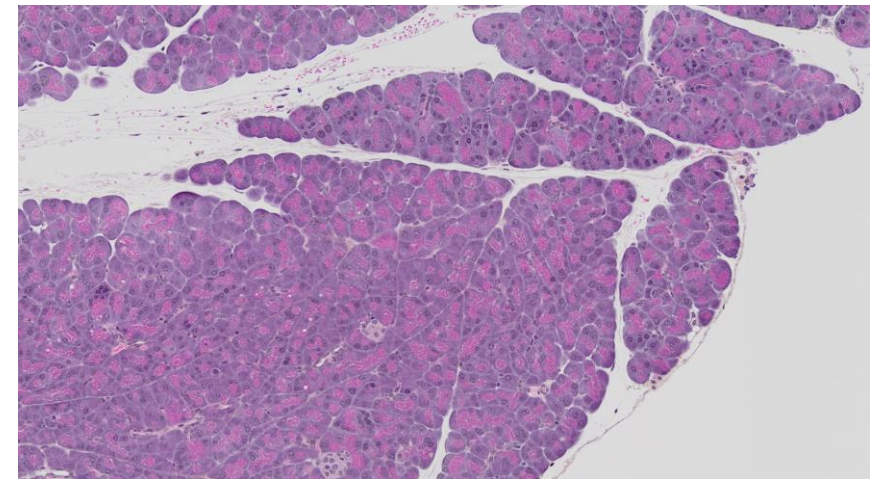


- Massive tumor
- Lymphoid cells
- Large light cells with spotted nuclei

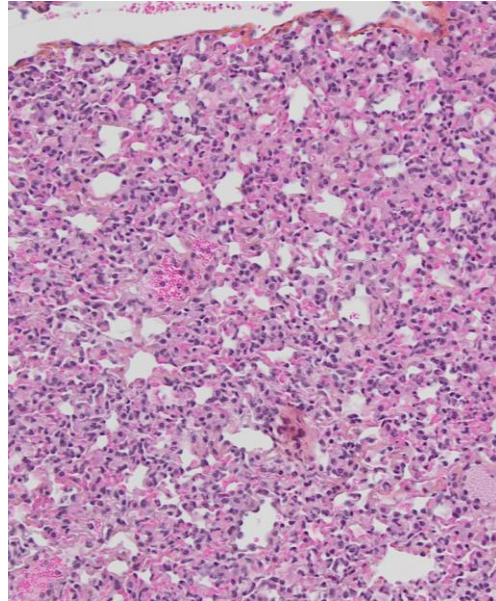
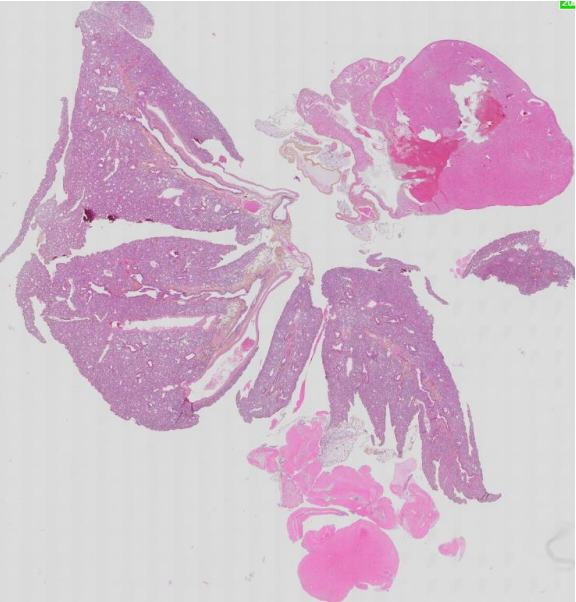
M25MP (spleen and pancreas)



- Spleen with dark defined nuclei and megakaryocytes and red blodspots/vains
- Pancreas looks normal



M25LH (Lungs and heart)



- Lungs look collapsed, might be from the preservation, fill lungs with formalin hereafter
- Lungs look healthy but cell dense

M25TV (tumor left shoulder) - lymphoma

- IHC staining of Ki67, and CD45
- EBER-ISH staining to detect EBV

Mouse

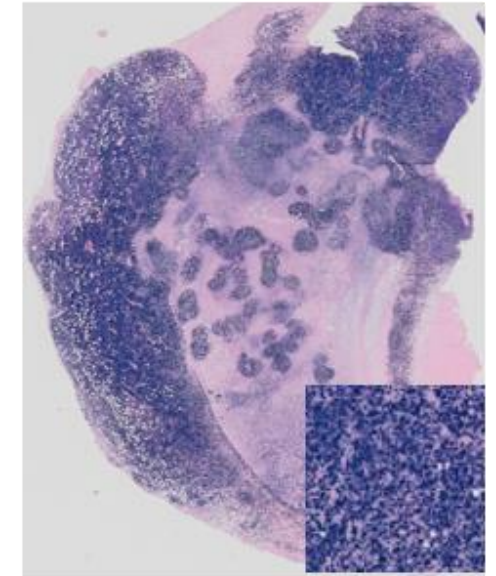
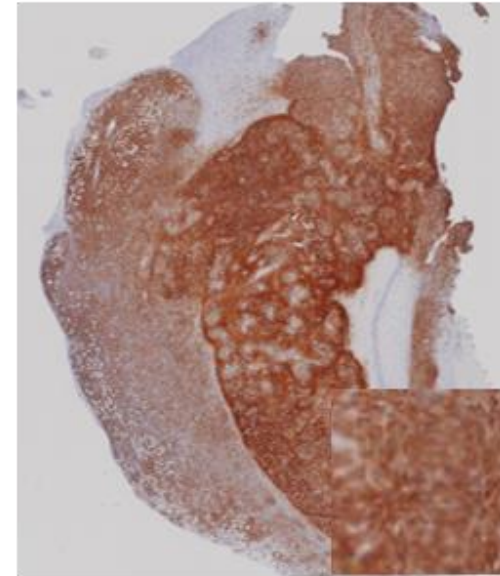
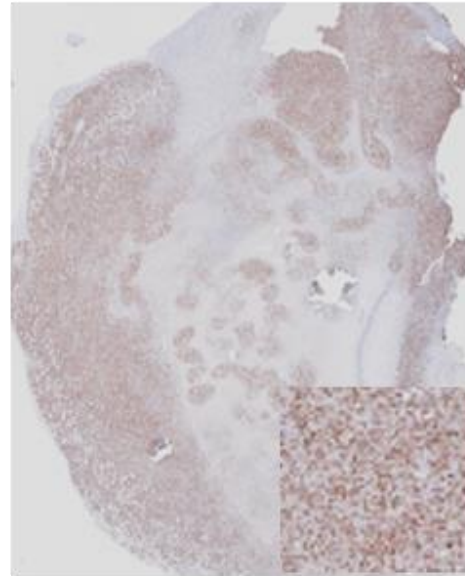
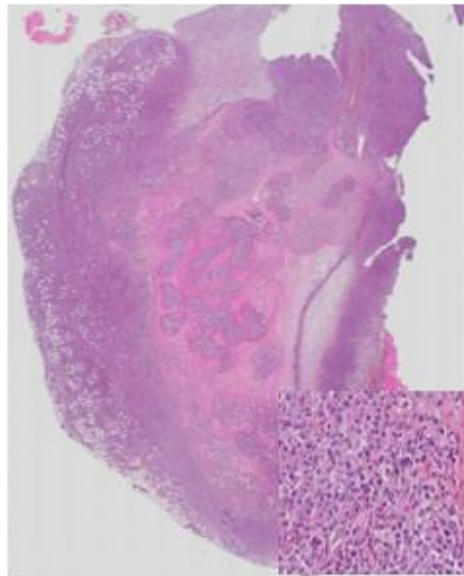
HES

Ki67

CD45

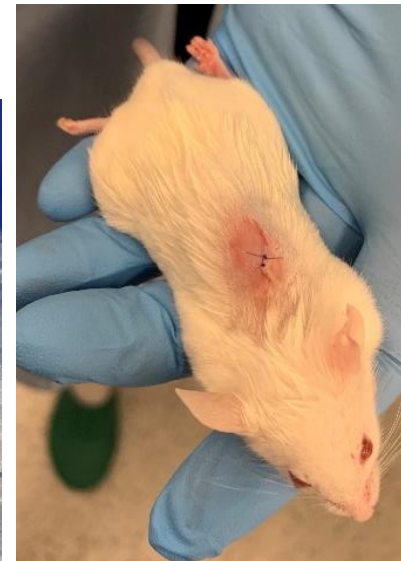
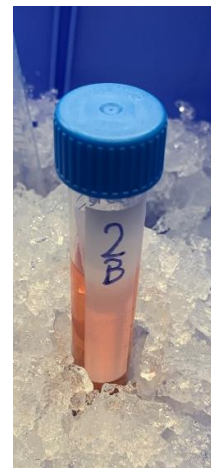
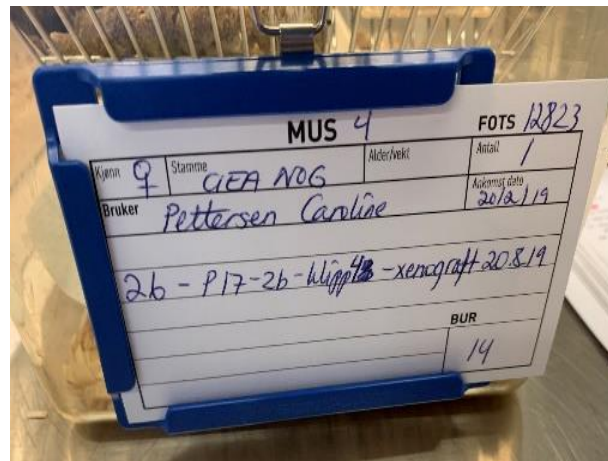
EBER-ISH

#25



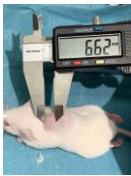
Mouse 26

- Surgery date: 20.08.19
 - Age (weeks) 31
 - Weight (g) 24.4
 - Tumor fragment P17-2B
 - Fragment size 3 x 3 mm
 - Ear mark 4



Supplementary figure 1-26-1. Pictures from the engraftment day

Supplementary figure 1-26-2. Pictures from follow up and tumor size measurement



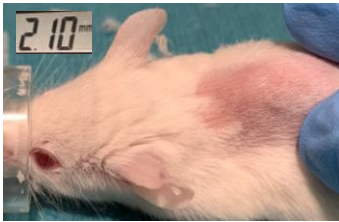
0w + 6d



1w + 6d



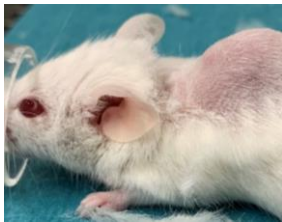
2w + 6d



3w + 5d



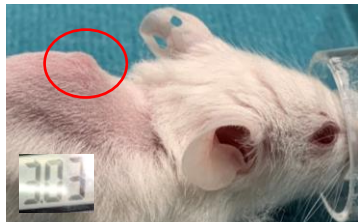
4w + 1d



4w + 6d



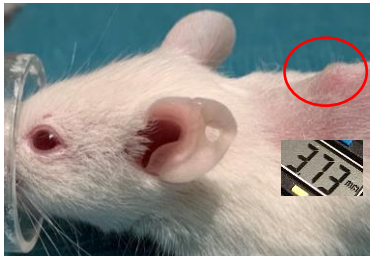
5w + 1d



5w + 6d



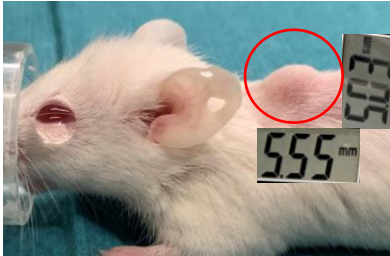
6w + 1d



7w + 0d



7w + 6d



8w + 1d



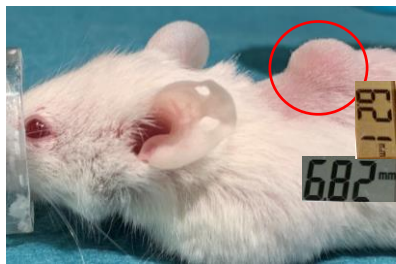
8w + 3d



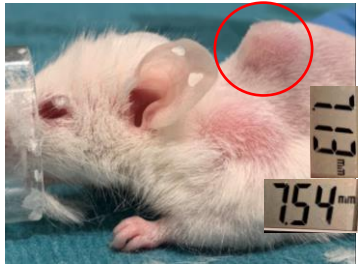
8w + 6d



9w + 2d



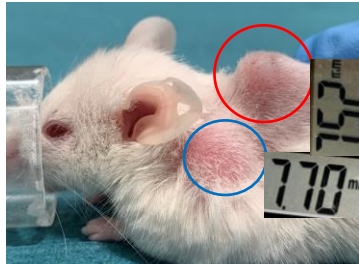
9w + 6d



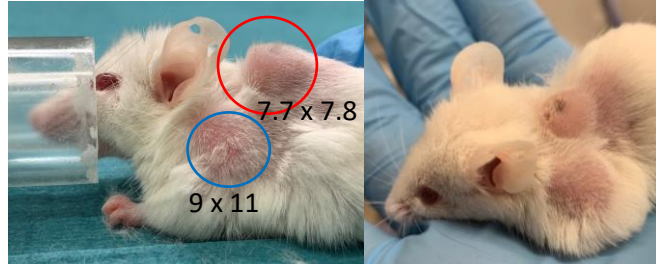
10w + 0d



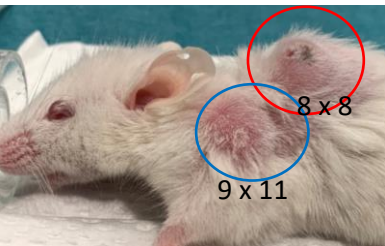
10w + 1d



10w + 3d



10w + 6d



Treatment:

- Smartfish Remune with fish oil
- Days/weeks
- Blood samples before/after treatment

~ OMEGA-3 ~

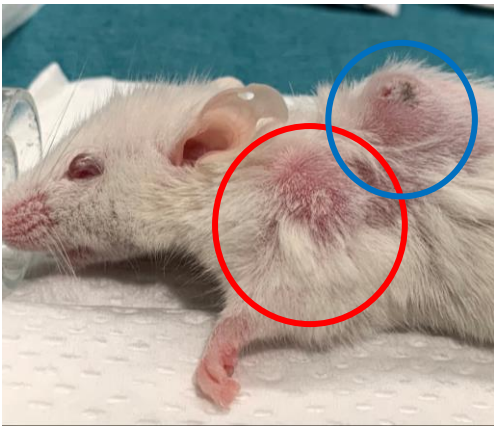
Antall gram per flaske før og etter 7 timer

		Weight (g)		ID mus	ID mus	ID mus
		Start	End			
		08.00	15.00			
	31.07.2019	142,5		26		
	01.08.2019					
	02.08.2019					
14.10	05.08.2019	142,5	129,6	26		
15.10	06.08.2019	138,4	129			
16.10	07.08.2019	142,9	128,1			
17.10	08.08.2019	141,3	125,9	(8 timer)		
18.10	09.08.2019	140,9	137			
21.10	12.08.2019	142,2	133,6	Har slått i 24t		
22.10	13.08.2019					
23.10	14.08.2019	142,2	126,3			
24.10	15.08.2019	142,5	126,7			
	16.08.2019	141,0	128,5			
28	19.08.2019	137,9	130,2			
29	20.08.2019	143,0	126,8			
30/10	21.08.2019	140,9	127,9			
31/10	22.08.2019	140,8	130,1			
1/11	23.08.2019	136,4	124,4			
4.11	26.08.2019	136,0	128,8			
5.11	27.08.2019					

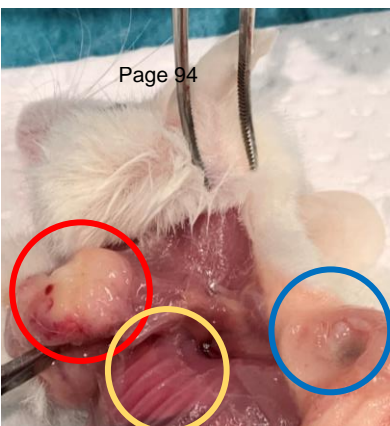
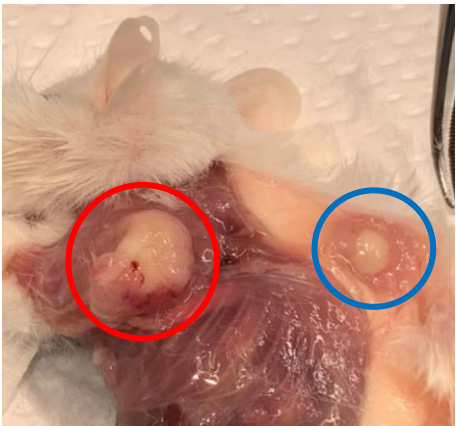
Supplementary figure 1-26-3. List over weight registrations of drinking bottle (with Smartfish Remune Peach) before and after treatment

Supplementary figure 1-26-4.
Pictures from euthanization 04.11.19

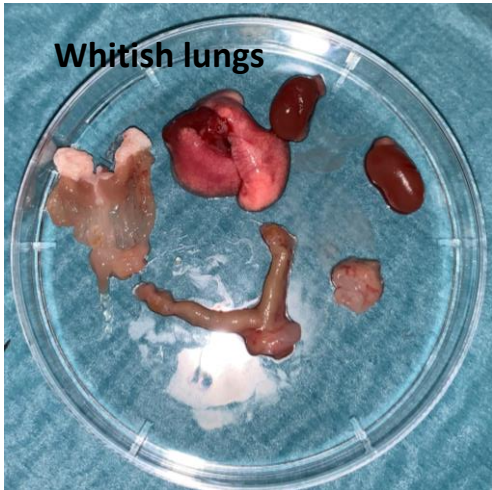
- Necroscopy
 - Xenograft size
 - Secondary tumor left shoulder
 - Secondary tumor right shoulder
 - Blood sample
 - Tumor tissue for
 - Histology
 - RNA isolation
 - Protein isolation



Blue; xenograft, Red; 2nd tumor



Whitish lungs



Whitish lungs



Enlarged spleen (2.2 cm) with white areas. Green; secondary tumor (right shoulder), Red; secondary tumor (left shoulder)



Xenograft

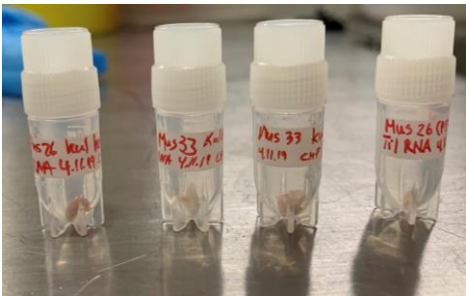
903™ Protein Saver Card
For Research Use Only
Not for use in diagnostic procedures

↑ Tuck Cover Here ↑

Name Mus 26 (P17-26) et al. beha. OMEGA3

Date 04.11.19 CHY-OMEGA3

Bloodcard for fatty acid profiling



Samples collected for histology/HES staining

Supplementary figure 1-26-5. Score sheets

NTNU Score sheet FOTS: Avdeling for komparativ medisin (AKM) Responsible researcher: Pettersen Animal ID: (P17-26) 26 Wipp 4

Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0	20/7	26/8	29/8	2/9	4/9	6/9	9/9	11/9	13/9	16/9	18/9
	Reduced grooming	1											
	Minor distention of abdomen, rough hair coat	3											
	Hunchback or distended abdomen, inactive	18											
Behaviour (Level of activity)	Normal	0											
	Slightly reduced	1											
	Moderately reduced	3											
	Distressed behaviour due to growing tumour	3											
	Obviously reduced	5											
Body weight (Compared to body weight before experiment)	Isolated, inactive, lethargic	18											
	Body weight:		24,6		23,4	23,5	23,8	23,1	24,2	24,9	23,6	23,5	
	No loss	0											
	Loss < 5%	1											
	Loss 5-9%	3											
Clinical signs (Infection, bleeding, discoloration)	Loss 10-14%	5											
	Loss > 15%	18											
	Normal	0											
	Minor irritation around surgical wound	1											
	Moderate irritation/infected surgical wound	3											

0-3: Normal
4-9: Pay attention to health state and consider treatment
10-13: Pay close attention to health state, consider treatment or euthanasia
14-18: Euthanasia *Start treatment with antibiotics. If no effect within 3 days, euthanize the animal

NTNU Score sheet FOTS: Avdeling for komparativ medisin (AKM) Responsible researcher: Pettersen Animal ID: (P17-26) 26 Wipp 4

Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0	20/7	22/7	25/7	30/7	2/10	4/10	8/10	11/10	14/10	15/10	
	Reduced grooming	1											
	Minor distention of abdomen, rough hair coat	3											
	Hunchback or distended abdomen, inactive	18											
Behaviour (Level of activity)	Normal	0											
	Slightly reduced	1											
	Moderately reduced	3											
	Distressed behaviour due to growing tumour	3											
	Obviously reduced	5											
Body weight (Compared to body weight before experiment)	Isolated, inactive, lethargic	18											
	Body weight:		24,2	24,8	23,7	24,7	25,2	24,2	23,8	23,2	23,1	23,3	
	No loss	0											
	Loss < 5%	1											
	Loss 5-9%	3											
Clinical signs (Infection, bleeding, discoloration)	Loss 10-14%	5											
	Loss > 15%	18											
	Normal	0											
	Minor irritation around surgical wound	1											
	Moderate irritation/infected surgical wound	3											

0-3: Normal
4-9: Pay attention to health state and consider treatment
10-13: Pay close attention to health state, consider treatment or euthanasia
14-18: Euthanasia *Start treatment with antibiotics. If no effect within 3 days, euthanize the animal

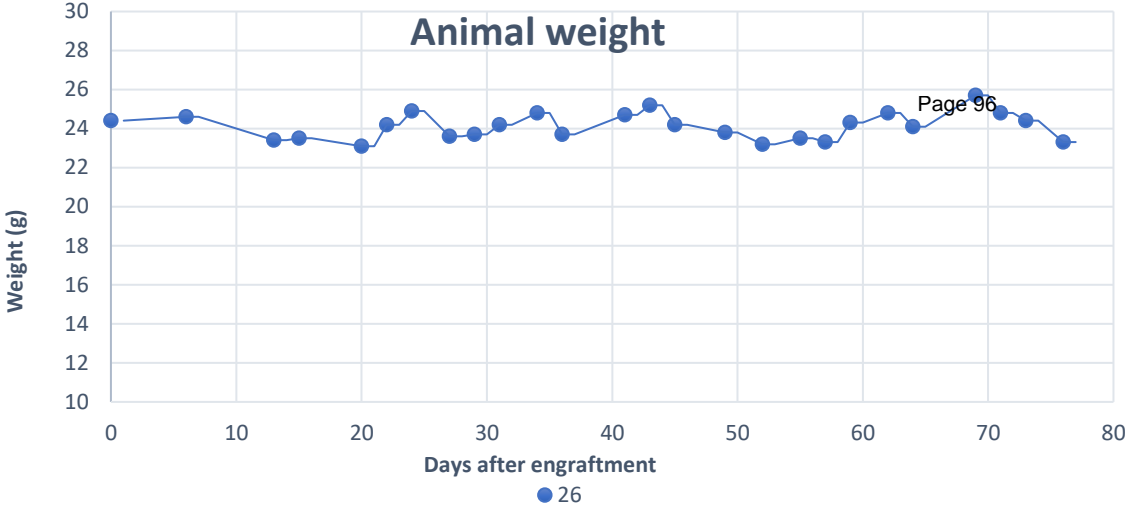
NTNU Score sheet FOTS: Avdeling for komparativ medisin (AKM) Responsible researcher: Pettersen Animal ID: (P17-26) 26 Wipp 4

Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0	16/10	19/10	21/10	23/10	23/10	29/10	29/10	30/10	1/11	8/11	
	Reduced grooming	1											
	Minor distention of abdomen, rough hair coat	3											
	Hunchback or distended abdomen, inactive	18											
Behaviour (Level of activity)	Normal	0											
	Slightly reduced	1											
	Moderately reduced	3											
	Distressed behaviour due to growing tumour	3											
	Obviously reduced	5											
Body weight (Compared to body weight before experiment)	Isolated, inactive, lethargic	18											
	Body weight:		23,3	24,3	24,8	24,1	25,7						
	No loss	0											
	Loss < 5%	1											
	Loss 5-9%	3											
Clinical signs (Infection, bleeding, discoloration)	Loss 10-14%	5											
	Loss > 15%	18											
	Normal	0											
	Minor irritation around surgical wound	1											
	Moderate irritation/infected surgical wound	3											

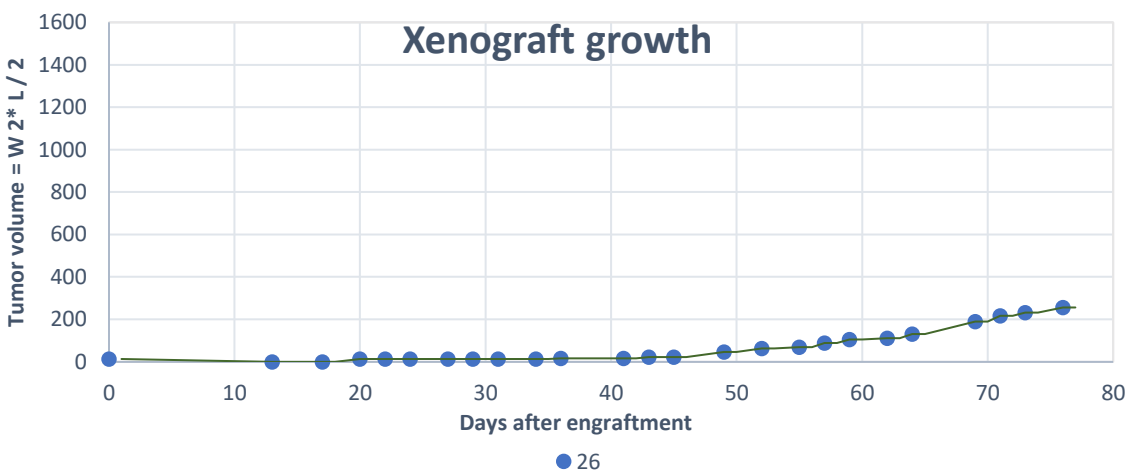
0-3: Normal
4-9: Pay attention to health state and consider treatment
10-13: Pay close attention to health state, consider treatment or euthanasia
14-18: Euthanasia *Start treatment with antibiotics. If no effect within 3 days, euthanize the animal

Supplementary figure 1-26-6.
Mouse, xenograft and
secondary tumor growth
curves

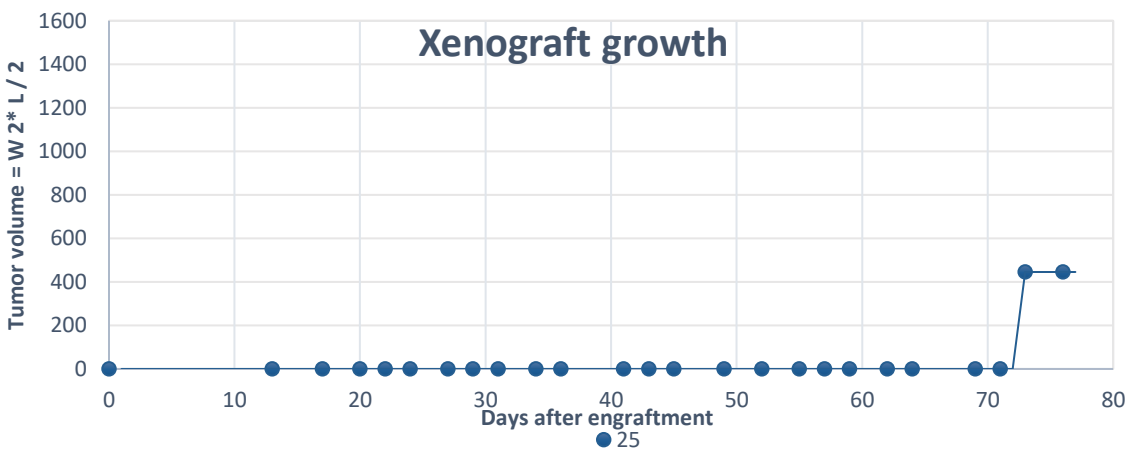
Weight curve



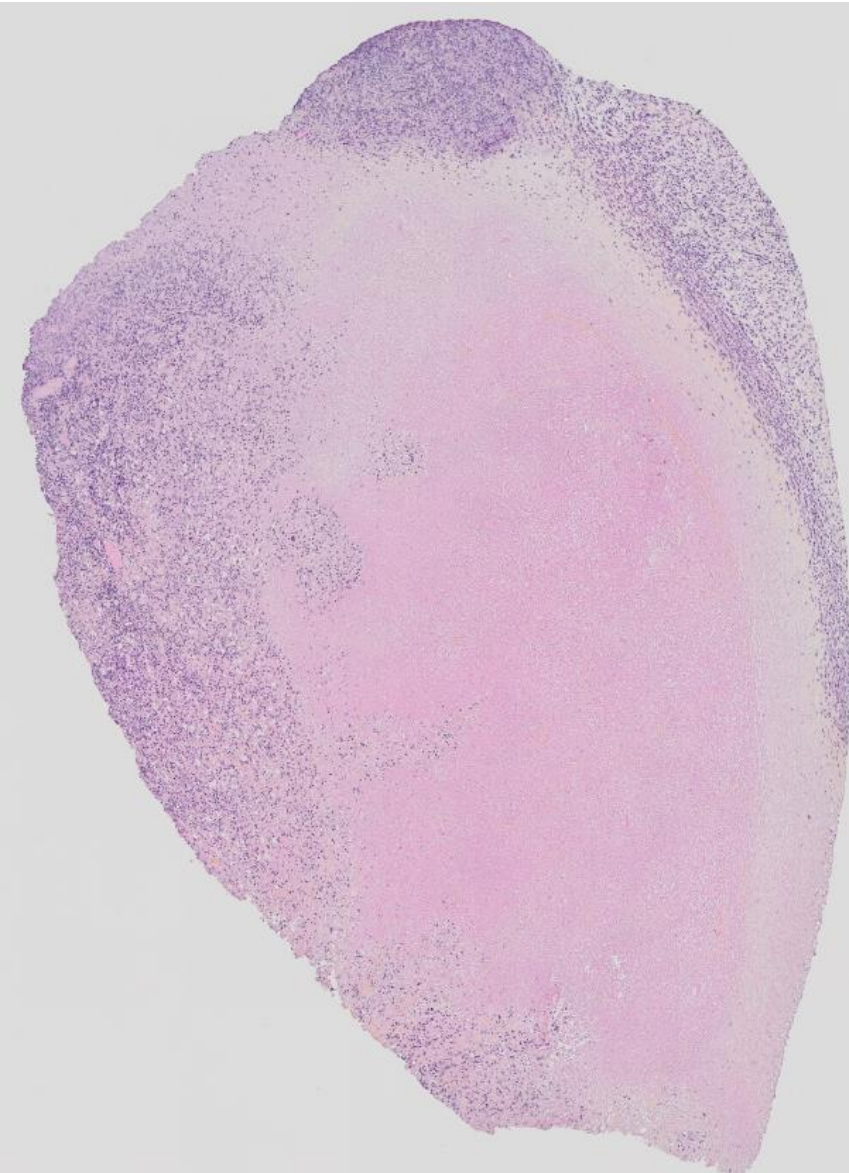
Xenograft growth curve



Secondary tumor growth curve



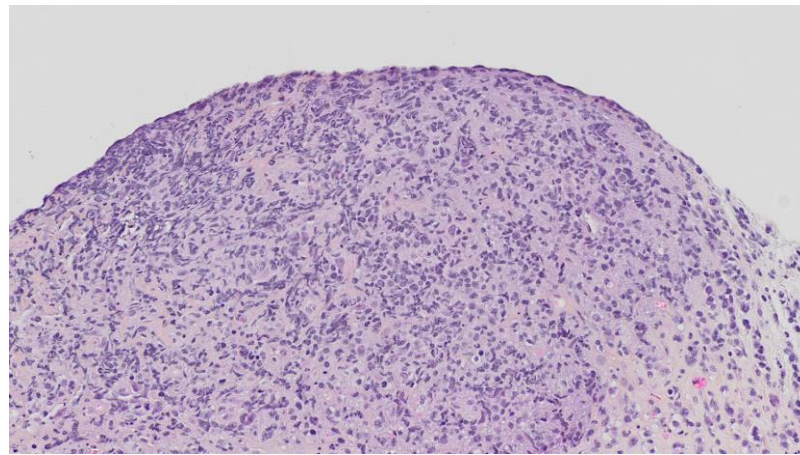
-
- A photograph of a single, irregularly shaped, light brown, translucent object, possibly a piece of wood or bark, resting on a dark, textured surface. The object has a mottled appearance with some darker spots and a slightly rough texture. The background is a dark, greenish-blue material with a fine, pebbled texture.



Mouse 26 X (xenograft)

- HES staining
 - Hematoxylin – blue – nuclear staining
 - Eosin – pink – Extracellular matrix and cytoplasm
 - Safran – yellow – stains collagen fibers/connective tissue
- Large necrotic area in the middle of the xenograft
- Lymphoid tumor cells surrounding the xenograft
- Seems like the lymphoid cells have «strangled» the xenograft

Supplementary figure 1-26-7.
Histology pictures

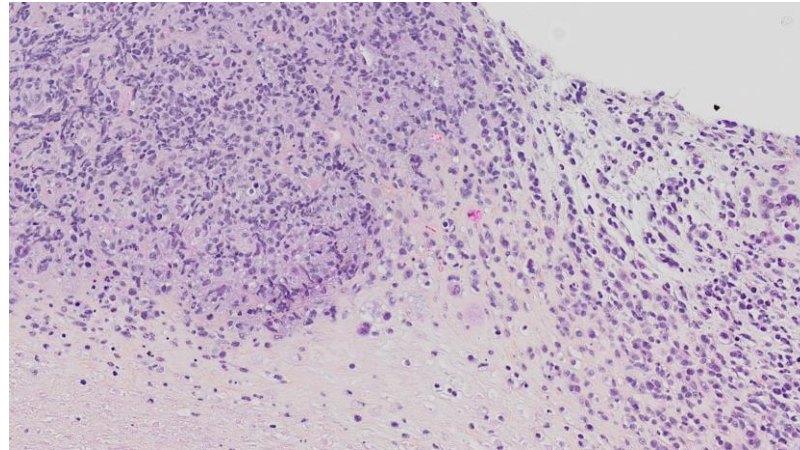


Mouse 26 X (xenograft)

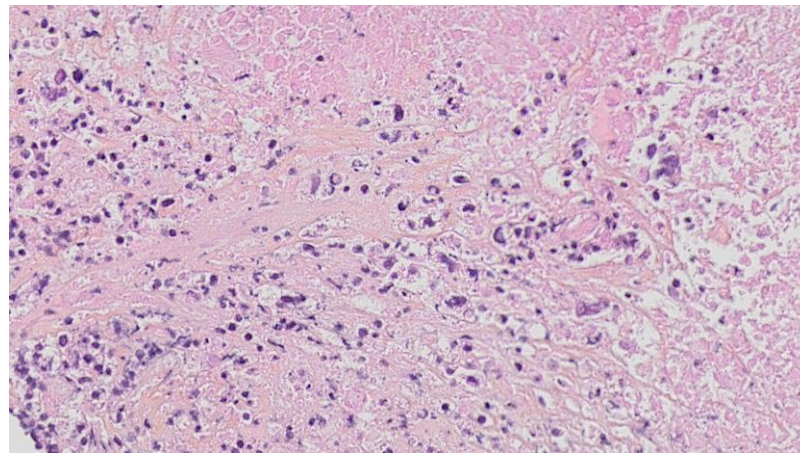
Page 99

Compact tissue with tumor cells

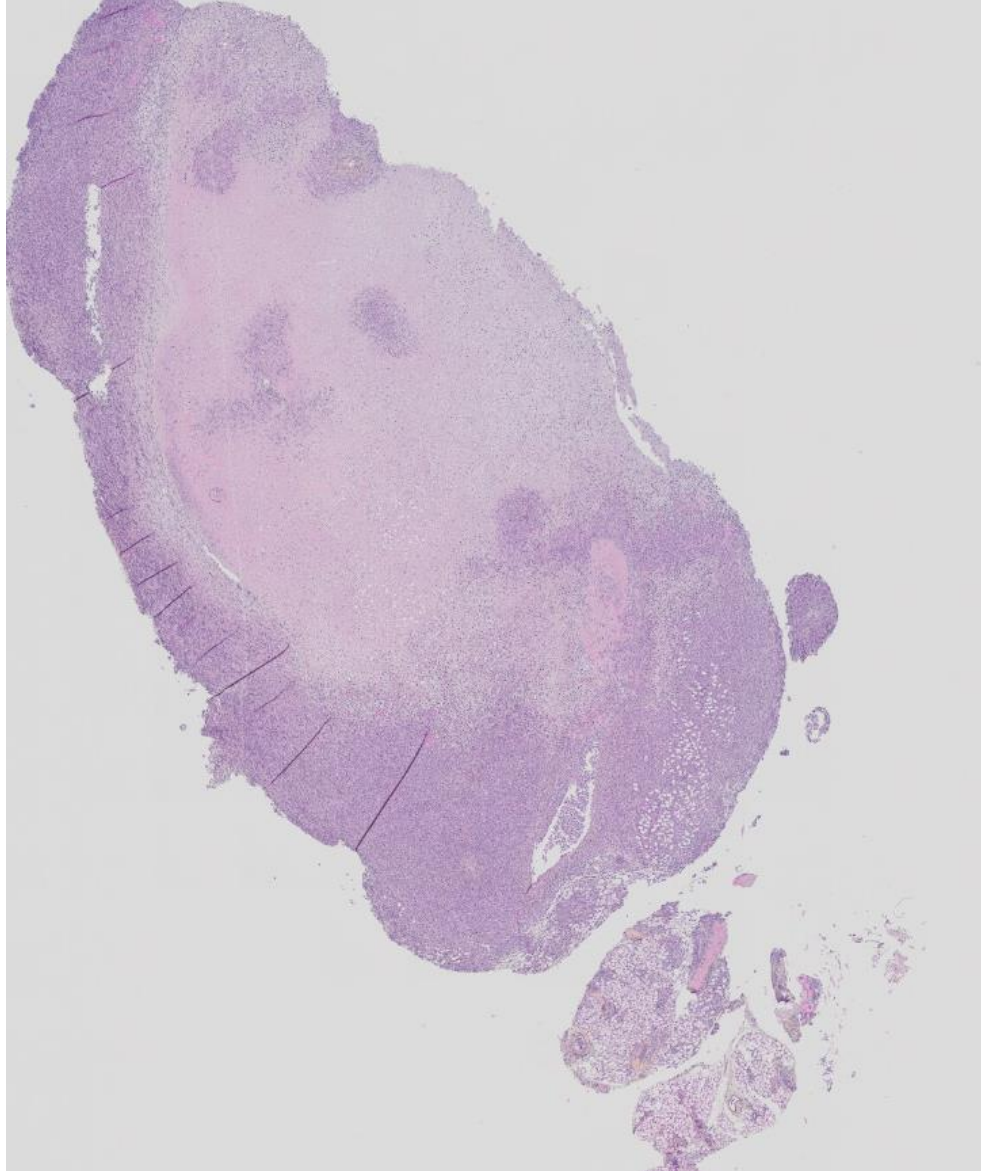
- Some unregular nuclei
- Several mitoses



Border from lymphoid cancer cells to
necrotic tissue

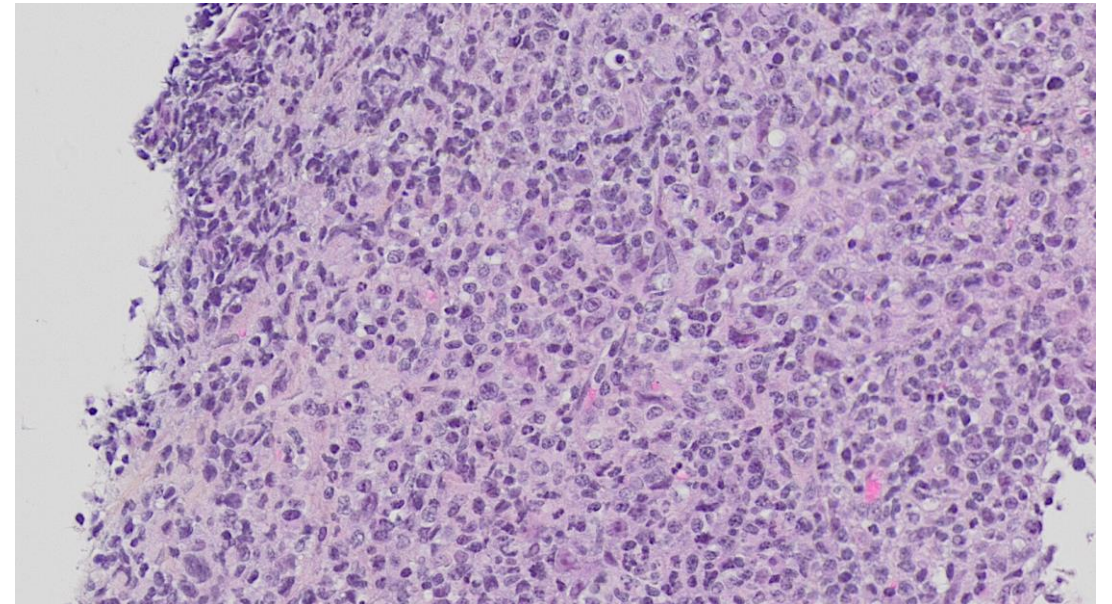


Necrotic tissue



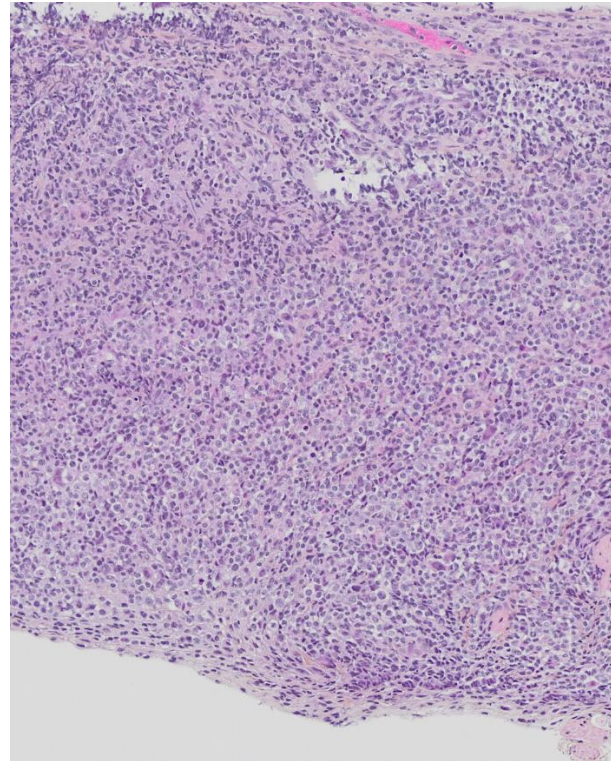
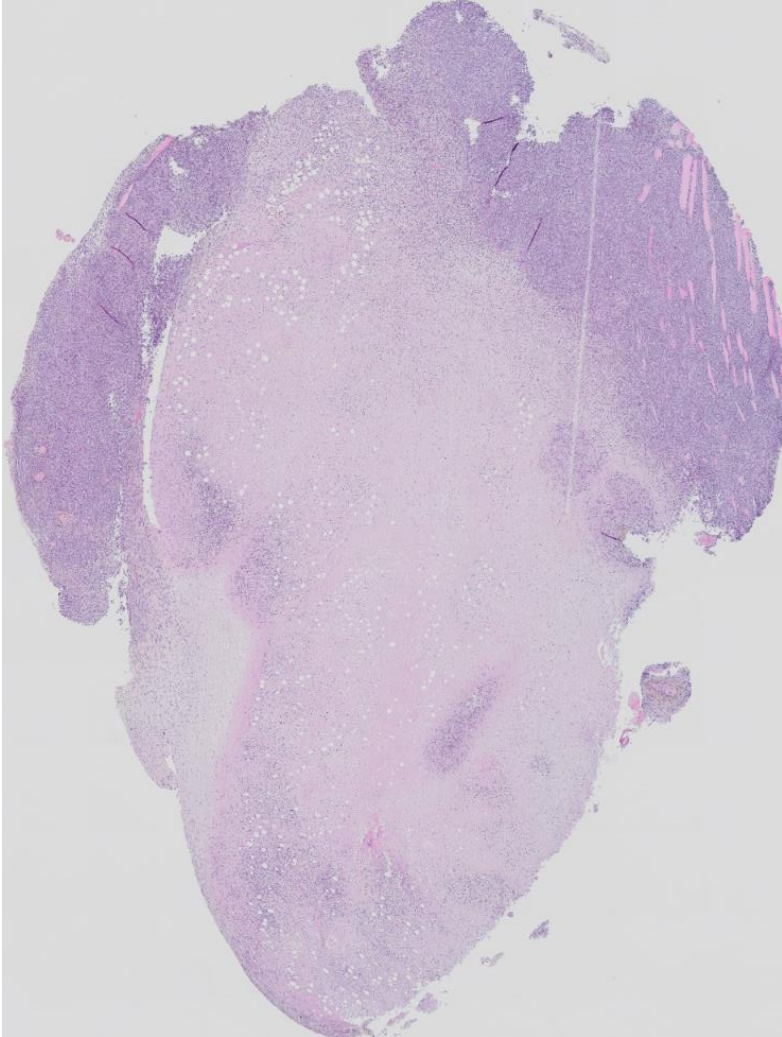
Mouse 26 H (tumor right shoulder)

- Necrotic tissue in the middle
- Lymphoid tumor cells



Mouse 26 V (tumor left shoulder)

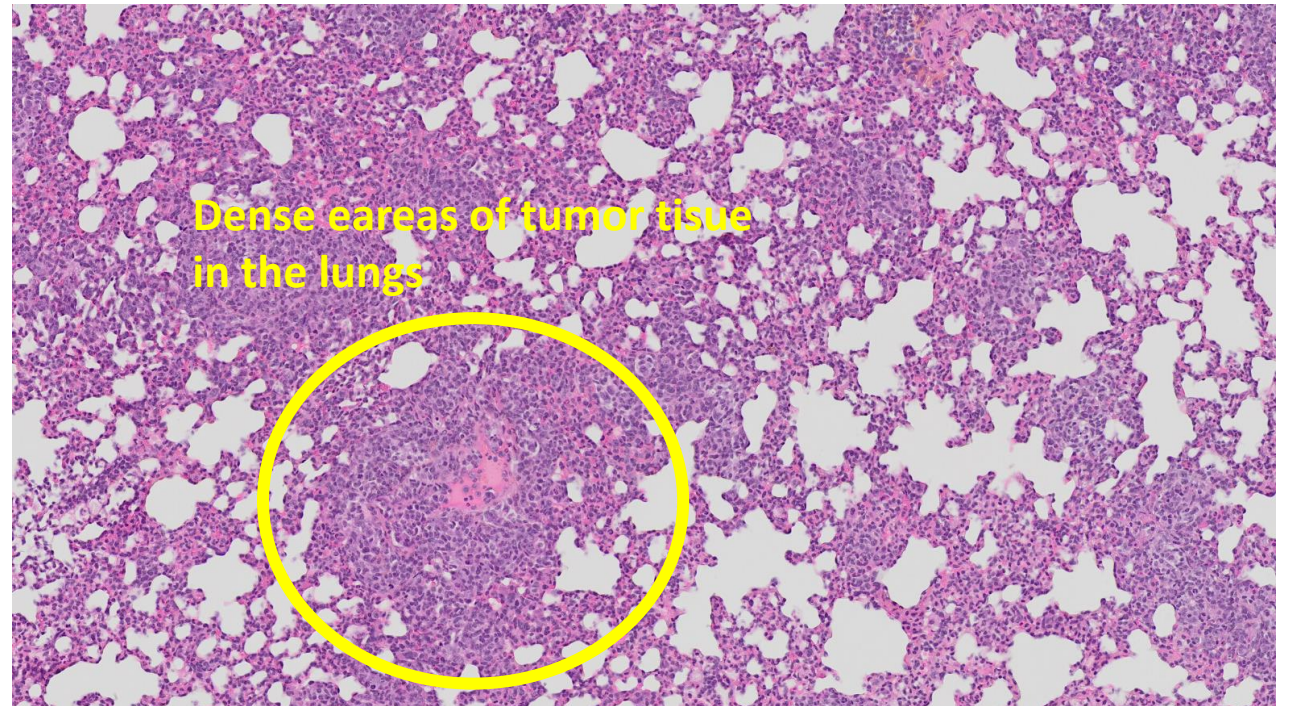
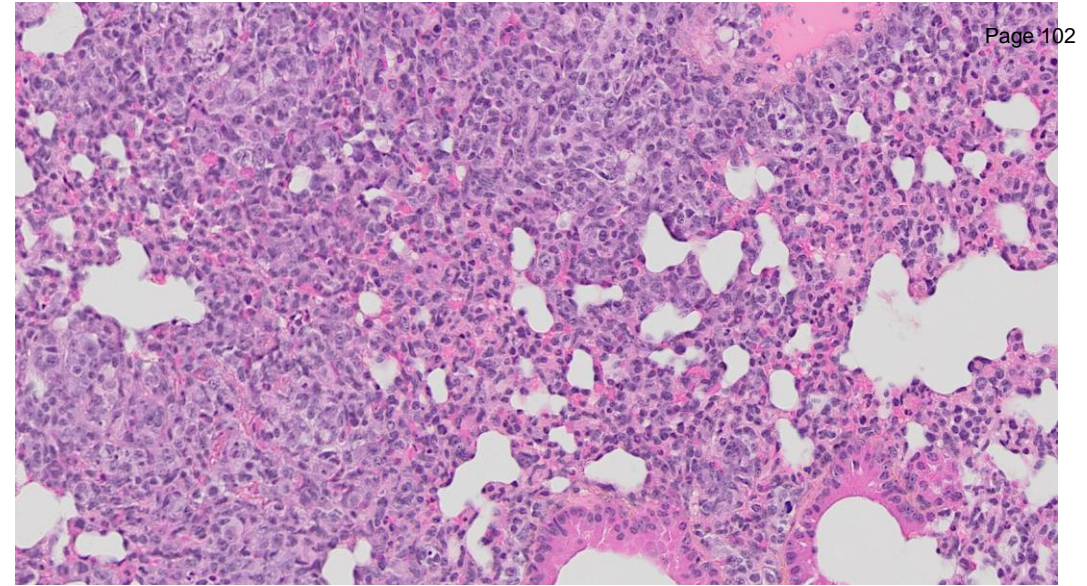
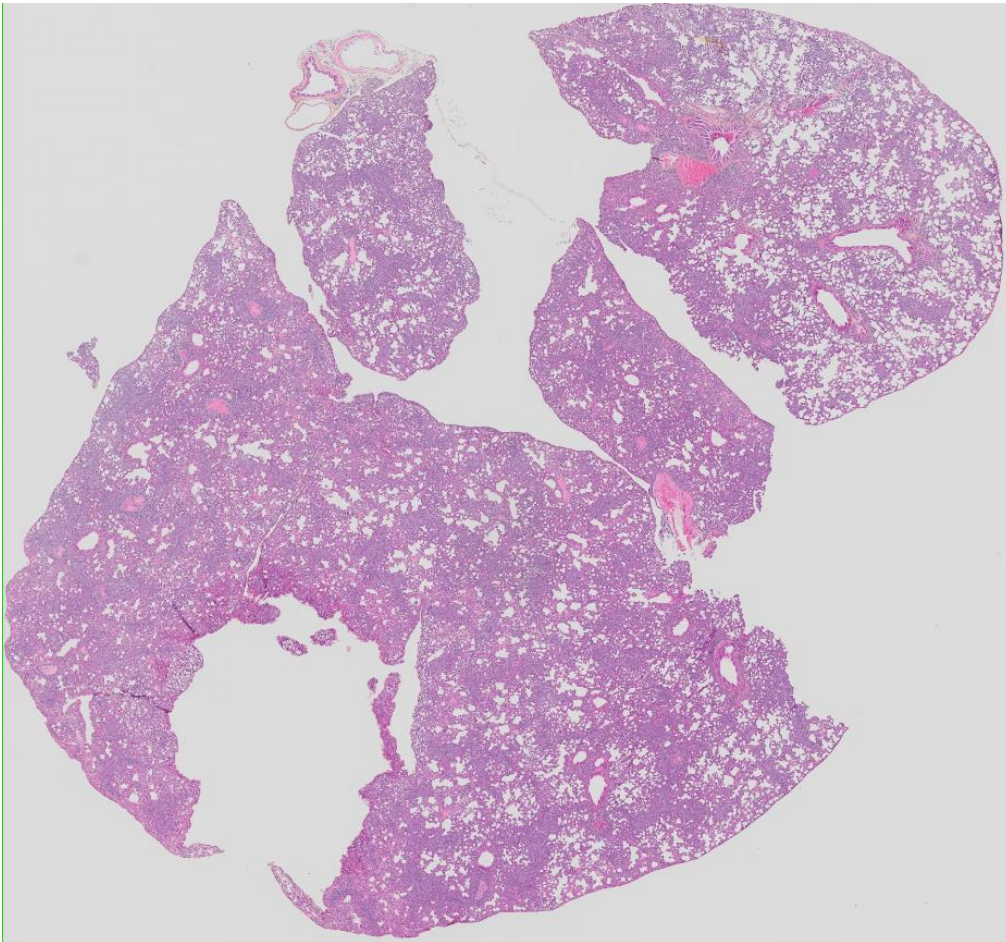
- Lymphoid tumor cells
- Necrosis in the middle



Supplementary figure 1-26-7. Histology pictures

Mouse 26 LH (Lung)

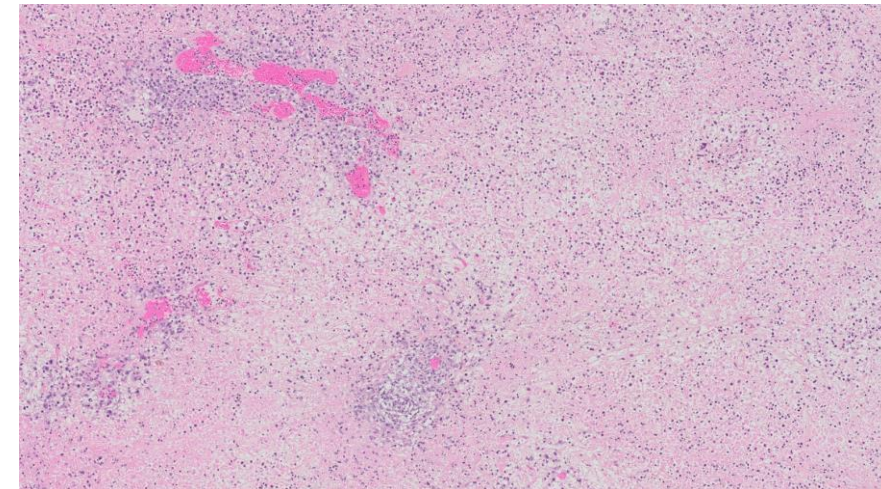
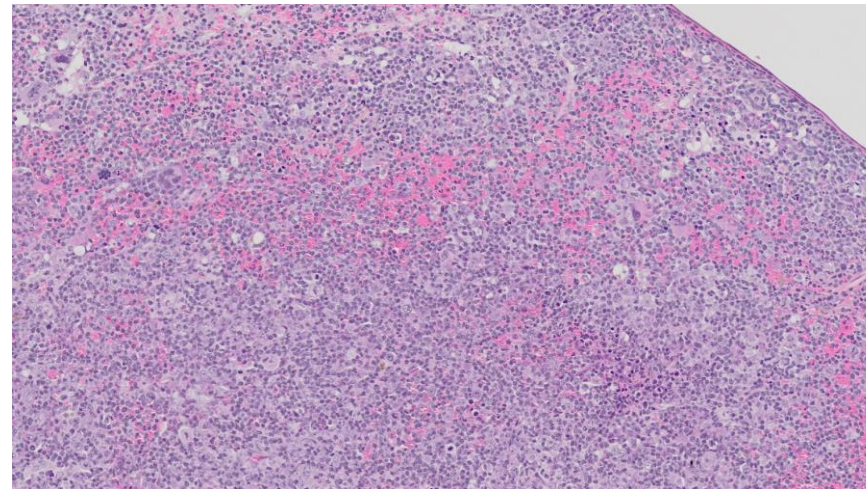
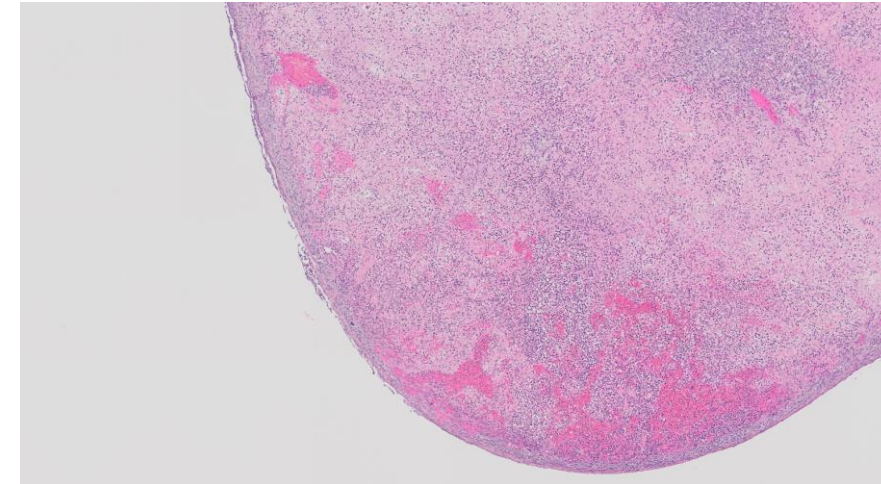
- Dense areas of tumor tissue in the lungs
- Lymphoid tumor cells



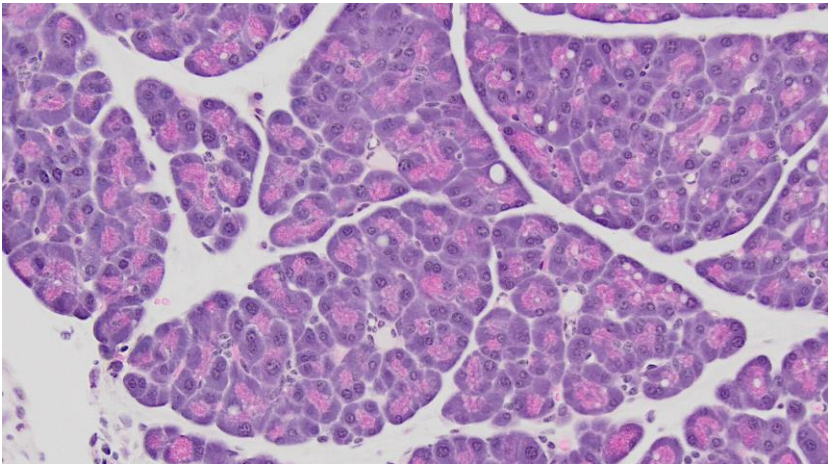


Mouse 26 M (Spleen)

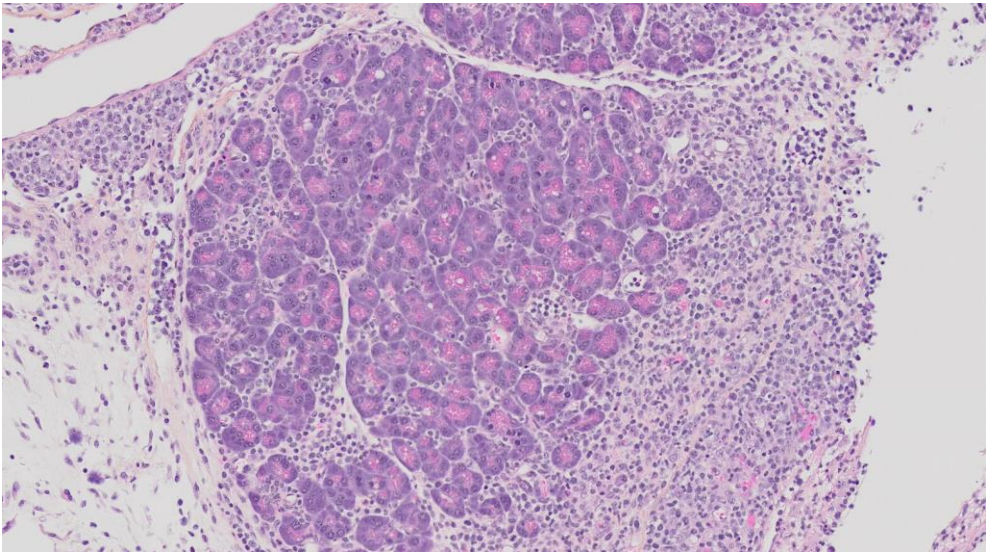
- Large spleen (2.2 cm, ca 3 when not bent)
- Pancreas attached
- White necrotic fields
- Plenty tumor cells in the spleen
- Possible bleedings in the spleen



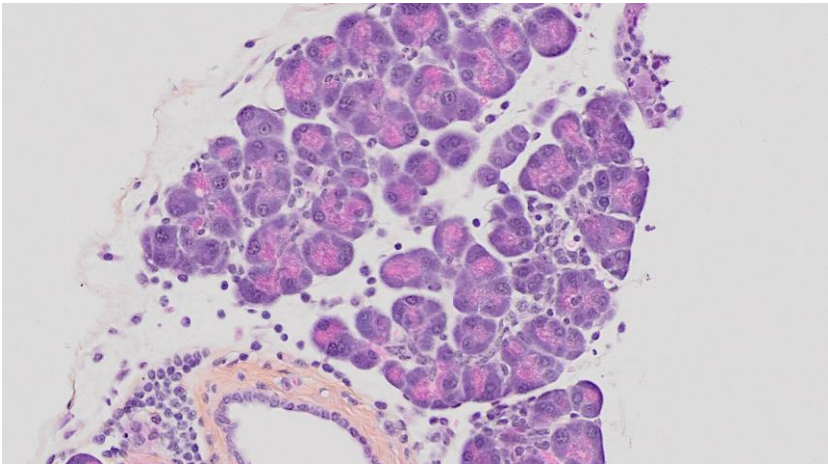
Supplementary figure 1-26-7. Histology pictures



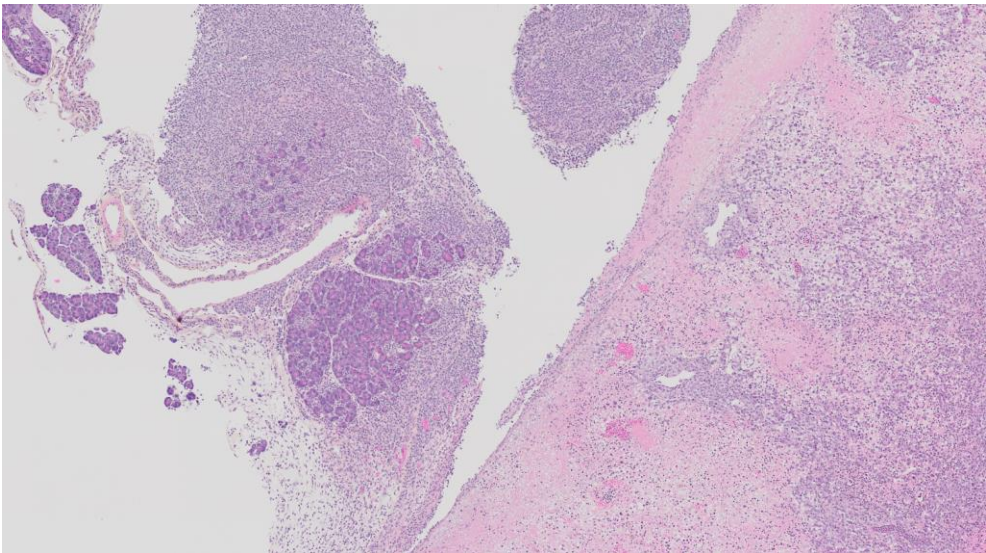
Pancreatic cells



Pancreatic cells infiltrated by tumor cells



Pancreatic cells infiltrated by tumor cells



Passage between the spleen and pancreas

Supplementary figure 1-26-8. Histology and immunohistochemistry pictures of secondary tumor (left)

Page 105

Mouse 26 V (tumor left shoulder)

- Lymphoma
- IHC staining of Ki67 and CD45
- EBER-ISH staining of EBV

Mouse

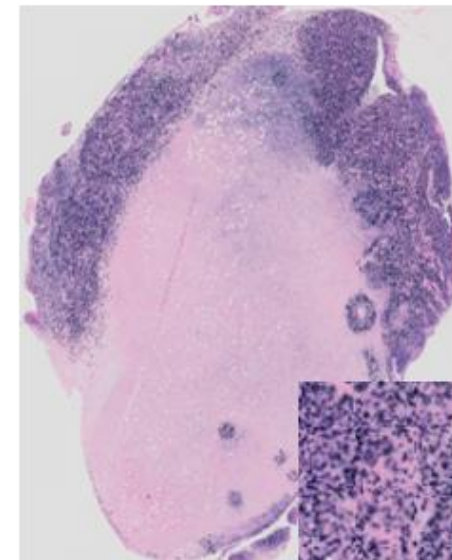
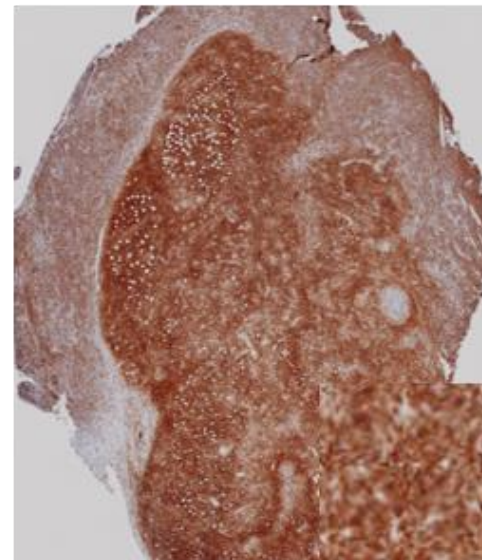
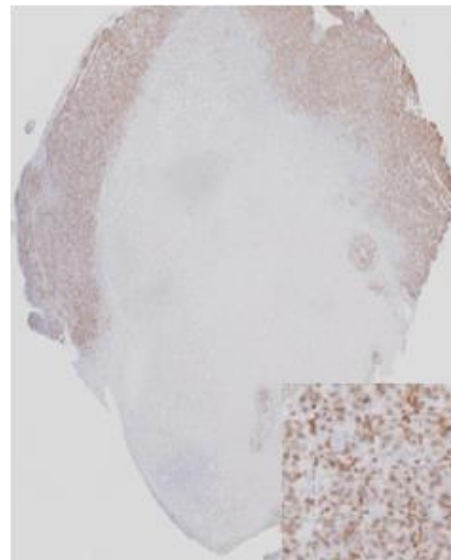
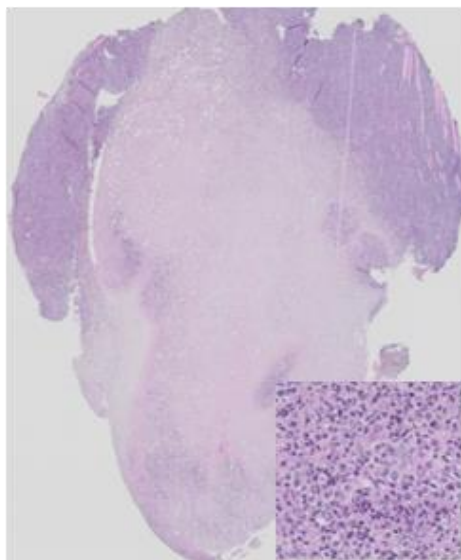
HES

Ki67

CD45

EBER-ISH

#26

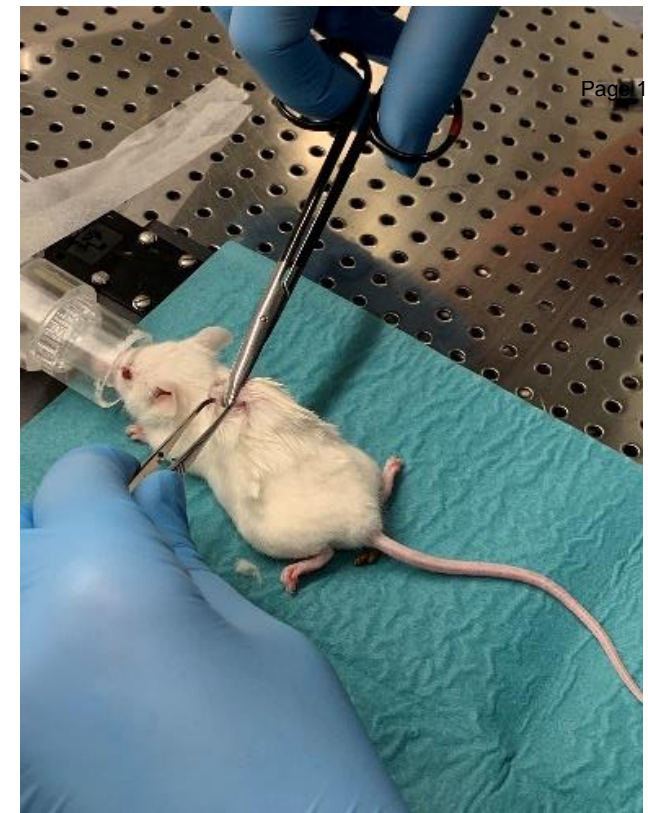
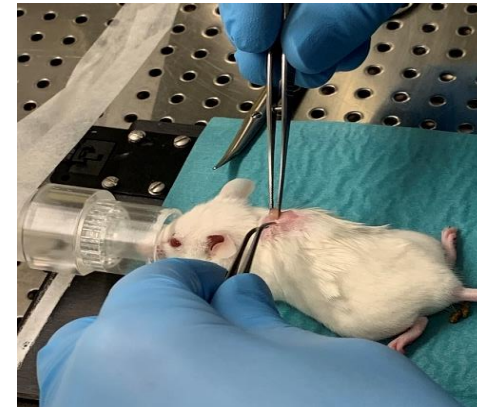
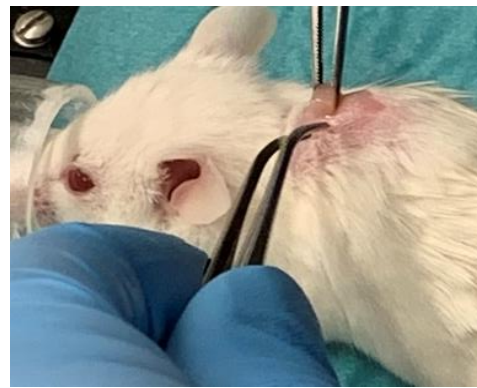


Mouse 27

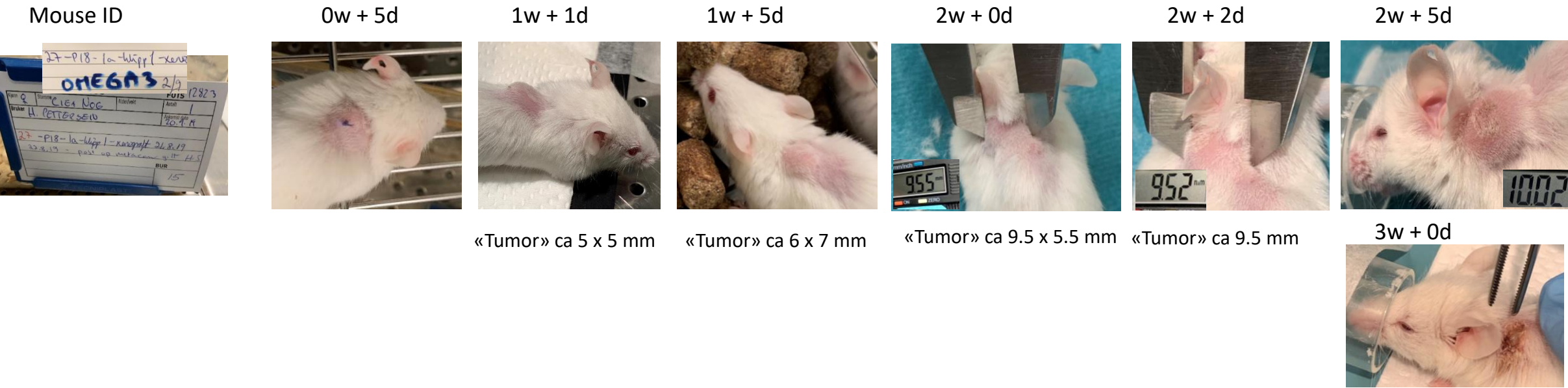
- Surgery date: 21.08.19
 - Age (weeks) 31
 - Weight (g) 22
 - Tumor fragment P18-1a
 - Fragment size 3 x 3
 - Ear mark 1

Supplementary figure 1-27-1.

Pictures from the engraftment day



Supplementary figure 1-27-2. Pictures from follow up and xenograft size measurement



Treatment:

- Smartfish Remune with fish oil
- Blodsamples taken before and after treatment

MUS			FOTS 12823
Kjønn ♀	Stamme CIEA M08	Alder/vekt	Antall 2 Page 108
Bruker Pettersen Caroline H			Ankomst dato 20.9.19
27-P18-1a-hipp(1)-xerografi 21.8.19			
29-P18-2a-hipp(3)-xerografi 21.8.19			
OMEGA 3 2/9			BUR
			15

~ OMEGA - 3 ~

30.08.2019			
02.09.2019	142,4g	131,3g	(27)
03.09.2019	142,8g	131,8g	
04.09.2019	144,5	133,9	(29)
05.09.2019	141,2	128,3	
06.09.2019	141,2	vekt?	
09.09.2019	141,2		
10.09.2019	140,7	128,0	
11.09.2019	141,4		avlivet
12.09.2019			

Supplementary figure 1-27-3. List over weight registrations of the drinking bottle (with Smartfish Remune Peach) before and after provided to the mice

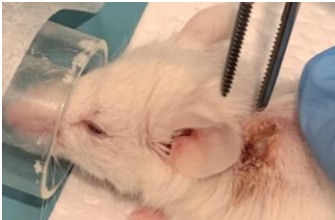
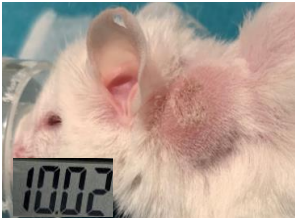
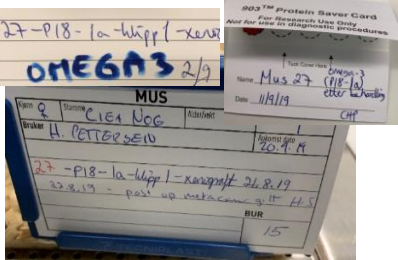
Supplementary figure 1-27-4. Pictures from euthanization (11.09.19)

- Not the xenograft, but an abscess that was growing

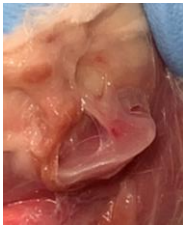
Mus ID

19 dager post op

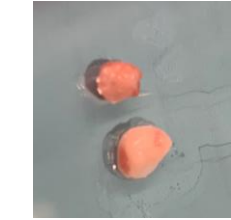
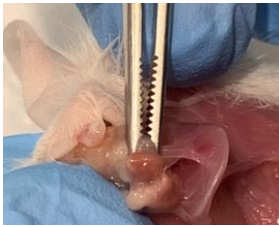
21 dager/avliving



Scurvy wound, the «tumor» has burst. Turned out it was an abscess and not the xenograft growing.



Small xenograft under the skin



The largest fragment was divided into the 3 sample tubes, and the smallest fragment in a «left over» tube.

Supplementary figure 1-27-5. Score sheet

NTNU

Score sheet FOTS:
Avdeling for komparativ medisin (AKM)

Responsible researcher:
Petterson

Animal ID:
(P18-1a) 27
Wipr 1

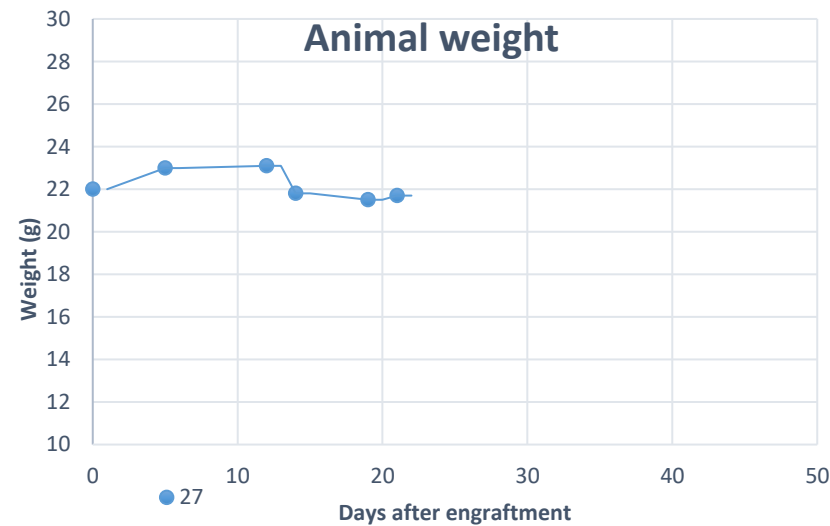
Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0	21/8	24/8	29/8	2/9	4/9	6/9	9/9	11/9		
	Reduced grooming	1										
	Minor distention of abdomen, rough hair coat	3										
	Hunchback or distended abdomen, inactive	18										
Behaviour (Level of activity)	Normal	0										
	Slightly reduced	1										
	Moderately reduced	3										
	Distressed behaviour due to growing tumour	3										
	Obviously reduced	5										
	Isolated, inactive, lethargic	18										
Body weight (Compared to body weight before experiment)	Body weight:		23	2	23,1g	21,8		21,5	21,7			
	No loss	0										
	Loss < 5%	1										
	Loss 5-9 %	3										
	Loss 10-14%	5										
	Loss ≥ 15%	18										
Clinical signs (Infection, bleeding, discoloration)	Normal	0										
	Minor irritation around surgical wound	1										
	Moderate irritation/infected surgical wound	3										
	Infected/open surgical wound	4 *										
	Tumour > 1,0 cm in diameter	10										
	Tumour > 1,5 cm in diameter	18										
	Ulcerous tumour	18										
Total:												
Comments, treatments etc:												

0-3: Normal
4-9: Pay attention to health state and consider treatment
10-13: Pay close attention to health state, consider treatment or euthanasia
14-18: Euthanasia *Start treatment with antibiotics. If no effect within 3 days, euthanize the animal

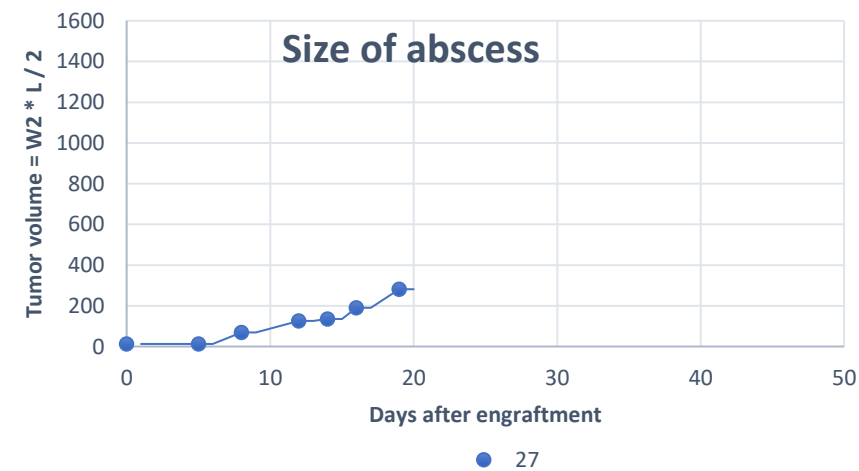
Abscess mistaken for rapidly growing xenograft

Supplementary figure 1-27-6.
Mouse and abscess growth curves

Weight curve

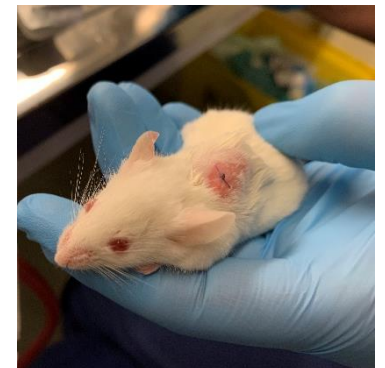


Size of abscess



Mouse 28

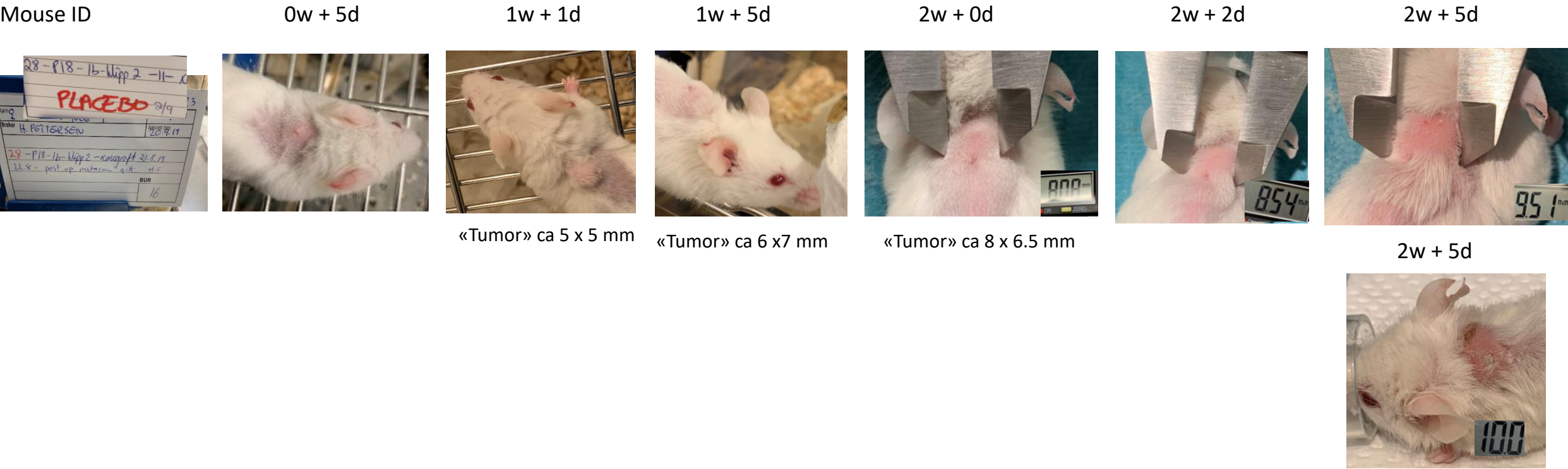
- Surgery date: 21.08.19
 - Age (weeks) 31
 - Weight (g) 22.6
 - Tumor fragment P18-1b
 - Fragment size 3 x 3 mm
 - Ear mark 2



Supplementary figure 1-28-1.

Pictures from the engraftment day

Supplementary figure 1-28-2. Pictures from follow up and xenograft size measurement



Treatment:

- Placebo (Smartfish Remune with Rapseed oil)
- Blodsamples taken before and after treatment

~PLACEBO~

30.08.2019			
02.09.2019	145,1g	138,1	28
03.09.2019	141,5g	129,2	
04.09.2019	145,9	134,9	
05.09.2019	147,8	135,5	
06.09.2019	142,2	128,5	
09.09.2019	146,4		
10.09.2019	146,4	132,3	
11.09.2019	142,4		active
12.09.2019			
13.09.2019			

MUS		FOTS	
Kønn	Stamme	Alder/vekt	Antall
♀	C10A MG		1
Bruker		Ankomst dato	
		20.1.19	
28-P18-1b-klipp 2 -11- Kongsrødt 21818			
PLACEBO 2/9		BUR	
		16	

Supplementary figure 1-28-3. List over weight registrations of the drinking bottle (with placebo) before and after provided to the mice

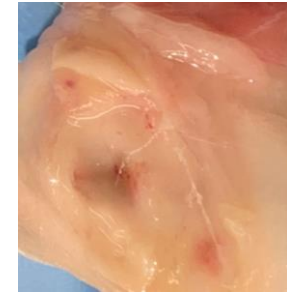
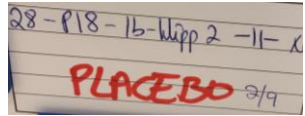
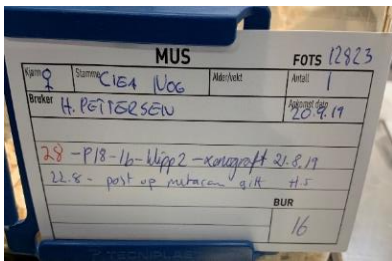
Supplementary figure 1-28-4. Pictures from euthanization (11.09.19)

- Not xenograft but an abscess growing
- Euthanized due to two other mice with bursting abscesses (mouse 27 and 29)

Mus ID

19 dager post op

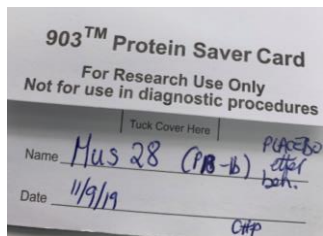
21 dager/avliving



Brown fields/scurvy forming
on the skin over the «tumor»
(abscess)

Green abscess. Green liquid coming out when pinched. Clearly not the xenograft.

Almost no xenograft visible,
nothing to sample



Supplementary figure 1-28-5. Score sheet

NTNU

Score sheet FOTS:
Avdeling for komparativ medisin (AKM)

Responsible researcher:
Petterson

Animal ID:
(P18-16) 28 W181 2

Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0	2/8	26/8	29/8	2/9	4/9	6/9	9/9	11/9		
	Reduced grooming	1										
	Minor distention of abdomen, rough hair coat	3										
	Hunchback or distended abdomen, inactive	18										
Behaviour (Level of activity)	Normal	0										
	Slightly reduced	1										
	Moderately reduced	3										
	Distressed behaviour due to growing tumour	3										
	Obviously reduced	5										
	Isolated, inactive, lethargic	18										
Body weight (Compared to body weight before experiment)	Body weight:			23,2	23,7	23,4	23,0		23,5	22,9		
	No loss	0										
	Loss < 5%	1										
	Loss 5-9%	3										
	Loss 10-14%	5										
	Loss ≥ 15%	18										
Clinical signs (Infection, bleeding, discoloration)	Normal	0										
	Minor irritation around surgical wound	1	Swiff inn	Har fort	Ser	Ser			Start	start		
	Moderate irritation/infected surgical wound	3	4x3x3	3x3x3	5x5x3	5x5x3			2x5	2x5		
	Infected/open surgical wound	4*	0,5x1	0,5x1	0,5x1	0,5x1			7x5	7x5		
	Tumour > 1,0 cm in diameter	10	5,3	5,3	5,3	5,3			10	10		
	Tumour > 1,5 cm in diameter	18										
	Ulcerous tumour	18										
Total:												
Comments, treatments etc:												

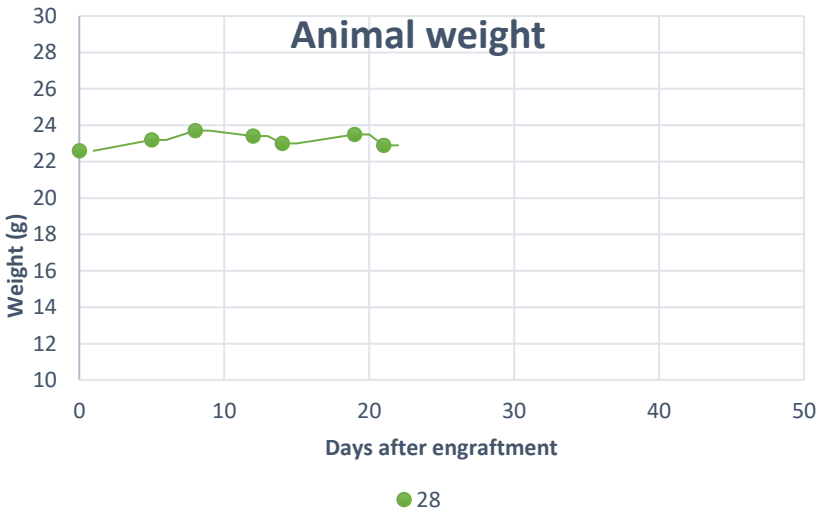
0-3: Normal
4-9: Pay attention to health state and consider treatment
10-13: Pay close attention to health state, consider treatment or euthanasia
14-18: Euthanasia *Start treatment with antibiotics. If no effect within 3 days, euthanize the animal

Swiff inn
Har fort
Ser
Ser
Start
start
2x5
2x5
7x5
7x5
10
10
5,3
5,3
5,3
5,3
10
10
9,5
7

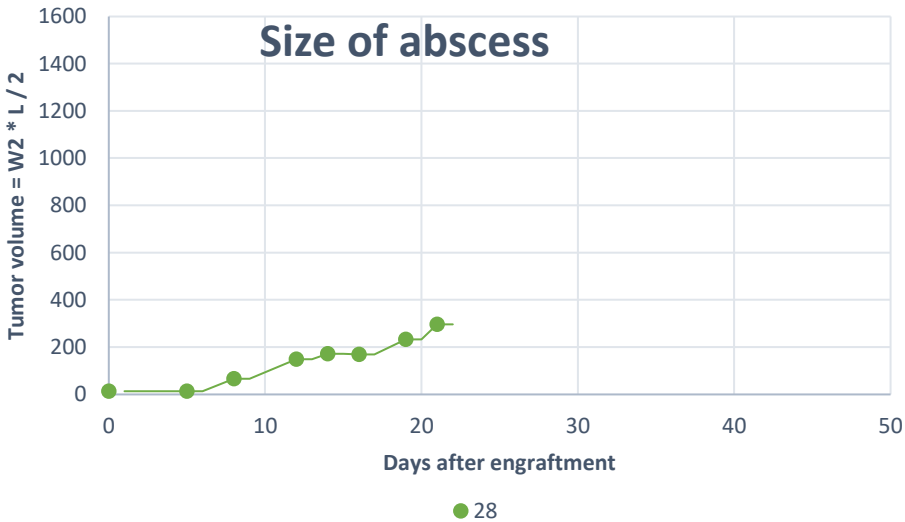
Note: numbers represent abscess size, not tumor growth.

Supplementary figure 1-28-6.
Mouse and abscess growth curve

Weight curve

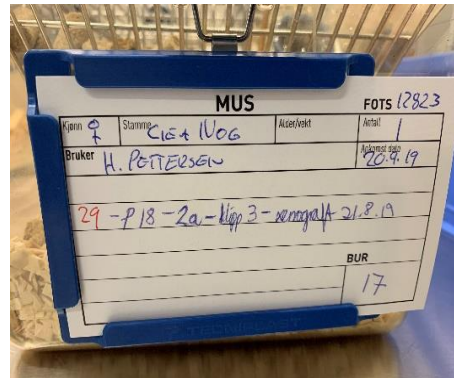


Size of abscess



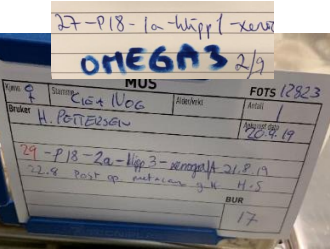

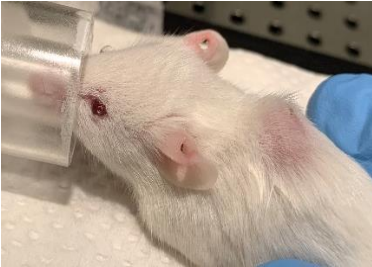

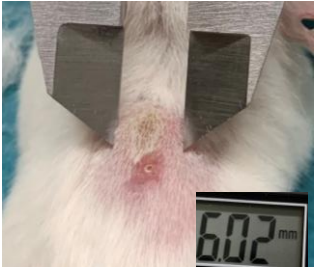
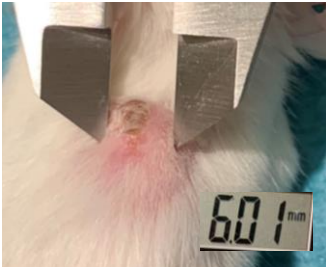
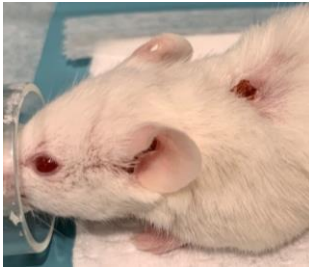
Mouse 29

- Surgery date: 21.08.19
 - Age (weeks) 31
 - Weight (g) 22.82
 - Tumor fragment P18-2a
 - Fragment size 3 x 3 mm
 - Ear mark 3
 - One stitch was opened by the mouse after 1 hour. Restitched.



Supplementary figure 1-29-1. Pictures from the engraftment day

Pictures from follow up

Mouse ID	0w + 5d	1w + 1d	1w + 5d	2w + 0d	2w + 2d	2w + 5d
						
		«tumor» ca 5 x 5 mm	«Tumor» ca 5 x 5 mm	«Tumor» ca 6 x 5,5 mm	«Tumor» ca 6 mm	Wound with «crater»

Treatment:

- Smartfish Remune with fishoil
- Blodsamples before/after

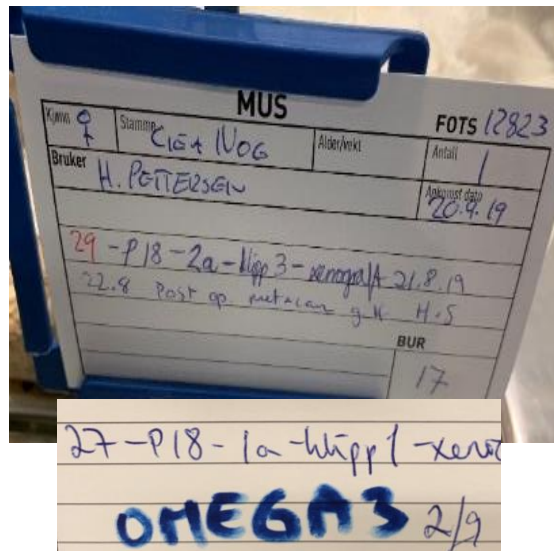
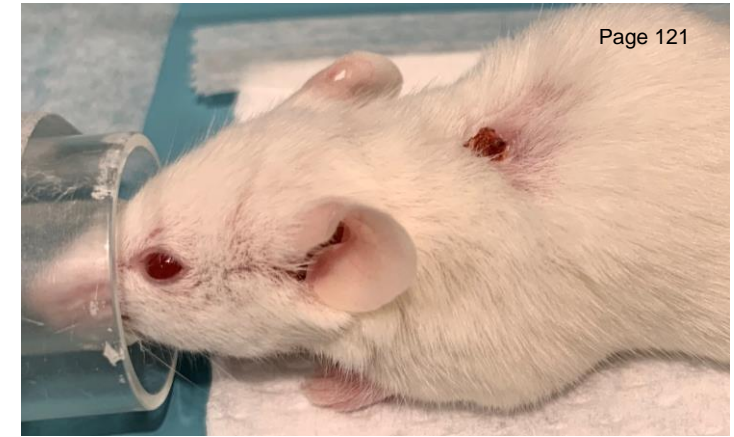
~ OMEGA-3 ~				
02.09.2019	142,4g	131,3g	278	
03.09.2019	142,8g	131,8g		
04.09.2019	144,5	133,9g		29
05.09.2019	141,2	128,3		
06.09.2019	141,2	vekt?		
09.09.2019	141,2			
10.09.2019	140,7	128,0		
11.09.2019	141,4		avlivet	
12.09.2019				

MUS			FOTS 12823
Kjønn ♀	Stamme CIEA N03	Alder/vekt	Antall 2
Bruker Pettersen Caroline H			Ankomst dato 20.9.19
27-P18-1a-hipp(1)-x-ray 21.8.19			
29-P18-2a-hipp(3)-x-ray 21.8.19			
OMEGA3 2/9			BUR
			15

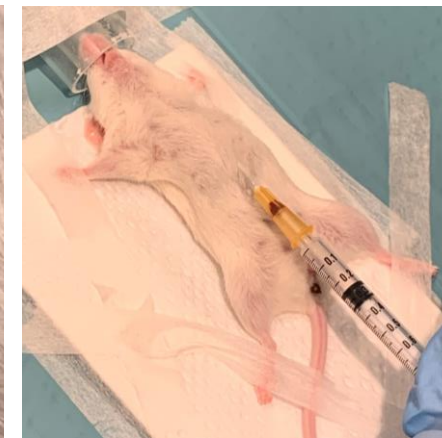
Supplementary figure 1-29-3. List over weight registrations of the drinking bottle (with Smartfish Remune Peach) before and after provided to the mice

Supplementary figure 1-29-4. Pictures from euthanization (11.09.19)

- It was not the xenograft, but an abscess growing.
Abscess bursted and left a wound in the xenograft aerea



Wound with a «crater». The xenograft seems to be gone.



Blood drained from the heart before opening the chest and cutting the aorta. Gave a higher volume for the blood sample compared to sample from the back vein.



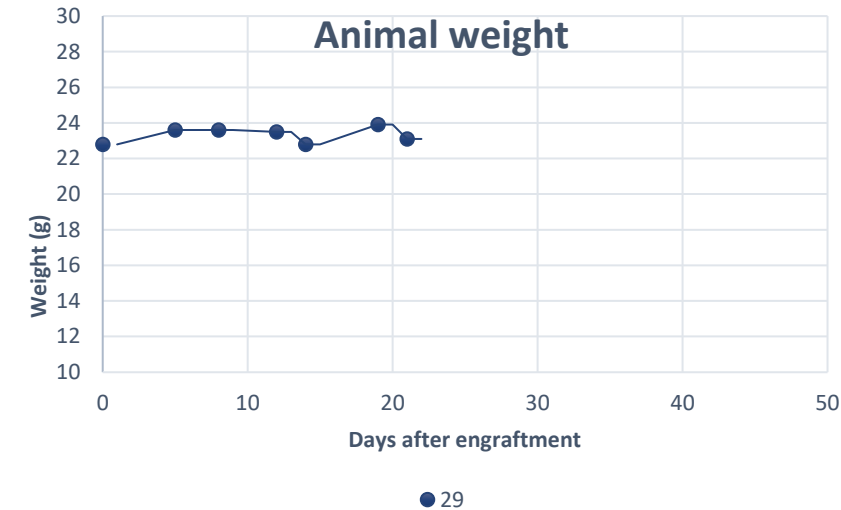
Only remainings of the xenograft was found.

Page 122

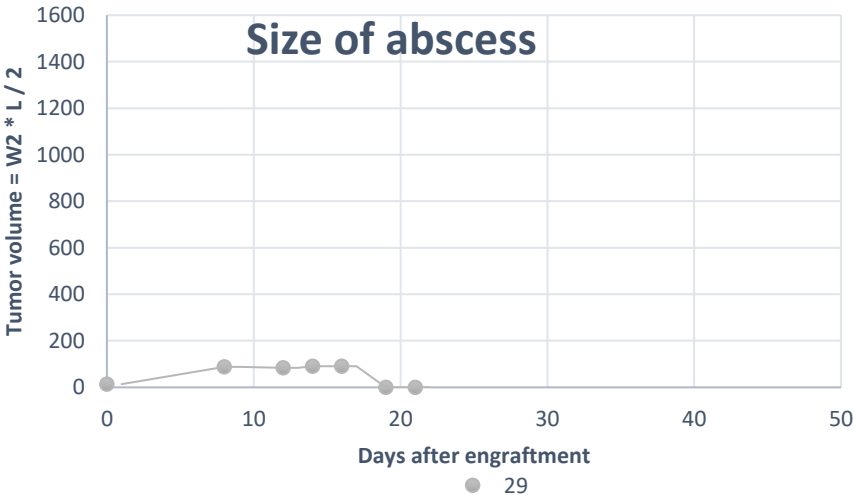
Abscess mistaken for rapidly growing xenograft

Supplementary figure 1-29-6.
Mouse and abscess growth curves

Weight curve

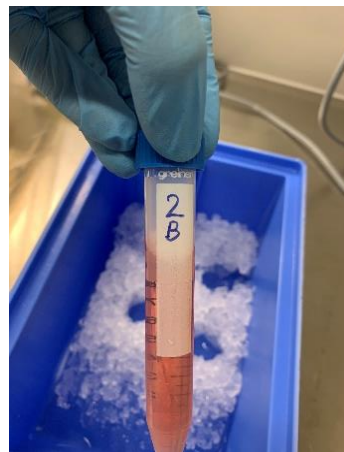
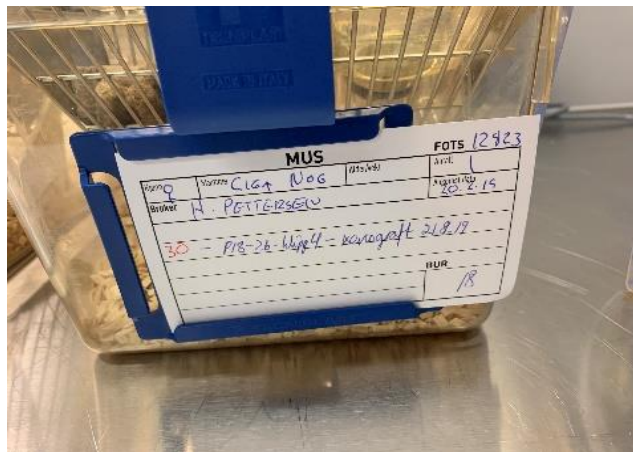


Size of abscess



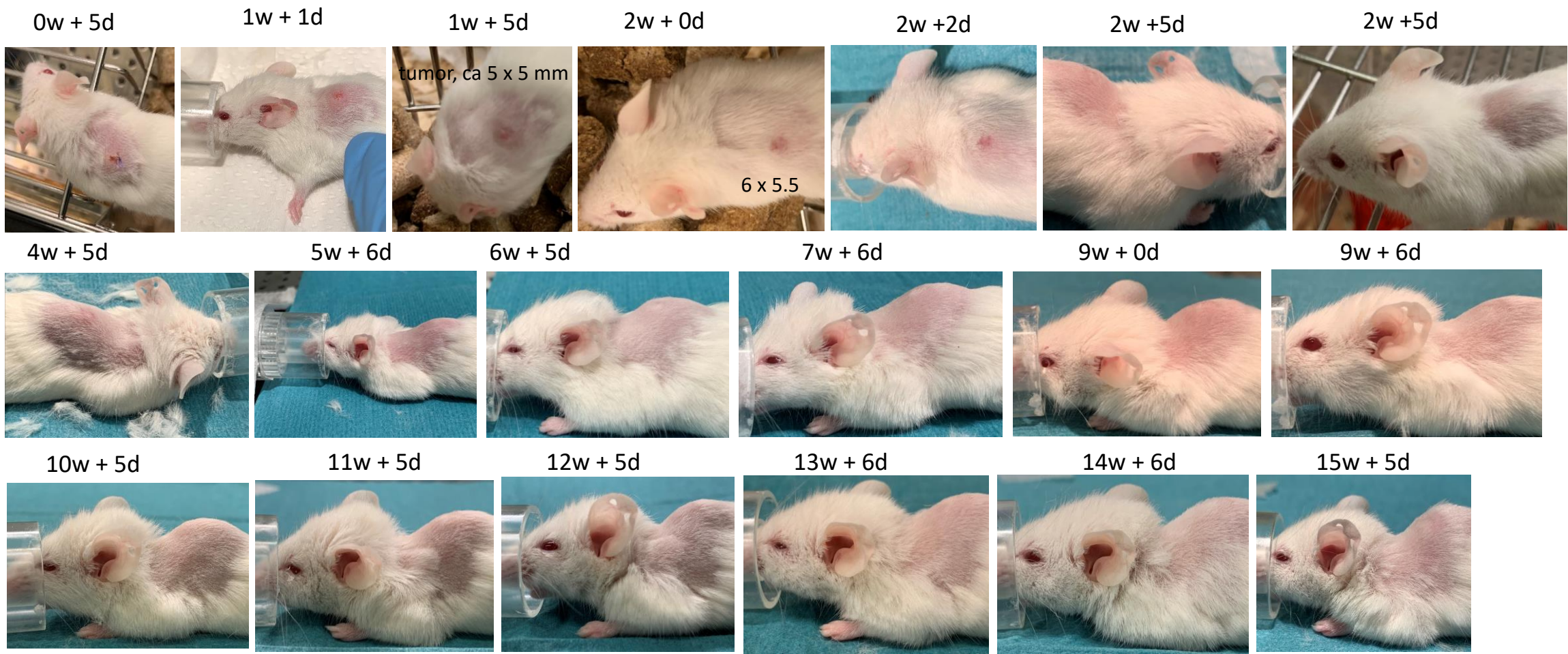
Mouse 30

- Surgery date: 21.08.19
 - Age (weeks) 31
 - Weight (g) 22.1
 - Tumor fragment P18-2b
 - Fragment size 3 x 3 mm
 - Ear mark 4

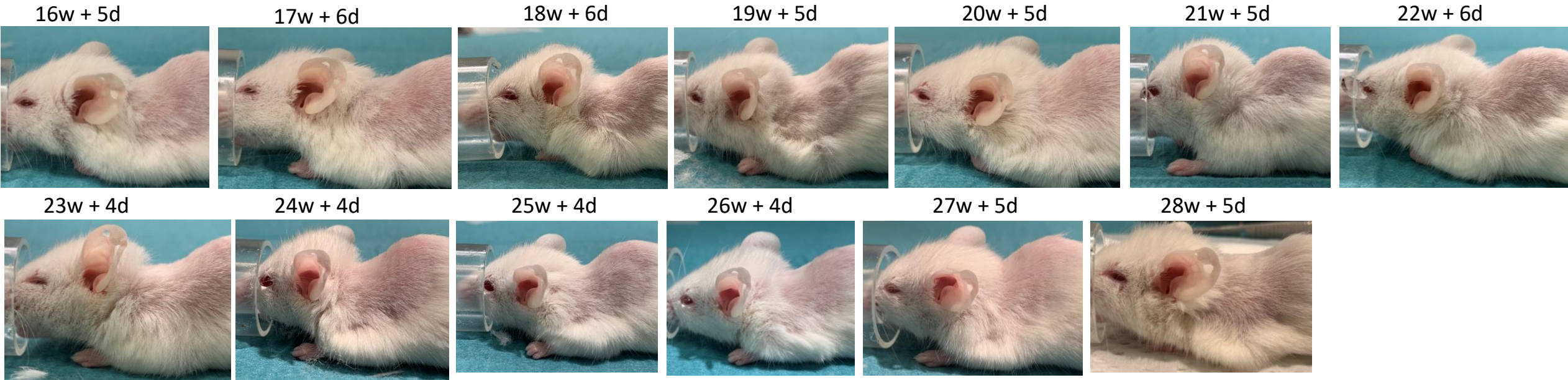


Supplementary figure 1-30-1. Pictures from the engraftment day

Supplementary figure 1-30-2. Pictures from follow up and xenograft size measurement



Supplementary figure 1-30-2. Pictures from follow up and xenograft size measurement



Supplementary figure 1-30-3. Pictures from euthanization (11.03.20)

- Xenograft size – not visible
- No treatment given
- Small/normal spleen
- Possibly small tumor on liver
- Euthanized due to xenograft not growing after 6 months

903™ Protein Saver Card
For Research Use Only
Not for use in diagnostic procedures

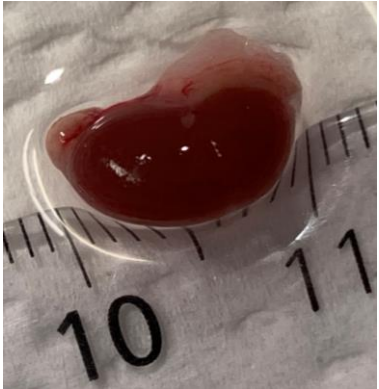
Tuck Cover Here

Name Mus 30 (P18-2b) Hipp 4
Date 11.03.20

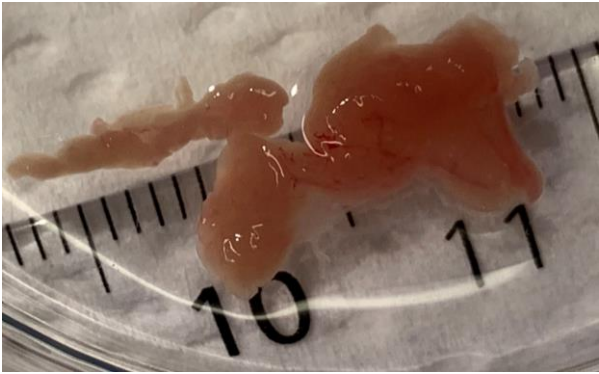
DMGAS3 CAP

Autopsy card modified from:
http://www.pathbase.net/Necropsy_of_the_Mouse/

NUMBER	Male	Female	STRAIN	BIRTH DATE	EXPERIMENT
30 - (P18-2b) Hipp 4			CIEA MGS		PDX - Xenograft 218 B
AGE AT DEATH	DEATH MODE	DATE	CLINICAL SYMPTOMS AT DEATH	GROUP	
		11.03.20		Petersen, Carline	
ORGAN WEIGHT		SECTION TAKEN			
ORGAN	WEIGHT	ORGAN	YES	GROSS OBSERVATION	
Femur		1) Lung + Heart	X	OK	
Liver		2) Liver	X	Fibula i liver	
Spleen		3) Kidney	X		
		4) Adrenal			
		5) Testis/Ovary			
		6) Spleen	X	size? < 1cm spleen	
Kidney		7) Lymph nodes			
		8) Bone marrow			
		9) Xenograft	X	visible?	



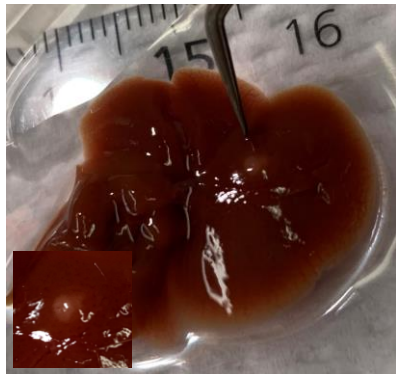
Normal kidney



Pancreas



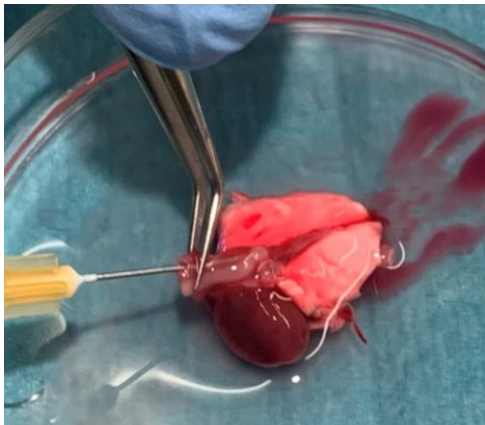
Thymus



Liver with «bump» (tumor?) Only a small «bump» of xenograft



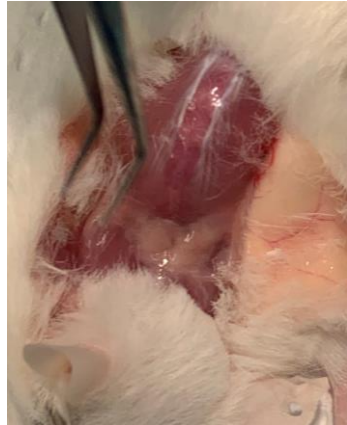
Normal heart and lungs



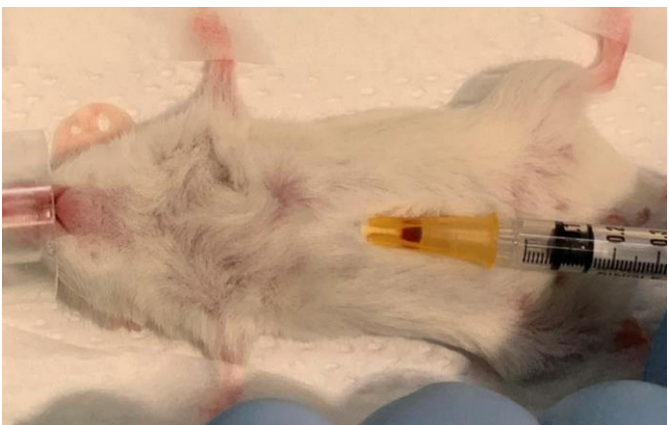
Lungs filled with formalin



Normal spleen



No tumors on shoulders



Blood sampling

Supplementary figure 1-30-4. Score sheets

NTNU Score sheet FOTS: Avdeling for komparativ medisin (AKM) Responsible researcher: Petterson Animal ID: (P18-26) 30 Wipf 4

Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0	21/8	26/8	27/8	2/9	4/9	6/9	9/9	11/9	13/9	16/9	19/9
	Reduced grooming	1											
	Minor distention of abdomen, rough hair coat	3											
	Hunchback or distended abdomen, inactive	18											
Behaviour (Level of activity)	Normal	0											
	Slightly reduced	1											
	Moderately reduced	3											
	Distressed behaviour due to growing tumour	3											
	Obviously reduced	5											
	Isolated, inactive, lethargic	18											
Body weight (Compared to body weight before experiment)	Body weight:		23,4	23,3	23	23,1		24,5	23,9	23,3	22,8	23,5	
	No loss	0											
	Loss < 5%	1											
	Loss 5-9%	3											
	Loss 10-14%	5											
	Loss > 15%	18											
Clinical signs (Infection, bleeding, discoloration)	Normal	0											
	Minor irritation around surgical wound	1											
	Moderate irritation/infected surgical wound	3											
	Infected/open surgical wound	4*											
	Tumour > 1,0 cm in diameter	10											
	Tumour > 1,5 cm in diameter	18											
	Ulcerous tumour	18											
Total:													
Comments, treatments etc:													

0-3: Normal
4-9: Pay attention to health state and consider treatment
10-13: Pay close attention to health state, consider treatment or euthanasia
14-18: Euthanasia *Start treatment with antibiotics. If no effect within 3 days, euthanize the animal

20/9
23,8
Wipf Xuro

NTNU Score sheet FOTS: Avdeling for komparativ medisin (AKM) Responsible researcher: Petterson Animal ID: (P18-26) 30 Wipf 4

Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0	20/9	23/9	25/9	30/9	2/10	4/10	8/10	11/10	14/10	18/10	
	Reduced grooming	1											
	Minor distention of abdomen, rough hair coat	3											
	Hunchback or distended abdomen, inactive	18											
Behaviour (Level of activity)	Normal	0											
	Slightly reduced	1											
	Moderately reduced	3											
	Distressed behaviour due to growing tumour	3											
	Obviously reduced	5											
	Isolated, inactive, lethargic	18											
Body weight (Compared to body weight before experiment)	Body weight:		23,8	23,9	22,3	22,6	23,7	23,5	23,9	22,4	22,7	23,3	
	No loss	0											
	Loss < 5%	1											
	Loss 5-9%	3											
	Loss 10-14%	5											
	Loss > 15%	18											
Clinical signs (Infection, bleeding, discoloration)	Normal	0											
	Minor irritation around surgical wound	1											
	Moderate irritation/infected surgical wound	3											
	Infected/open surgical wound	4*											
	Tumour > 1,0 cm in diameter	10											
	Tumour > 1,5 cm in diameter	18											
	Ulcerous tumour	18											
Total:													
Comments, treatments etc:													

0-3: Normal
4-9: Pay attention to health state and consider treatment
10-13: Pay close attention to health state, consider treatment or euthanasia
14-18: Euthanasia *Start treatment with antibiotics. If no effect within 3 days, euthanize the animal

NTNU Score sheet FOTS: Avdeling for komparativ medisin (AKM) Responsible researcher: Petterson Animal ID: (P18-26) 30 Wipf 4

Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0	16/10	18/10	21/10	23/10	23/10	26/10	1/11	4/11	6/11	13/11	13/11
	Reduced grooming	1											
	Minor distention of abdomen, rough hair coat	3											
	Hunchback or distended abdomen, inactive	18											
Behaviour (Level of activity)	Normal	0											
	Slightly reduced	1											
	Moderately reduced	3											
	Distressed behaviour due to growing tumour	3											
	Obviously reduced	5											
	Isolated, inactive, lethargic	18											
Body weight (Compared to body weight before experiment)	Body weight:		23,3	23,5	23,9	22,7	22,5	22,5	22	23,1	24,0	22,5	
	No loss	0											
	Loss < 5%	1											
	Loss 5-9%	3											
	Loss 10-14%	5											
	Loss > 15%	18											
Clinical signs (Infection, bleeding, discoloration)	Normal	0											
	Minor irritation around surgical wound	1											
	Moderate irritation/infected surgical wound	3											
	Infected/open surgical wound	4*											
	Tumour > 1,0 cm in diameter	10											
	Tumour > 1,5 cm in diameter	18											
	Ulcerous tumour	18											
Total:													
Comments, treatments etc:													

0-3: Normal
4-9: Pay attention to health state and consider treatment
10-13: Pay close attention to health state, consider treatment or euthanasia
14-18: Euthanasia *Start treatment with antibiotics. If no effect within 3 days, euthanize the animal

NTNU Score sheet FOTS: Avdeling for komparativ medisin (AKM) Responsible researcher: Petterson Animal ID: (P18-26) 30 Wipf 4

Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0	15/11	18/11	20/11	25/11	27/11	2/12	5/12	9/12	11/12	13/12	14/12
	Reduced grooming	1											
	Minor distention of abdomen, rough hair coat	3											
	Hunchback or distended abdomen, inactive	18											
Behaviour (Level of activity)	Normal	0											
	Slightly reduced	1											
	Moderately reduced	3											
	Distressed behaviour due to growing tumour	3											
	Obviously reduced	5											
	Isolated, inactive, lethargic	18											
Body weight (Compared to body weight before experiment)	Body weight:		22,5	22,9	23,4	24,0	23,9	22,8	22,3	23,2	22,5	22,3	22,9
	No loss	0											
	Loss < 5%	1											
	Loss 5-9%	3											
	Loss 10-14%	5											
	Loss > 15%	18											
Clinical signs (Infection, bleeding, discoloration)	Normal	0											
	Minor irritation around surgical wound	1											
	Moderate irritation/infected surgical wound	3											
	Infected/open surgical wound	4*											
	Tumour > 1,0 cm in diameter	10											
	Tumour > 1,5 cm in diameter	18											
	Ulcerous tumour	18											
Total:													
Comments, treatments etc:													

0-3: Normal
4-9: Pay attention to health state and consider treatment
10-13: Pay close attention to health state, consider treatment or euthanasia
14-18: Euthanasia *Start treatment with antibiotics. If no effect within 3 days, euthanize the animal

Supplementary figure 1-30-4. Score sheets

NTNU

Score sheet FOTS:
Avdeling for komparativ medisin (AKM)

Responsible researcher:
Pettersen

Animal ID:
(P18-2b)

30
Wapp
4

Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0	18/12	22/12	23/12	24/12	30/12	31/12	1/1	2/1	13/1	15/1	16/1
	Reduced grooming	1											
	Minor distention of abdomen, rough hair coat	3											
	Hunched back or distended abdomen, inactive	18											
Behaviour (Level of activity)	Normal	0											
	Slightly reduced	1											
	Moderately reduced	3											
	Distressed behaviour due to growing tumour	3											
	Obviously reduced	5											
Body weight (Compared to body weight before experiment)	Isolated, inactive, lethargic	18	23.8	23.4	22.8	23.0	23.7	23.8	24.5	23.5	24.4	24.4	24.4
	Body weight:												
	No loss	0											
	Loss < 5%	1											
	Loss 5-9%	3											
	Loss 10-14%	5											
Clinical signs (Infection, bleeding, discoloration)	Loss ≥ 15%	18											
	Normal	0											
	Minor irritation around surgical wound	1	ser	-1-	-1-	-1-	-1-	-1-	-1-	-1-	-1-	-1-	-1-
	Moderate irritation/infected surgical wound	3	ser	-1-	-1-	-1-	-1-	-1-	-1-	-1-	-1-	-1-	-1-
	Infected/open surgical wound	4*	ser	-1-	-1-	-1-	-1-	-1-	-1-	-1-	-1-	-1-	-1-
	Tumour > 1.0 cm in diameter	10											
	Tumour > 1.5 cm in diameter	18											
	Ulcerous tumour	18											
Total:													
Comments, treatments etc:													

NTNU

Score sheet FOTS:
Avdeling for komparativ medisin (AKM)

Responsible researcher:
Pettersen

Animal ID:
(P18-2b)

30
Wapp
4

Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0	20/1	22/1	24/1	27/1	29/1	30/1	3/2	5/2	7/2	11/2	
	Reduced grooming	1											
	Minor distention of abdomen, rough hair coat	3											
	Hunched back or distended abdomen, inactive	18											
Behaviour (Level of activity)	Normal	0											
	Slightly reduced	1											
	Moderately reduced	3											
	Distressed behaviour due to growing tumour	3											
	Obviously reduced	5											
Body weight (Compared to body weight before experiment)	Isolated, inactive, lethargic	18	23.4	22.8	23	24.2	24.2	23.5	22.5	23.1	24.4		
	Body weight:												
	No loss	0											
	Loss < 5%	1											
	Loss 5-9%	3											
	Loss 10-14%	5											
Clinical signs (Infection, bleeding, discoloration)	Loss ≥ 15%	18											
	Normal	0											
	Minor irritation around surgical wound	1	ser	-1-	-1-	-1-	-1-	-1-	-1-	-1-	-1-	-1-	-1-
	Moderate irritation/infected surgical wound	3	ser	-1-	-1-	-1-	-1-	-1-	-1-	-1-	-1-	-1-	-1-
	Infected/open surgical wound	4*	ser	-1-	-1-	-1-	-1-	-1-	-1-	-1-	-1-	-1-	-1-
	Tumour > 1.0 cm in diameter	10											
	Tumour > 1.5 cm in diameter	18											
	Ulcerous tumour	18											
Total:													
Comments, treatments etc:													

NTNU

Score sheet FOTS:
Avdeling for komparativ medisin (AKM)

Responsible researcher:
Pettersen

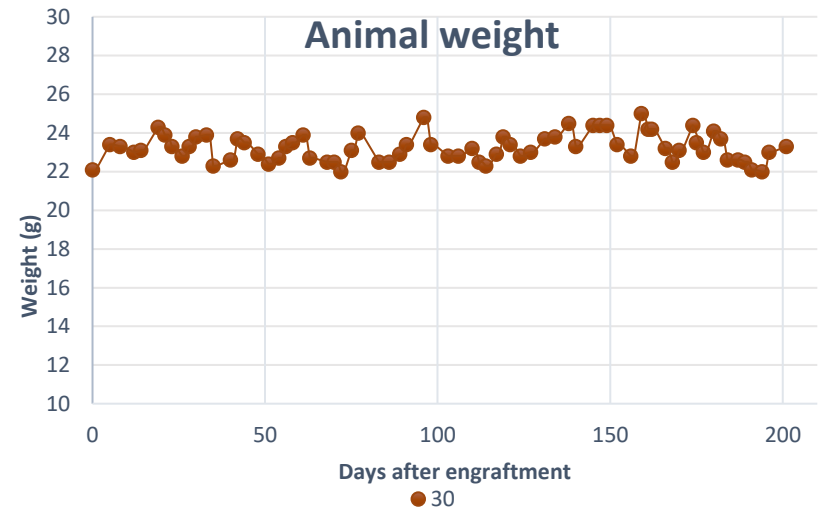
Animal ID:
(P18-2b)

30
Wapp
4

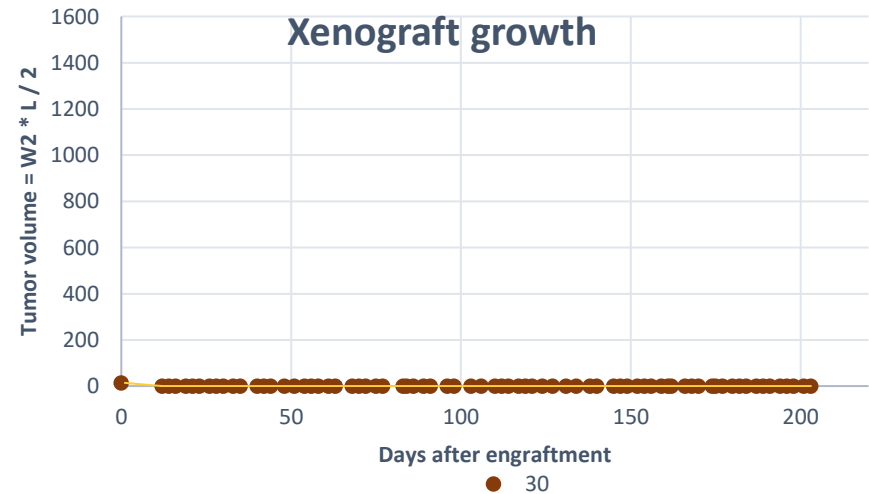
Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0	11/2	12/2	14/2	17/2	19/2	21/2	24/2	26/2	28/2	29/2	9/3
	Reduced grooming	1											
	Minor distention of abdomen, rough hair coat	3											
	Hunched back or distended abdomen, inactive	18											
Behaviour (Level of activity)	Normal	0											
	Slightly reduced	1											
	Moderately reduced	3											
	Distressed behaviour due to growing tumour	3											
	Obviously reduced	5											
Body weight (Compared to body weight before experiment)	Isolated, inactive, lethargic	18	24.4	23.5	23	24.1	23.7	22.6	22.6	22.5	22.1	22	23
	Body weight:												
	No loss	0											
	Loss < 5%	1											
	Loss 5-9%	3											
	Loss 10-14%	5											
Clinical signs (Infection, bleeding, discoloration)	Loss ≥ 15%	18											
	Normal	0											
	Minor irritation around surgical wound	1	ser	-1-	-1-	-1-	-1-	-1-	-1-	-1-	-1-	-1-	-1-
	Moderate irritation/infected surgical wound	3	ser	-1-	-1-	-1-	-1-	-1-	-1-	-1-	-1-	-1-	-1-
	Infected/open surgical wound	4*	ser	-1-	-1-	-1-	-1-	-1-	-1-	-1-	-1-	-1-	-1-
	Tumour > 1.0 cm in diameter	10											
	Tumour > 1.5 cm in diameter	18											
	Ulcerous tumour	18											
Total:													
Comments, treatments etc:													

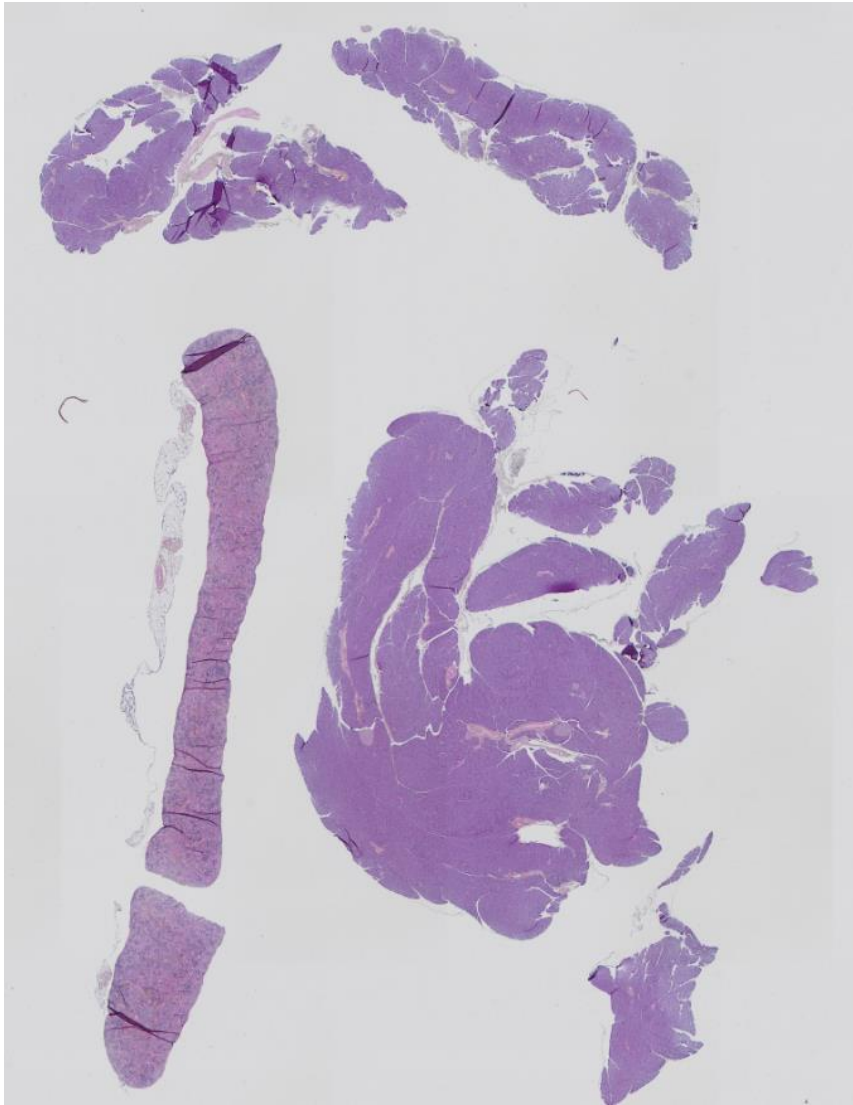
Supplementary figure 1-30-5.
Mouse and xenograft growth curves

Weight curve



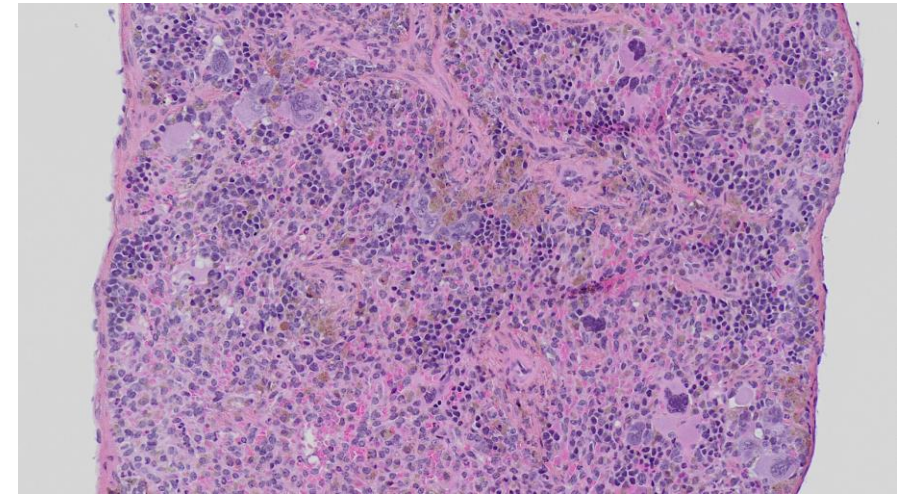
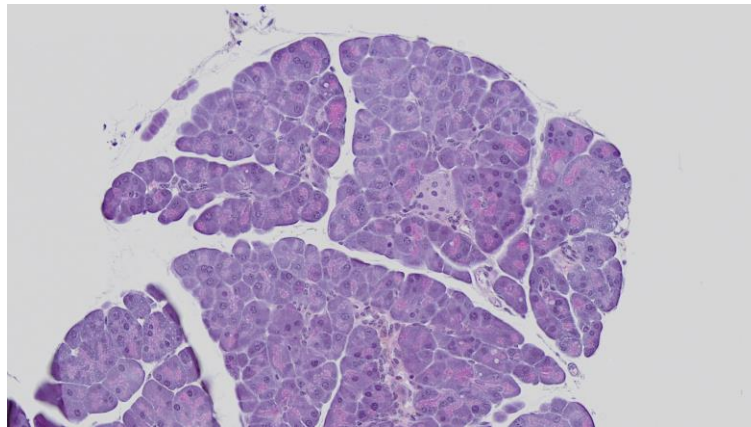
Xenograft growth curve



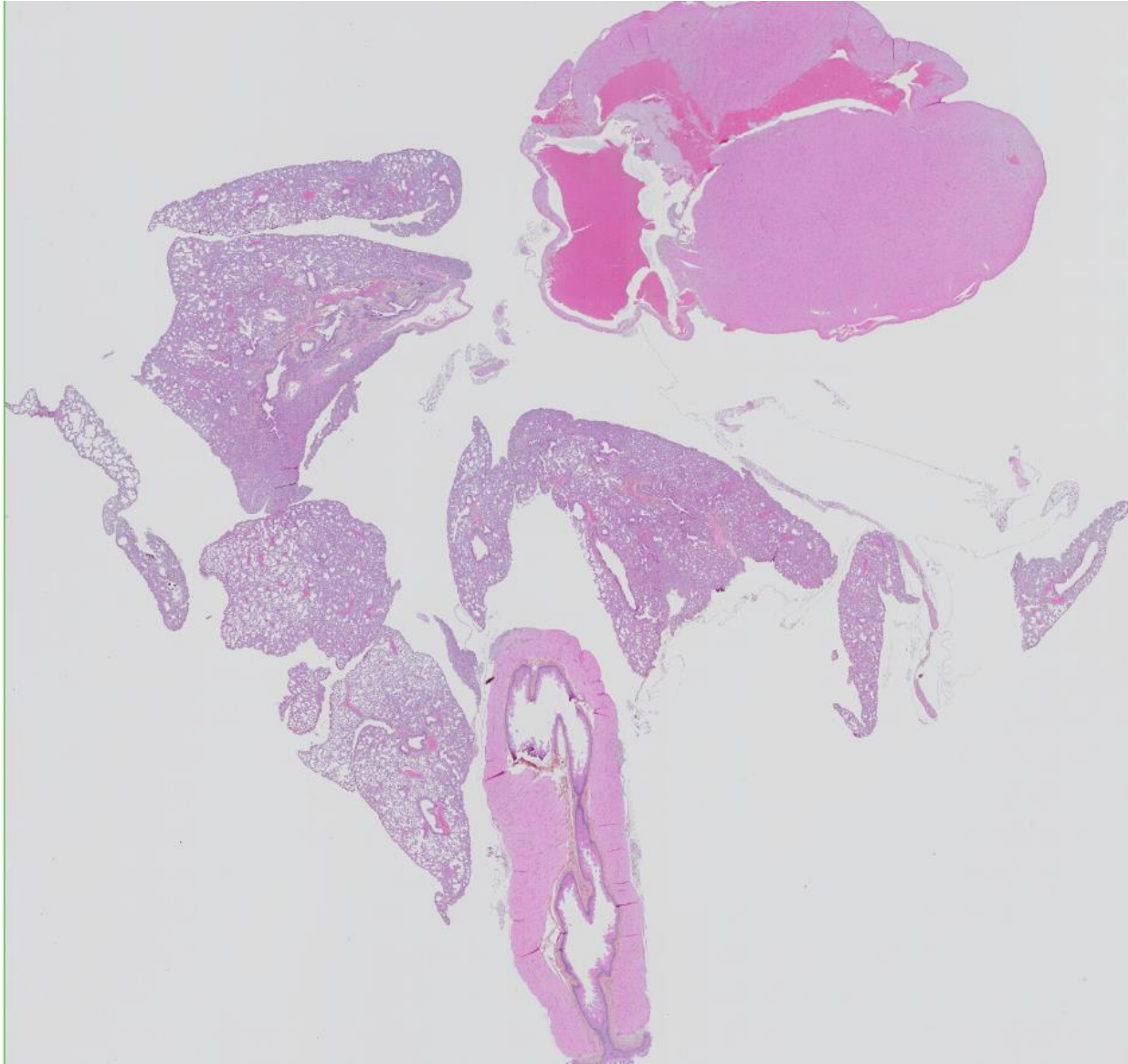


M30MP – Spleen and pancreas

- Look normal



Supplementary figure 1-30-6. Histology pictures

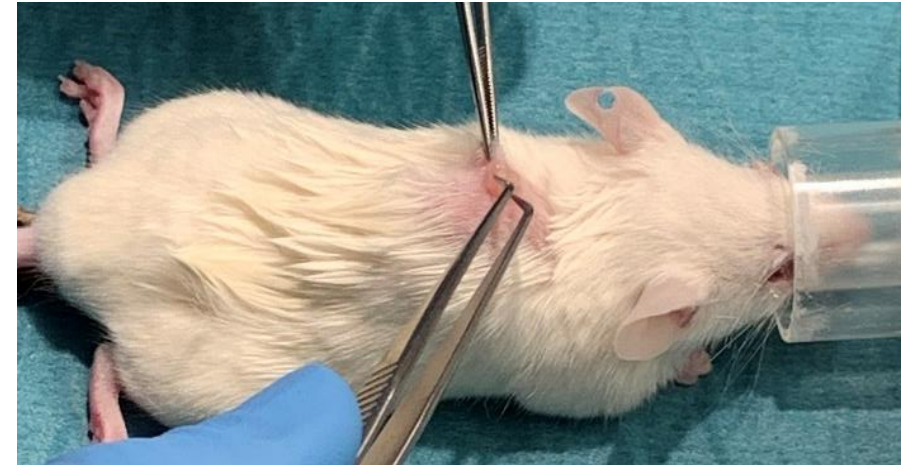
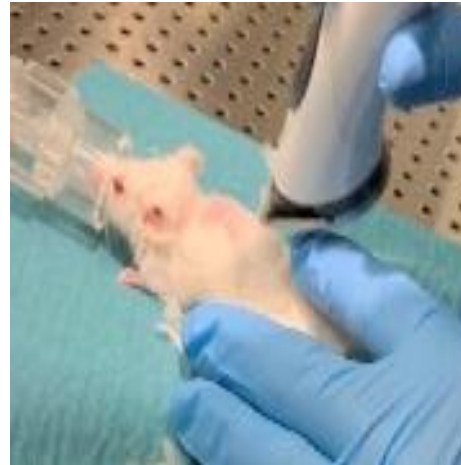
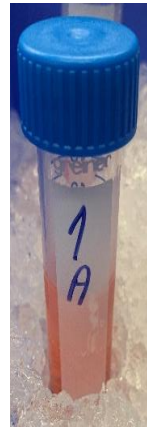


M30LH – Lungs and heart

- Look normal

Mouse 31

- Surgery date: 03.09.19
 - Age (weeks) 33
 - Weight (g) 23.8
 - Tumor fragment P19-1a
 - Fragment size 3 x 3 mm
 - Ear marks 1



Supplementary figure 1-31-1. Pictures from the engraftment day

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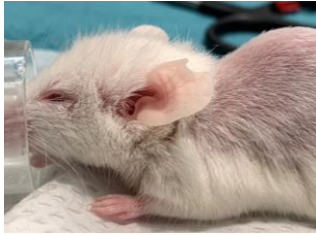
$$2w + 1d$$

$$7w + 2d$$

$$14w + 0d$$

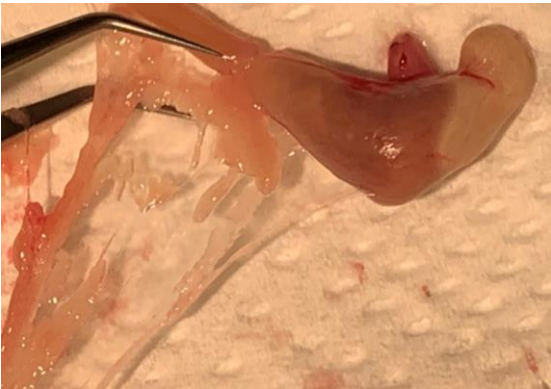
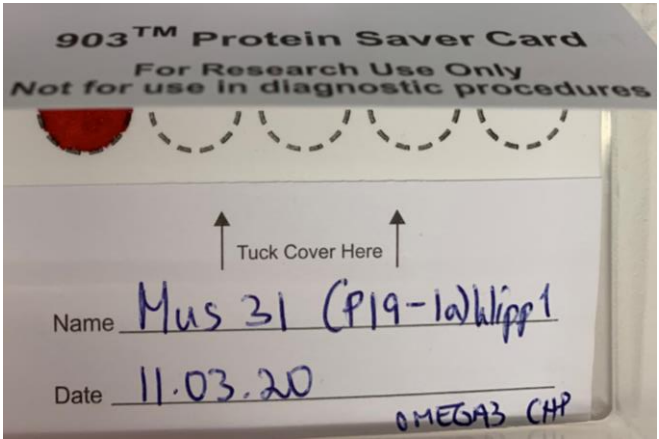
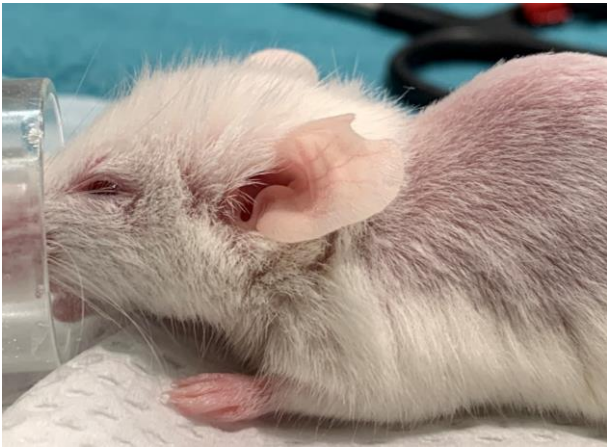
$$21w + 1d$$


27w + 0d

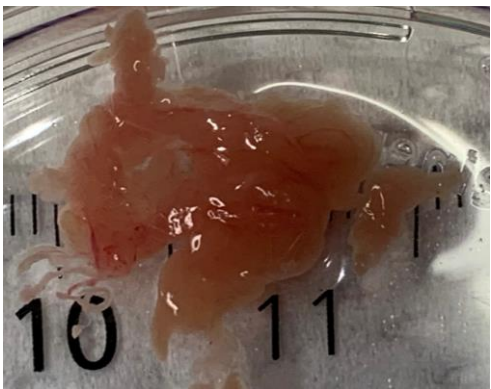


Supplementary figure 1-31-3. Pictures from euthanization (11.03.20)

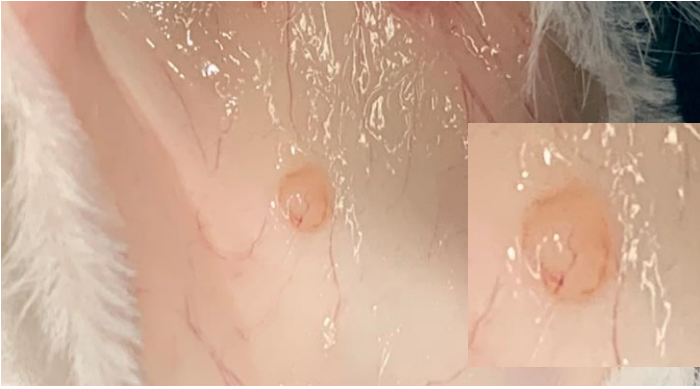
- No treatment given (no xenograft growth)
- Xenograft size – not visible
- Small/normal spleen
- Euthanized due to xenograft not growing after 6 months



Stomach and pancreatic tissue



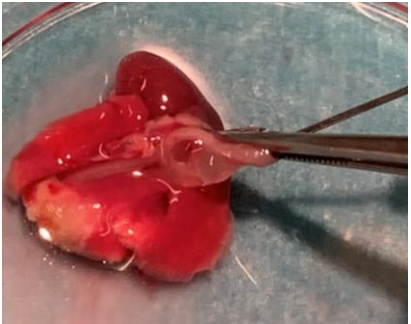
Pancreas



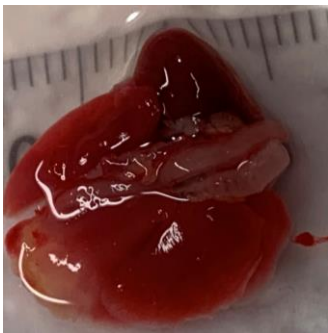
Small xenograft under the skin



Blood sampling



Lungs filled with formalin



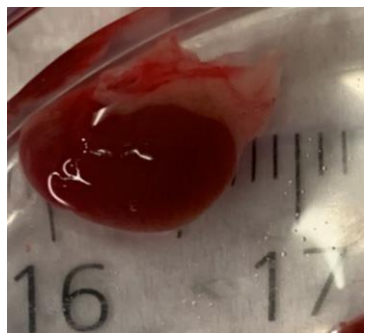
Normal lungs and heart



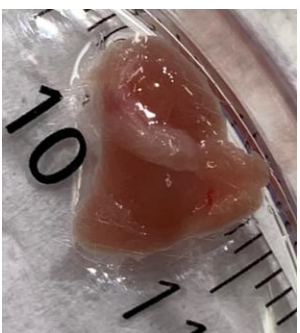
Normal spleen



Normal liver



Normal kidney



Thymus

Supplementary figure 1-31-4. Autopsy card filled out during necroscopy

AUTOPSY CARD

NUMBER 31 (P19-1a) Wipp1	Male Female ♀	STRAIN UEA NO3	BIRTH DATE	EXPERIMENT POX - xenograft 3/9/19
AGE AT DEATH	DEATH MODE DATE 11.03.20			GROUP Pettersen, Caroline
	CLINICAL SYMPTOMS AT DEATH Fisk/healthy			
ORGAN WEIGHT		SECTION TAKEN		
ORGAN	WEIGHT	ORGAN	YES	GROSS OBSERVATION
Femur	LH	1) Lung + Heart	X	OK, fylt 4 formelin
	L	2) Liver	X	OK
Liver	RV	3) Kidney	X	OK
		4) Adrenal		
Spleen		5) Testis/Ovary		
	HP	6) Spleen + pancreas	X	size? ca 1,5 cm, normal, litt hvite fett
Kidney		7) Lymph nodes		
		8) Bone marrow		
Testis/Ovary	X	9) xenograft	X	visible? pen liten forhogning, huden, tatt ut til HES
	T	10) thymus	X	
		11)		
		12)		
		13)		

Notes: Blod host ✓
Blod plasma ✓
Bilder ✓

Autopsy card modified from: http://www.pathbase.net/Necropsy_of_the_Mouse/

Supplementary figure 1-31-5. Score sheets

NTNU Score sheet FOTS: Avdeling for komparativ medisin (AKM) Responsible researcher: Pettersen Animal ID: (P19-1a) 31 klipp 1

Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0	24	4/9	6/9	9/9	11/9	13/9	16/9	17/9	20/9	23/9
	Reduced grooming	1										
	Minor distention of abdomen, rough hair coat	3										
	Hunchback or distended abdomen, inactive	18										
Behaviour (Level of activity)	Normal	0										
	Slightly reduced	1										
	Moderately reduced	3										
	Distressed behaviour due to growing tumour	3										
	Obviously reduced	5										
Body weight (Compared to body weight before experiment)	Isolated, inactive, lethargic	18										
	Body weight:		23,8	23,2	23,4	23,2	24,5	23,6	24,2	23,5	23,3	
	No less	0										
	Loss < 5%	1										
	Loss 5-9%	3										
Clinical signs (Infection, bleeding, discoloration)	Loss 10-14%	5										
	Loss > 15%	18										
	Normal	0										
	Minor irritation around surgical wound	1										
	Moderate irritation/infected surgical wound	3										
Total:	Infected/open surgical wound	4*										
	Tumour > 1,0 cm in diameter	10										
	Tumour > 1,5 cm in diameter	18										
	Ulcerous tumour	18										
	Comments, treatments etc:											

0-3: Normal
4-9: Pay attention to health state and consider treatment
10-13: Pay close attention to health state, consider treatment or euthanasia
14-18: Euthanasia *Start treatment with antibiotics. If no effect within 3 days, euthanize the animal

NTNU Score sheet FOTS: Avdeling for komparativ medisin (AKM) Responsible researcher: Pettersen Animal ID: (P19-1a) 31 klipp 1

Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0	25/9	30/9	2/10	4/10	8/10	11/10	14/10	16/10	18/10	21/10
	Reduced grooming	1										
	Minor distention of abdomen, rough hair coat	3										
	Hunchback or distended abdomen, inactive	18										
Behaviour (Level of activity)	Normal	0										
	Slightly reduced	1										
	Moderately reduced	3										
	Distressed behaviour due to growing tumour	3										
	Obviously reduced	5										
Body weight (Compared to body weight before experiment)	Isolated, inactive, lethargic	18										
	Body weight:		23,3	23,7	24,3	23,2	22,8	23,7	23,9	25,1	25	23,9
	No less	0										
	Loss < 5%	1										
	Loss 5-9%	3										
Clinical signs (Infection, bleeding, discoloration)	Loss 10-14%	5										
	Loss > 15%	18										
	Normal	0										
	Minor irritation around surgical wound	1										
	Moderate irritation/infected surgical wound	3										
Total:	Infected/open surgical wound	4*										
	Tumour > 1,0 cm in diameter	10										
	Tumour > 1,5 cm in diameter	18										
	Ulcerous tumour	18										
	Comments, treatments etc:											

0-3: Normal
4-9: Pay attention to health state and consider treatment
10-13: Pay close attention to health state, consider treatment or euthanasia

NTNU Score sheet FOTS: Avdeling for komparativ medisin (AKM) Responsible researcher: Pettersen Animal ID: (P19-1a) 31 klipp 1

Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0	21/10	23/10	28/10	30/10	1/11	4/11	9/11	13/11	13/11	15/11
	Reduced grooming	1										
	Minor distention of abdomen, rough hair coat	3										
	Hunchback or distended abdomen, inactive	18										
Behaviour (Level of activity)	Normal	0										
	Slightly reduced	1										
	Moderately reduced	3										
	Distressed behaviour due to growing tumour	3										
	Obviously reduced	5										
Body weight (Compared to body weight before experiment)	Isolated, inactive, lethargic	18										
	Body weight:		23,9	23,8	23,2	23,6	23,4	24	24,4	25,2		
	No less	0										
	Loss < 5%	1										
	Loss 5-9%	3										
Clinical signs (Infection, bleeding, discoloration)	Loss 10-14%	5										
	Loss > 15%	18										
	Normal	0										
	Minor irritation around surgical wound	1										
	Moderate irritation/infected surgical wound	3										
Total:	Infected/open surgical wound	4*										
	Tumour > 1,0 cm in diameter	10										
	Tumour > 1,5 cm in diameter	18										
	Ulcerous tumour	18										
	Comments, treatments etc:											

0-3: Normal
4-9: Pay attention to health state and consider treatment
10-13: Pay close attention to health state, consider treatment or euthanasia
14-18: Euthanasia *Start treatment with antibiotics. If no effect within 3 days, euthanize the animal

NTNU Score sheet FOTS: Avdeling for komparativ medisin (AKM) Responsible researcher: Pettersen Animal ID: (P19-1a) 31 klipp 1

Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0	18/11	20/11	25/11	28/11	2/12	5/12	9/12	11/12	13/12	14/12
	Reduced grooming	1										
	Minor distention of abdomen, rough hair coat	3										
	Hunchback or distended abdomen, inactive	18										
Behaviour (Level of activity)	Normal	0										
	Slightly reduced	1										
	Moderately reduced	3										
	Distressed behaviour due to growing tumour	3										
	Obviously reduced	5										
Body weight (Compared to body weight before experiment)	Isolated, inactive, lethargic	18										
	Body weight:		24,1	24,5	24,7	24,6	23,4	23,2	23,5	24,4	24,1	
	No less	0										
	Loss < 5%	1										
	Loss 5-9%	3										
Clinical signs (Infection, bleeding, discoloration)	Loss 10-14%	5										
	Loss > 15%	18										
	Normal	0										
	Minor irritation around surgical wound	1										
	Moderate irritation/infected surgical wound	3										
Total:	Infected/open surgical wound	4*										
	Tumour > 1,0 cm in diameter	10										
	Tumour > 1,5 cm in diameter	18										
	Ulcerous tumour	18										
	Comments, treatments etc:											

0-3: Normal
4-9: Pay attention to health state and consider treatment
10-13: Pay close attention to health state, consider treatment or euthanasia
14-18: Euthanasia *Start treatment with antibiotics. If no effect within 3 days, euthanize the animal

Supplementary figure 1-31-5. Score sheets

NTNU

Avdeling for komparativ medisin (AKM)

Responsible for:

Petersen

Animal ID: (31)

Wgpr ①

Score sheet FOTS:

Adveling for komparativ medisin (AKM)

Parameter	State	Assessment scale	Date 18/12	Date 20/12	Date 23/12	Date 26/12	Date 30/12	Date 01/10	Date 06/10	Date 31/1	Date 13/1	Date 15/1	Date 17/1
General appearance	Normal	0											
	Reduced grooming	1											
	Minor distention of abdomen, rough hair coat	3											
	Hunchback or distended abdomen, inactive	18											
Behaviour (Level of activity)	Normal	0											
	Slightly reduced	1											
	Moderately reduced	3											
	Distressed behaviour due to growing tumour	3											
	Obviously reduced	5											
Body weight (Compared to body weight before experiment)	Isolated, inactive, lethargic	18											
	Body weight		23,9	23	23,5	23,0	24,9	24,8	23,2	24,2	25,1	24,0	23,3
	No loss	0											
	Loss < 5%	1											
	Loss 5-9%	3											
	Loss 10-14%	5											
Clinical signs (Infection, bleeding, discoloration)	Loss > 15%	18											
	Normal	0											
	Minor irritation around surgical wound	1											
	Moderate irritation/infected surgical wound	3											
	Infected/open surgical wound	4*											
	Tumour > 1.0 cm in diameter	10											
Tumour > 1.5 cm in diameter	18												
	18												
	Uterine tumour	18											
Total:													
Comments, treatments etc:													

0-3: Normal

4-9: Pay attention to health state and consider treatment

10-13: Pay close attention to health state, consider treatment or euthanasia

14-18: Euthanasia *Start treatment with antibiotics. If no effect within 3 days, euthanize the animal

NTNU Score sheet FOTS: Avdeling for komparativt medisin (AKM)		Responsible researcher: Petersen		Animal ID: (31)		Wkpt (1)						
Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	
General appearance	Normal	0	20/1	22/1	24/1	27/1	31/1	30	32	5/2	7/2	11/2
	Reduced grooming	1										
	Minor distention of abdomen, rough hair coat	3										
	Hunchback or distended abdomen, inactive	18										
Behaviour (Level of activity)	Normal	0										
	Slightly reduced	1										
	Moderately reduced	3										
	Distressed behaviour due to growing tumour	3										
	Obviously reduced	5										
	Isolated, inactive, lethargic	18										
Body weight (Compared to body weight before experiment)	Body weight	0	23/4	24/2	24/3	24/5	25/7	25	24	24/4		
	No loss	1										
	Loss < 5%	3										
	Loss 5-9 %	3										
	Loss 10-14%	5										
	Loss > 15%	18										
Clinical signs (Infection, bleeding, discoloration)	Normal	0										
	Minor irritation around surgical wound	1										
	Moderate irritation/infected surgical wound	3										
	Infected/open surgical wound	4*										
	Tumour > 1.0 cm in diameter	10										
	Tumour > 1.5 cm in diameter	18										
	Ulcerous tumour	18										
Total:												
Comments, treatments etc:												

0-3: Normal
4-9: Pay attention to health state and consider treatment
10-13: Pay close attention to health state, consider treatment or euthanasia
14-18: Euthanasia *Start treatment with antibiotics. If no effect within 3 days, euthanize the animal

23-25g

NTU Source sheet FOTS:
Avdeling for komparativ medisin (AKM)

Responsible researcher:
Pettersen

Animal ID: 31

Klipp
1

Parameter	State	Assessment scale	Date 1/2	Date 13/2	Date 14/2	Date 17/2	Date 19/2	Date 21/2	Date 24/2	Date 26/2	Date 28/2	Date 29/2	
General appearance	Normal	0											4/3 9/3
	Reduced grooming	1											
	Minor distention of abdomen, rough hair coat	3											
	Hunched or distended abdomen, inactive	18											
Behaviour (Level of activity)	Normal	9											
	Slightly reduced	1											
	Moderately reduced	3											
	Diminished behaviour due to growing tumour	3											
	Obviously reduced	5											
	Isolated, inactive, lethargic	18											
Body weight (Compared to body weight before experiment)	Body weight		24.1	22.9	24.1	24.9	25	25.8	23.4	25.6	22.8	23.1	24.3 24.0
	No loss	0											
	Loss < 5%	1											
	Loss 5-9%	3											
	Loss 10-14%	5											
	Loss > 14%	18											
Clinical signs (Infection, bleeding, discoloration)	Normal	0											
	Minor irritation around surgical wound	1											
	Moderate irritation/infected surgical wound	3											
	Infected/open surgical wound	4 +											
	Tumour > 1.0 cm in diameter	10											
	Tumour > 1.5 cm in diameter	18											
	Ulcerous tumour	18											
Total:													
Comments, treatments etc:													

0-3: Normal

4-9: Pay attention to health state and consider treatment

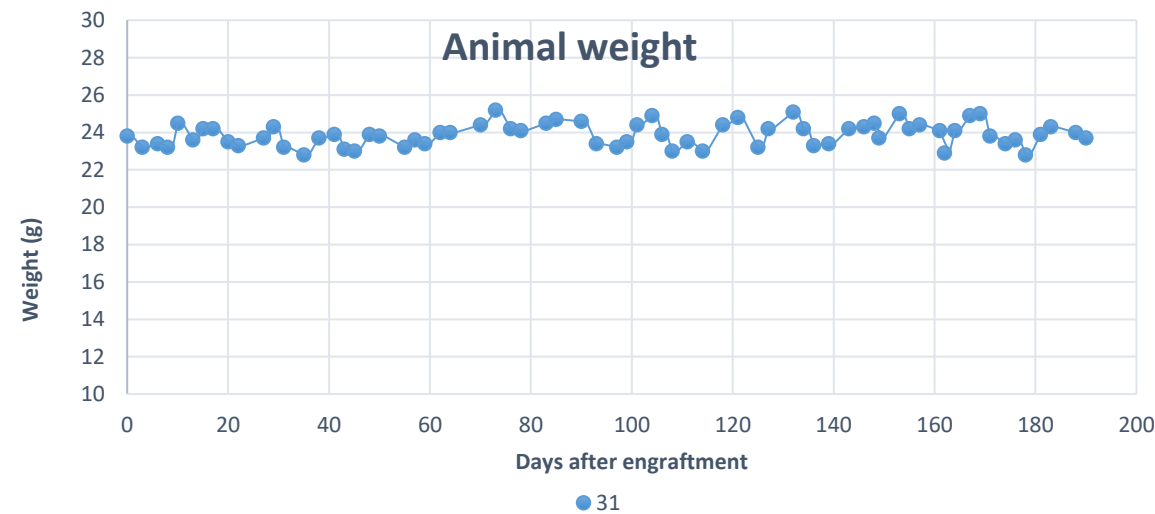
10-15: Pay close attention to health state, consider treatment or euthanasia

16-18: Euthanasia *Start treatment with antibiotics. If no effect within 3 days, euthanize the animal

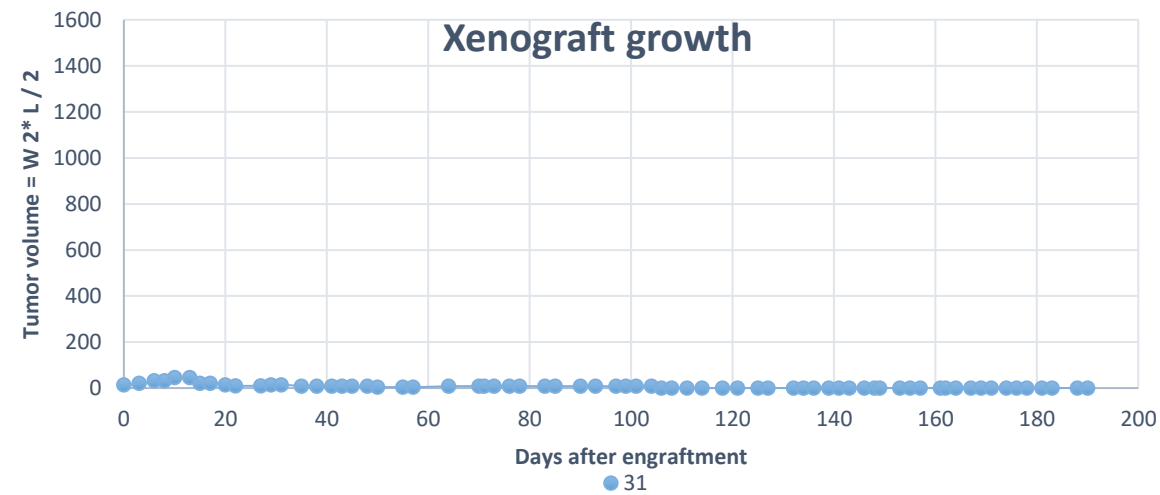
11/3
23.7
-11-
ankret

Supplementary figure 1-31-6.
Mouse and xenograft growth curves

Weight curve

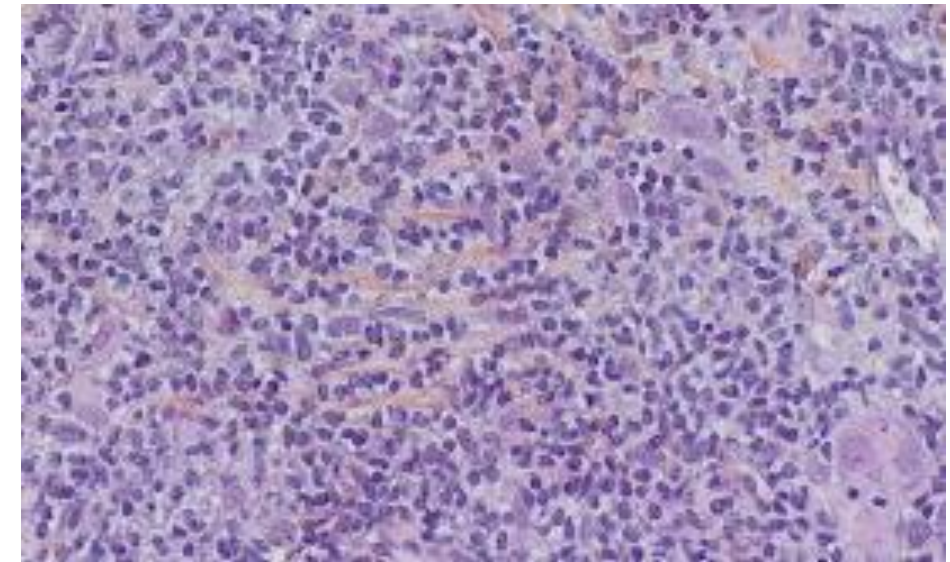
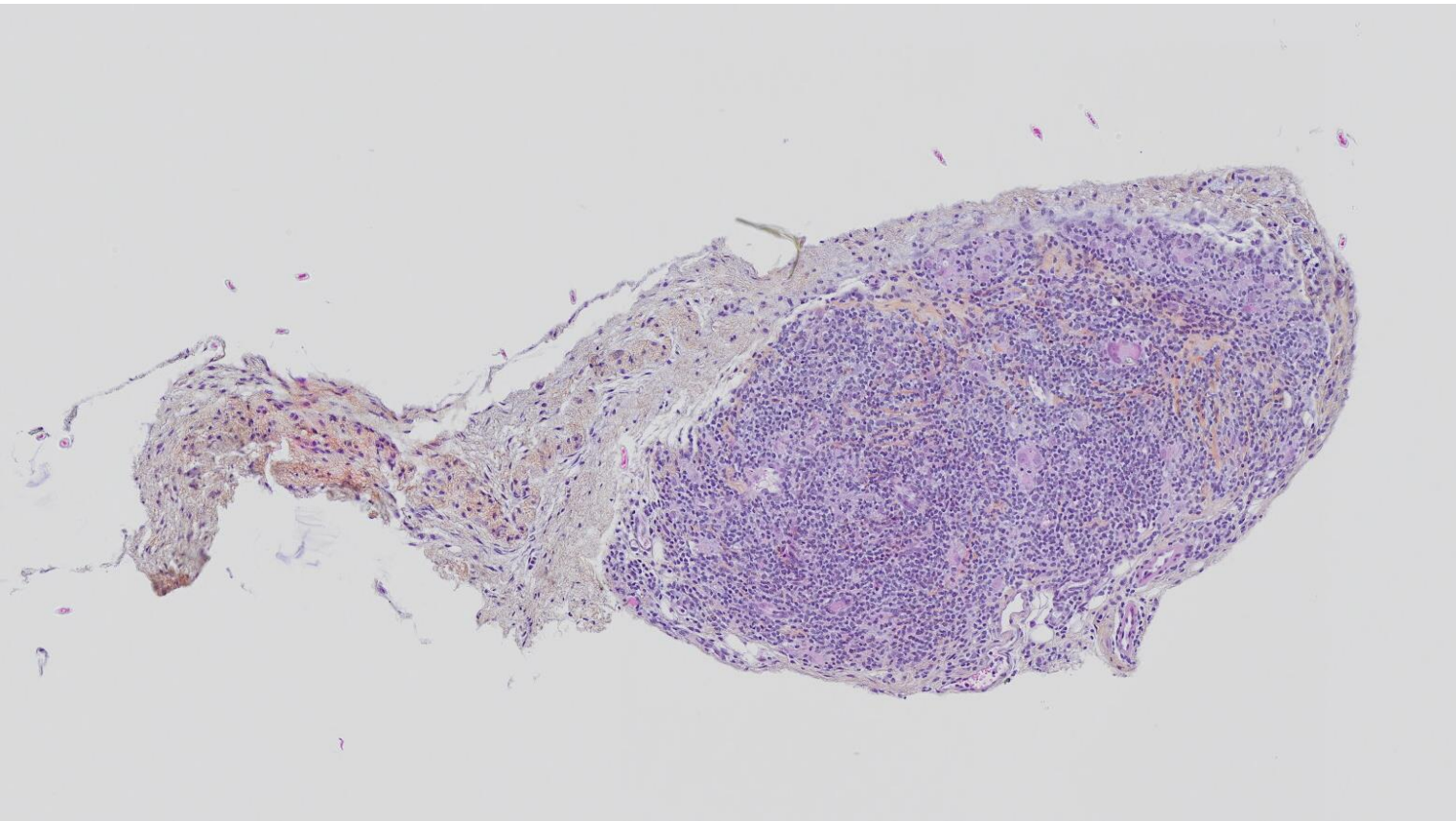


Xenograft growth curve



M31X – Remainings of xenograft?

- Looks like an inflammatory reaction that might have killed the xenograft
- Can see multinuclear and lymphoid cells



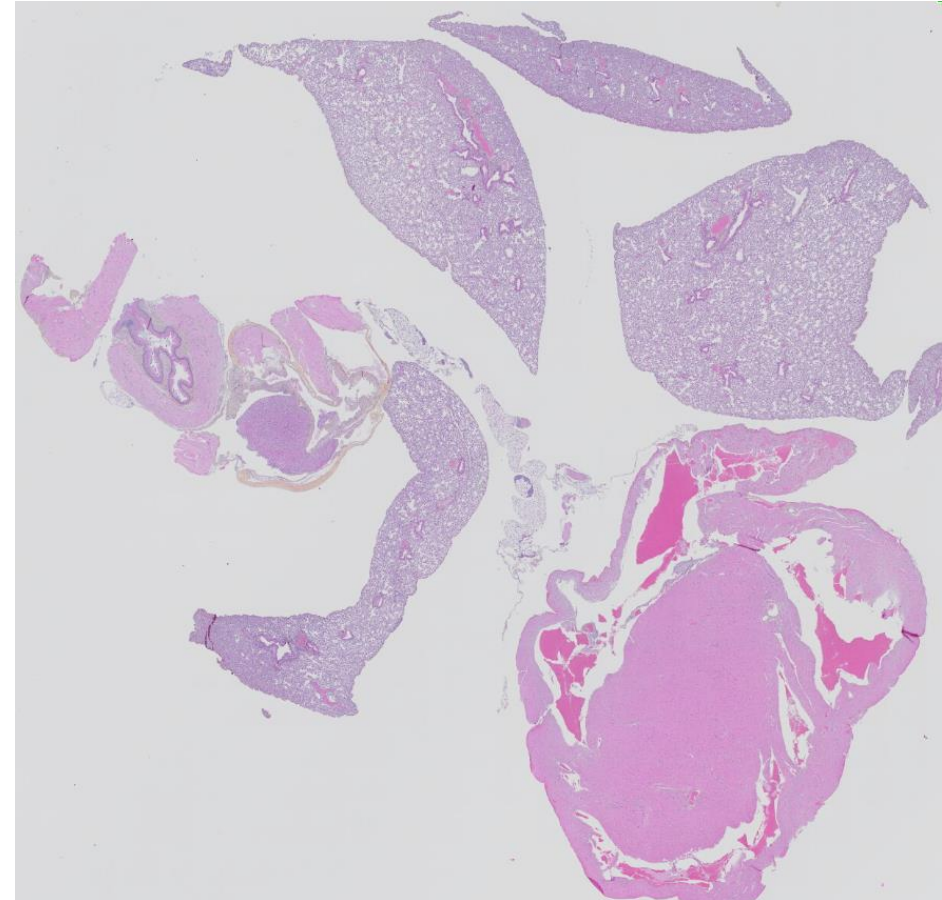
M31MP – Spleen and pancreas

- Looks normal



M31LH – Lungs and heart

- Looks normal



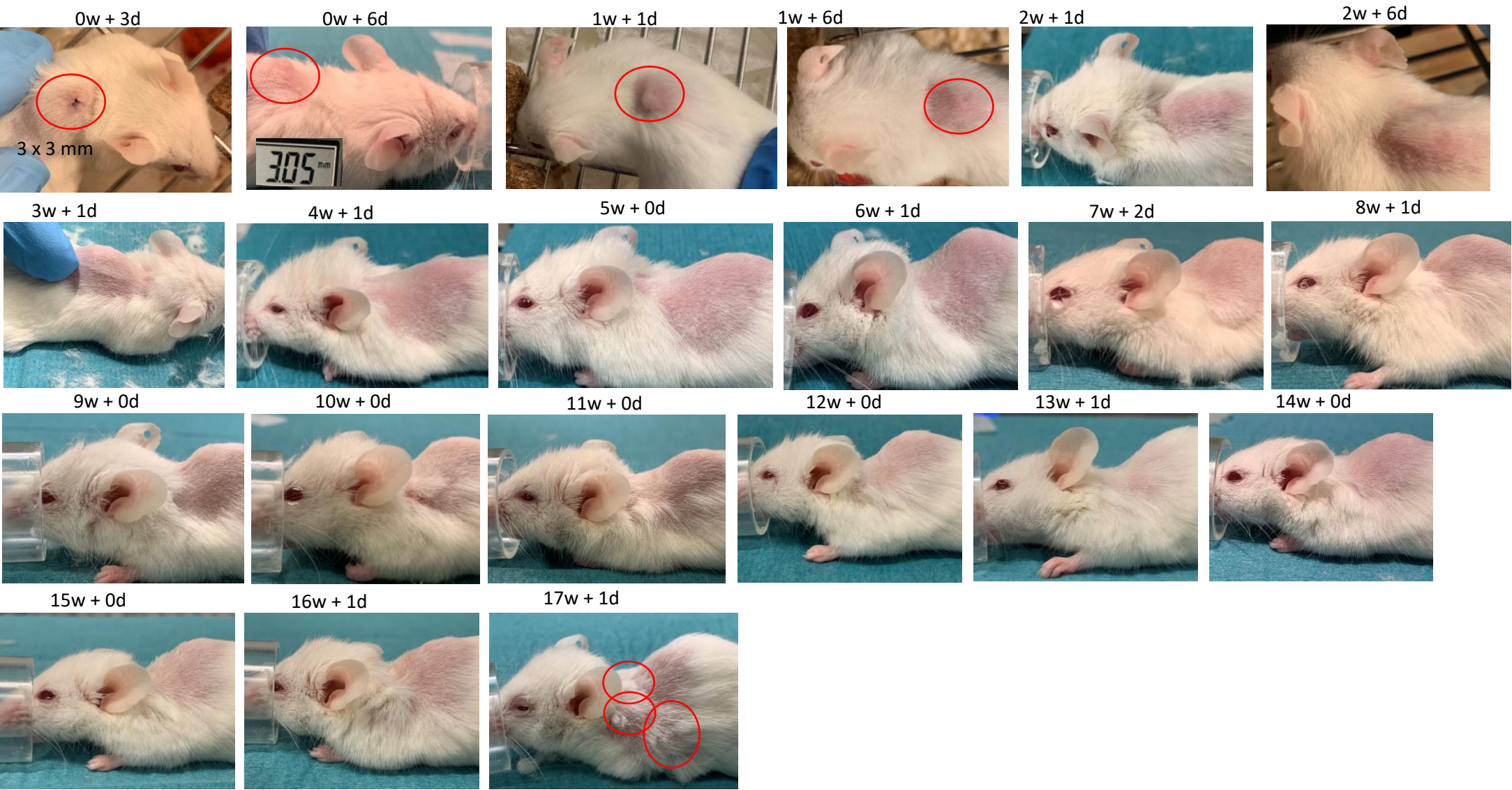
Mouse 32

- Surgery date: 03.09.19
 - Age (weeks) 33
 - Weight (g) 22.2
 - Tumor fragment P19-1b
 - Fragment size 3 x 3 mm
 - Ear marks 2



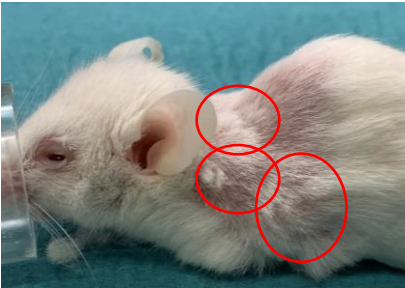
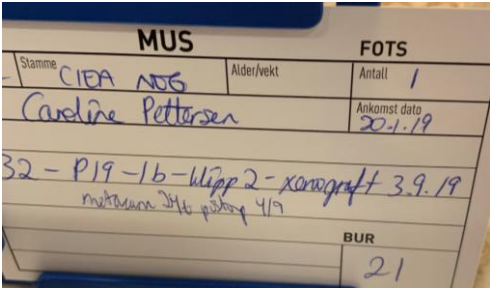
Supplementary figure 1-32-1. Pictures from the engraftment day

Supplementary figure 1-32-2. Pictures from follow up and xenograft size measurement

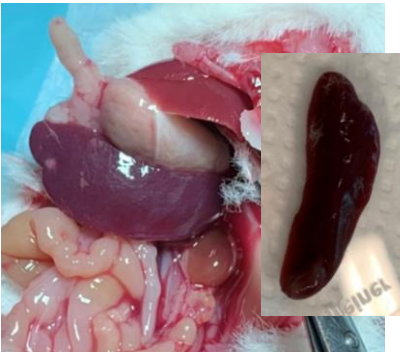


Supplementary figure 1-32-3. Pictures from euthanization (02.01.20)

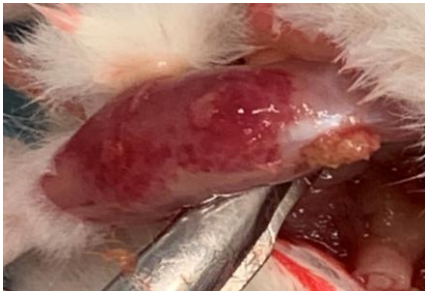
- No treatment given
- Euthanized due to reduced health and development of secondary tumors before growth of xenograft was established



Reduced health, Thick wounded skin at the neck, Liquid in the eye/rinning eye, 3 secondary tumors, The mouse seemed anemic, could not be drawn blood from,



Large spleen, > 2 cm



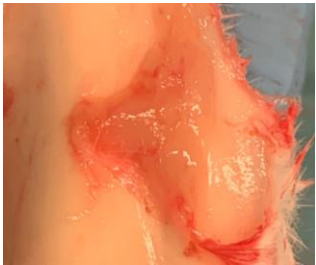
Red svollen legs



Red marks and svollen left shoulder. Tumor?



Tumor subcutaneous over the ribs left side



Xenograft? Not growing



Red marks and svollen right shoulder. Tumor?



Red marks on the spine



White lungs

Euthanization mouse #32 (P19-1b) 02.01.2020

Before euthanization:

- Reduced health
- Breathing heavily
- Thick irritated skin at the neck for at least 2 weeks
- Rinning eye
- Shoulders seemed enlarged

After euthanization:

- Could not be taken blood sample (anemic?)
- Enlarged spleen >2 cm
- White lungs
- All legs/shoulders red/svollen
- Red marks on the spine
- Xenograft did not seem to have grown
- Subcutaneous tumor flat over the ribs

Histology samples:

M32X	Xenograft
M32TS	Tumor Right Shoulder
M32M	Milt
M32LH	Lung and Heart
M32TR	Tumor over ribs right side
M32L	Leg left

Supplementary figure 1-32-4. Score sheets

NTNU

Score sheet FOTS:
Avdeling for komparativ medisin (AKM)

Responsible researcher:
Petterson

Animal ID:
(P19-16) (32) 462pp (2)

Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0											
	Reduced grooming	1											
	Minor distention of abdomen, rough hair coat	3											
	Hunchback or distended abdomen, inactive	18											
Behaviour (Level of activity)	Normal	0											
	Slightly reduced	1											
	Moderately reduced	3											
	Distressed behaviour due to growing tumour	3											
	Obviously reduced	5											
Body weight (Compared to body weight before experiment)	Isolated, inactive, lethargic	18											
	Body weight:		22,8		23,8	23,8	23,1	23,4	23,4	23,6	23,5	23,5	22,38
	No loss	0											
	Loss < 5%	1											
	Loss 5-9%	3											
Clinical signs (Infection, bleeding, discoloration)	Loss 10-14%	5											
	Loss ≥ 15%	18											
	Normal	0											
	Minor irritation around surgical wound	1											
	Moderate irritation/infected surgical wound	3											
Total:	Infected/open surgical wound	4 *											
	Tumour > 1.0 cm in diameter	10											
	Tumour > 1.5 cm in diameter	18											
	Ulcerous tumour	18											
	Comments, treatments etc:												

0-3: Normal

4-9: Pay attention to health state and consider treatment

10-13: Pay close attention to health state, consider treatment or euthanasia

14-18: Euthanasia *Start treatment with antibiotics. If no effect within 3 days, euthanize the animal

NTNU

Score sheet FOTS:
Avdeling for komparativ medisin (AKM)

Responsible researcher:
Petterson

Animal ID:
(P19-16) (32) 462pp (2)

Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0											
	Reduced grooming	1											
	Minor distention of abdomen, rough hair coat	3											
	Hunchback or distended abdomen, inactive	18											
Behaviour (Level of activity)	Normal	0											
	Slightly reduced	1											
	Moderately reduced	3											
	Distressed behaviour due to growing tumour	3											
	Obviously reduced	5											
Body weight (Compared to body weight before experiment)	Isolated, inactive, lethargic	18											
	Body weight:		22,3	22,3	22,6	23,7	24,5	22,3	23,6	22,7	22,5	22,6	
	No loss	0											
	Loss < 5%	1											
	Loss 5-9%	3											
Clinical signs (Infection, bleeding, discoloration)	Loss 10-14%	5											
	Loss ≥ 15%	18											
	Normal	0											
	Minor irritation around surgical wound	1											
	Moderate irritation/infected surgical wound	3											
Total:	Infected/open surgical wound	4 *											
	Tumour > 1.0 cm in diameter	10											
	Tumour > 1.5 cm in diameter	18											
	Ulcerous tumour	18											
	Comments, treatments etc:												

0-3: Normal

4-9: Pay attention to health state and consider treatment

10-13: Pay close attention to health state, consider treatment or euthanasia

14-18: Euthanasia *Start treatment with antibiotics. If no effect within 3 days, euthanize the animal

NTNU

Score sheet FOTS:
Avdeling for komparativ medisin (AKM)

Responsible researcher:
Petterson

Animal ID:
(P19-16) (32) 462pp (2)

Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0											
	Reduced grooming	1											
	Minor distention of abdomen, rough hair coat	3											
	Hunchback or distended abdomen, inactive	18											
Behaviour (Level of activity)	Normal	0											
	Slightly reduced	1											
	Moderately reduced	3											
	Distressed behaviour due to growing tumour	3											
	Obviously reduced	5											
Body weight (Compared to body weight before experiment)	Isolated, inactive, lethargic	18											
	Body weight:		22,6	23,8	23,8	21,9	23,2	24,2	22,6	23,7			
	No loss	0											
	Loss < 5%	1											
	Loss 5-9%	3											
Clinical signs (Infection, bleeding, discoloration)	Loss 10-14%	5											
	Loss ≥ 15%	18											
	Normal	0											
	Minor irritation around surgical wound	1											
	Moderate irritation/infected surgical wound	3											
Total:	Infected/open surgical wound	4 *											
	Tumour > 1.0 cm in diameter	10											
	Tumour > 1.5 cm in diameter	18											
	Ulcerous tumour	18											
	Comments, treatments etc:												

0-3: Normal

4-9: Pay attention to health state and consider treatment

10-13: Pay close attention to health state, consider treatment or euthanasia

14-18: Euthanasia *Start treatment with antibiotics. If no effect within 3 days, euthanize the animal

NTNU

Score sheet FOTS:
Avdeling for komparativ medisin (AKM)

Responsible researcher:
Petterson

Animal ID:
(P19-16) (32) 462pp (2)

Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0											
	Reduced grooming	1											
	Minor distention of abdomen, rough hair coat	3											
	Hunchback or distended abdomen, inactive	18											
Behaviour (Level of activity)	Normal	0											
	Slightly reduced	1											
	Moderately reduced	3											
	Distressed behaviour due to growing tumour	3											
	Obviously reduced	5											
Body weight (Compared to body weight before experiment)	Isolated, inactive, lethargic	18											
	Body weight:		24,4	24,4	23,6	23,5	24,7	24,9	24,2	23,9	24,2	24,2	
	No loss	0											
	Loss < 5%	1											
	Loss 5-9%	3											
Clinical signs (Infection, bleeding, discoloration)	Loss 10-14%	5											
	Loss ≥ 15%	18											
	Normal	0											
	Minor irritation around surgical wound	1											
	Moderate irritation/infected surgical wound	3											
Total:	Infected/open surgical wound	4 *											
	Tumour > 1.0 cm in diameter	10											
	Tumour > 1.5 cm in diameter	18											
	Ulcerous tumour	18											
	Comments, treatments etc:												

0-3: Normal

4-9: Pay attention to health state and consider treatment

10-13: Pay close attention to health state, consider treatment or euthanasia

14-18: Euthanasia *Start treatment with antibiotics. If no effect within 3 days, euthanize the animal

NTNU

Score sheet FOTS:
Avdeling for komparativ medisin (AKM)

Responsible researcher:
Petterson

Animal ID:
(P19-16) (32) 462pp (2)

Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0											
	Reduced grooming	1											
	Minor distention of abdomen, rough hair coat	3											
	Hunchback or distended abdomen, inactive	18											
Behaviour (Level of activity)	Normal	0											
	Slightly reduced	1											
	Moderately reduced	3											
	Distressed behaviour due to growing tumour	3											
	Obviously reduced	5											
Body weight (Compared to body weight before experiment)	Isolated, inactive, lethargic	18											
	Body weight:		24,4	24,4	23,5	24,2	24,4	24,4	24,4	24,4	24,4	24,4	
	No loss	0											
	Loss < 5%	1											
	Loss 5-9%	3											
Clinical signs (Infection, bleeding, discoloration)	Loss 10-14%	5											
	Loss ≥ 15%	18											
	Normal	0											
	Minor irritation around surgical wound	1											
	Moderate irritation/infected surgical wound	3											
Total:	Infected/open surgical wound	4 *											
	Tumour > 1.0 cm in diameter	10											
	Tumour > 1.5 cm in diameter	18											
	Ulcerous tumour	18											
	Comments, treatments etc:												

0-3: Normal

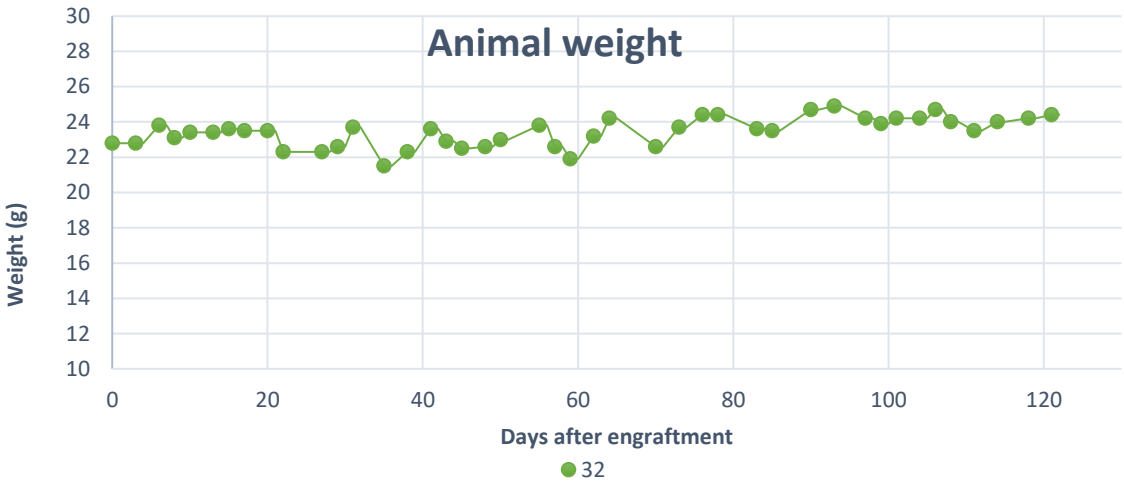
4-9: Pay attention to health state and consider treatment

10-13: Pay close attention to health state, consider treatment or euthanasia

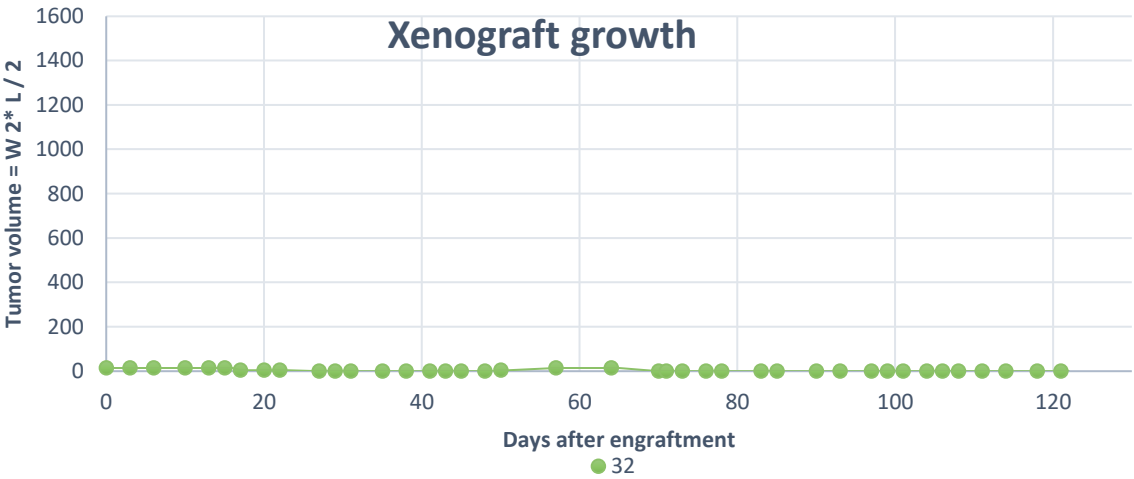
14-18: Euthanasia *Start treatment with antibiotics. If no effect within 3 days, euthanize the animal

Supplementary figure 1-32-5.
Mouse and xenograft growth curves

Weight curve



Xenograft growth curve



Secondary tumor growth curve

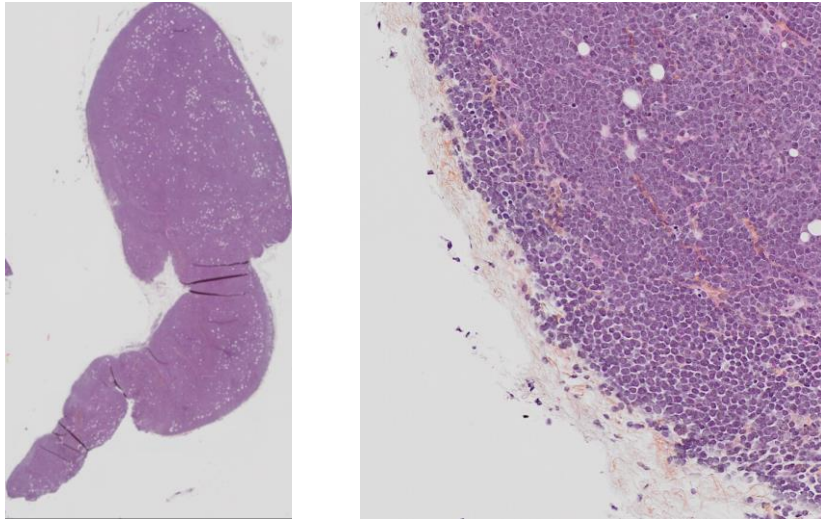
3 secondary tumors found at the day of euthanization.
Size was not measured.

Supplementary figure 1-32-6. Histology pictures

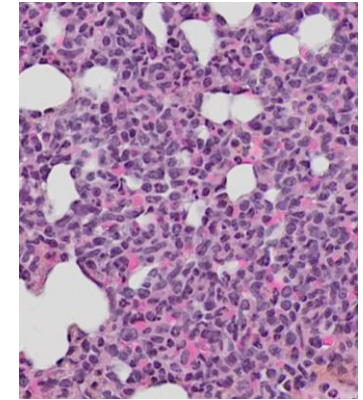
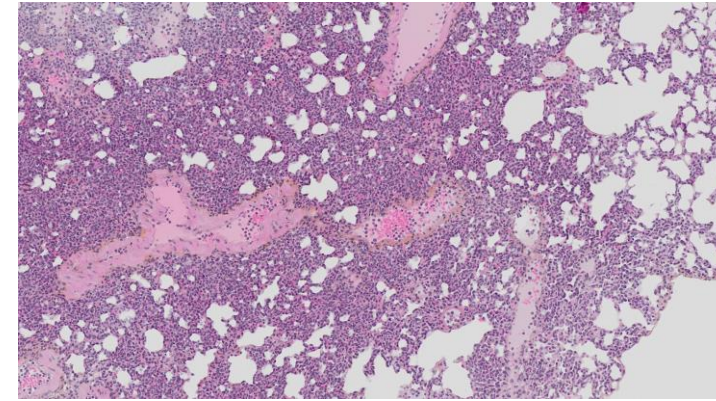
M32LH

Page 148

M32X

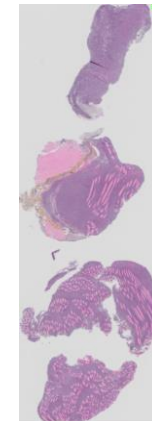
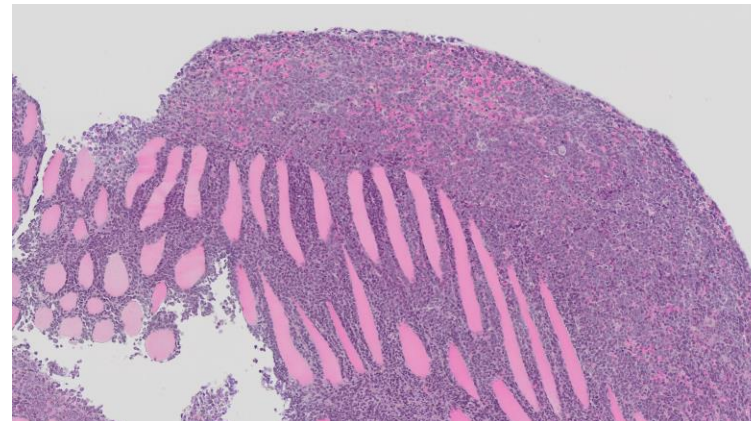


- Xenograft did not grow. During necropsy what was believed to be remainings of the xenograft was sampled. However HES staining showed that it was probably not the xenograft, but another tissue structure.



- Dense areas in the lungs consisting of lymphoid cells

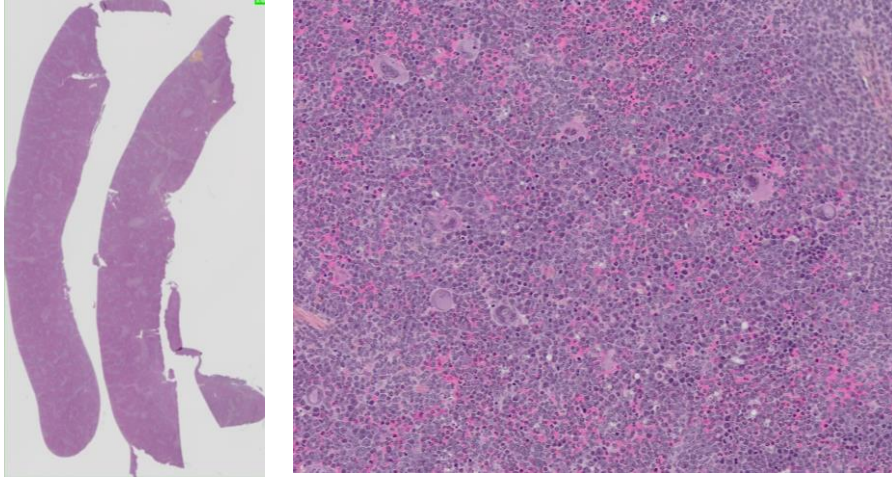
M32L



- Red swollen leg
- Lymphoid tumor cells present
- Bone structures

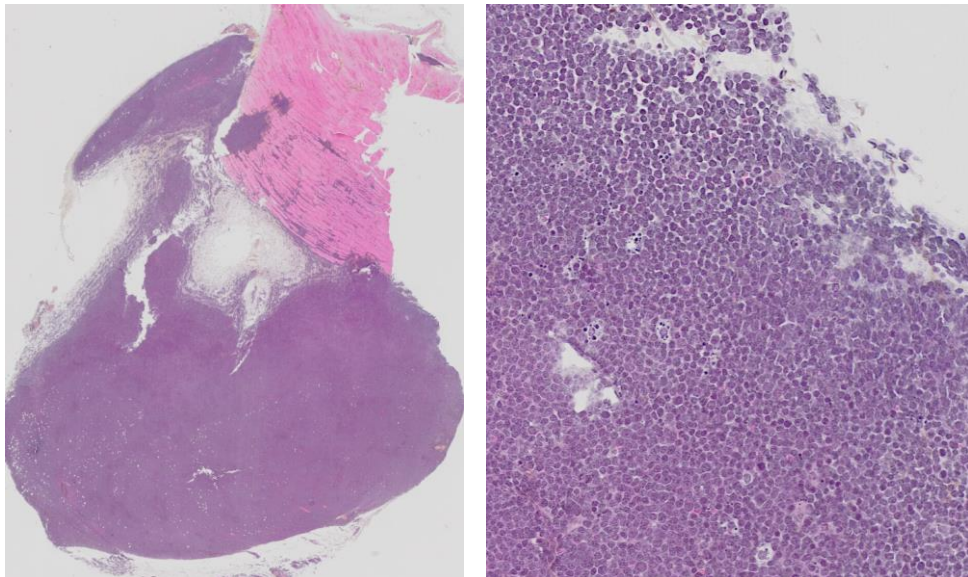
Supplementary figure 1-32-6. Histology pictures

M32M



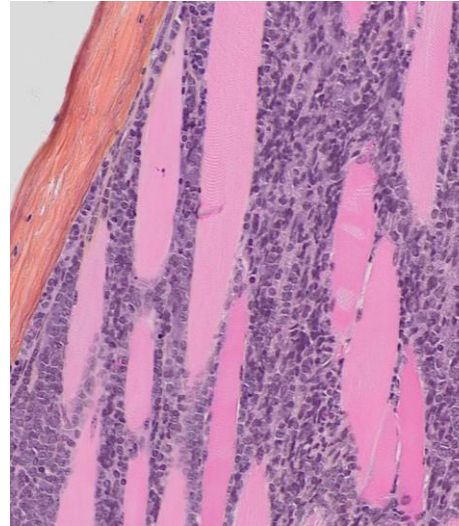
- Large spleen > 2 cm with lymphoid cells

M32TR – secondary tumor



- Lymphoid tumor cells

M32TS



- Ca 1 cm tumor on right shoulder
- Bone structures
- Lymphoid tumor cells

Supplementary figure 1-32-7. Histology and immunohistochemistry pictures

M32TR – secondary tumor

- Lymphoma
- IHC staining for human specific Ki67 and CD45 negative
- EBER-ISH staining for EBV negative
- Most likely a mouse tumor

Mouse

HES

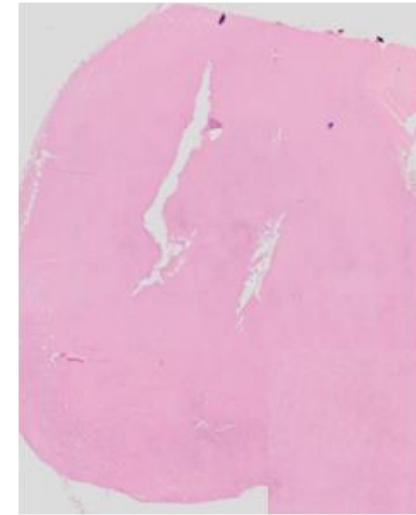
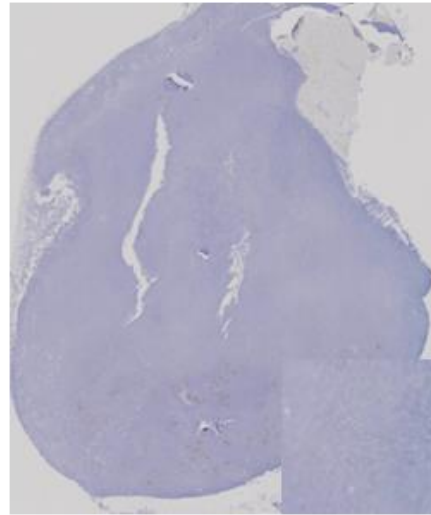
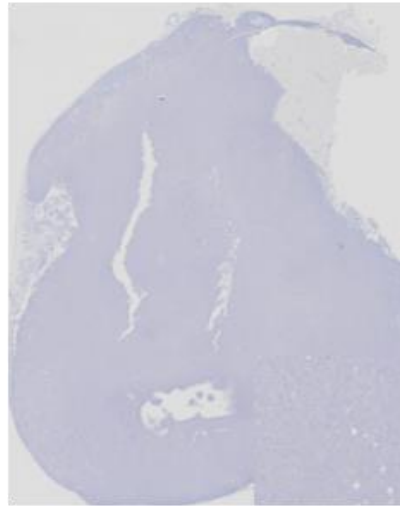
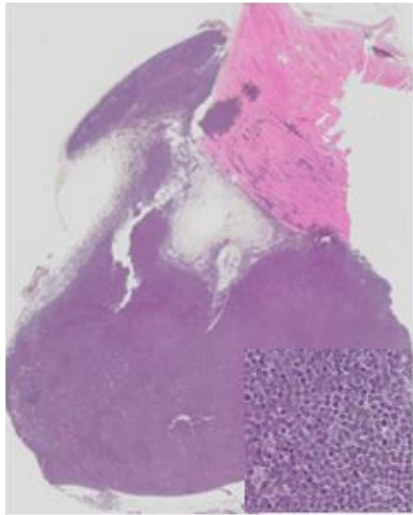
Ki67

CD45

EBER-ISH

CD20

#32



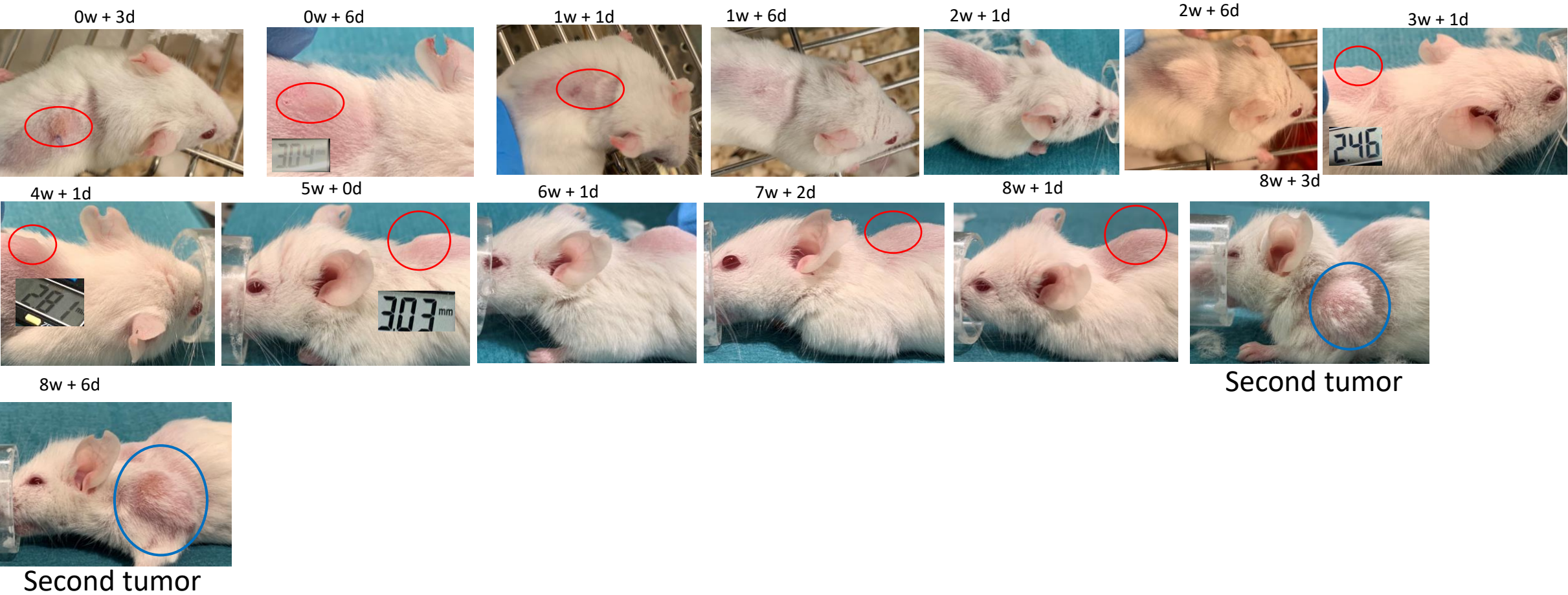
Mouse 33

- Surgery date: 03.09.19
 - Age (weeks) 33
 - Weight (g) 21.9
 - Tumor fragment P19-2a
 - Fragment size 3 x 3 mm
 - Ear marks 3



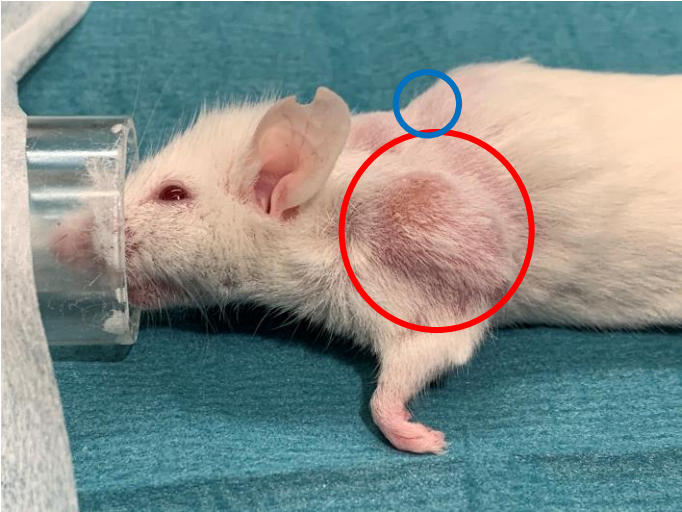
Supplementary figure 1-33-1. Pictures from the engraftment day

Supplementary figure 1-33-2. Pictures from follow up and xenograft size measurement

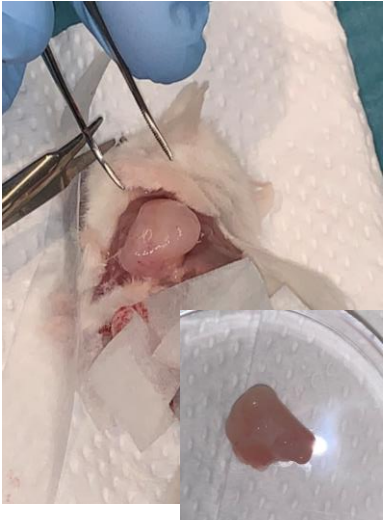


Supplementary figure 1-33-3. Pictures from euthanization (04.11.19)

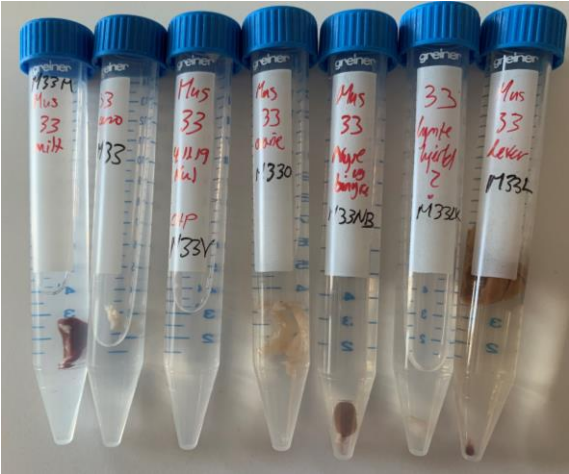
- No treatment given (xenograft not growing)
- Euthanized due to large secondary tumor before growth of xenograft was established
- Secondary tumor: size: 14 x 9 mm



Blue; no visible xenograft
Red; secondary tumor



Secondary tumor



Histology samples

Mus 33		
Mus 33	xenograft 4.11	M33
Mus 33	4.11.19 Milt	M33M
Mus 33	4.11.19 Kul venstre	M33V
-11-	ovarie	M33O
-11-	nyre og binyre	M33NB
-11-	lymfekjærl ?	M33LK
-11-	lever	M33L

Xenograft
Spleen
Tumor left
Ovary
Kidney
Lymph node?
Liver

Naming of histology samples



Enlarged spleen

903™ Protein Saver Card
For Research Use Only
Not for use in diagnostic procedures

Tuck Cover Here

Name ØMus 33 (P19-2a) Kul

Date 04.11.19 CHP



Blood sampling

Supplementary figure 1-33-4. Score sheets

NTNU Score sheet FOTS: Avdeling for komparativ medisin (AKM) Responsible researcher: Pettersen Animal ID: (P19-2a) 33 WUPB 3

Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0	3/9	4/9	6/9	9/9	11/9	13/9	16/9	18/9	20/9	23/9	25/9
	Reduced grooming	1											
	Minor distention of abdomen, rough hair coat	3											
	Hunchback or distended abdomen, inactive	18											
Behaviour (Level of activity)	Normal	0											
	Slightly reduced	1											
	Moderately reduced	3											
	Distressed behaviour due to growing tumour	3											
	Obviously reduced	5											
Body weight (Compared to body weight before experiment)	Isolated, inactive, lethargic	18											
	Body weight:		21.9		21.7	22.5	22.6	23.0	22.6	23.2	23.5	22.6	22.3
	No loss	0											
	Loss < 5%	1											
	Loss 5-9%	3											
Clinical signs (Infection, bleeding, discoloration)	Loss 10-14%	5											
	Loss ≥ 15%	18											
	Normal	0											
	Minor irritation around surgical wound	1											
	Moderate irritation/infected surgical wound	3											

Comments, treatments etc:

6-3: Normal
4-9: Pay attention to health state and consider treatment
10-13: Pay close attention to health state, consider treatment or euthanasia
14-18: Euthanasia *Start treatment with antibiotics. If no effect within 3 days, euthanize the animal

NTNU Score sheet FOTS: Avdeling for komparativ medisin (AKM) Responsible researcher: Pettersen Animal ID: (P19-2a) 33 WUPB 3

State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
Normal	0	25/9	30/9	2/10	4/10	8/10	11/10	14/10	16/10	18/10	21/10		
Reduced grooming	1												
Minor distention of abdomen, rough hair coat	3												
Hunchback or distended abdomen, inactive	18												
Normal	0												
Slightly reduced	1												
Moderately reduced	3												
Distressed behaviour due to growing tumour	3												
Obviously reduced	5												
Isolated, inactive, lethargic	18												
Body weight:		22.3	22.3	22.5	22.3	22	21.6	22.1	21.6	22.1	22.9		
No loss	0												
Loss < 5%	1												
Loss 5-9%	3												
Loss 10-14%	5												
Loss ≥ 15%	18												
Normal	0												
Minor irritation around surgical wound	1												
Moderate irritation/infected surgical wound	3												
Infected/open surgical wound	4 *												
Tumour > 1.0 cm in diameter	10												
Tumour > 1.5 cm in diameter	18												
Ulcerous tumour	18												
Total:													
Comments, treatments etc:													

NTNU Score sheet FOTS: Avdeling for komparativ medisin (AKM) Responsible researcher: Pettersen Animal ID: (P19-2a) 33 WUPB 3

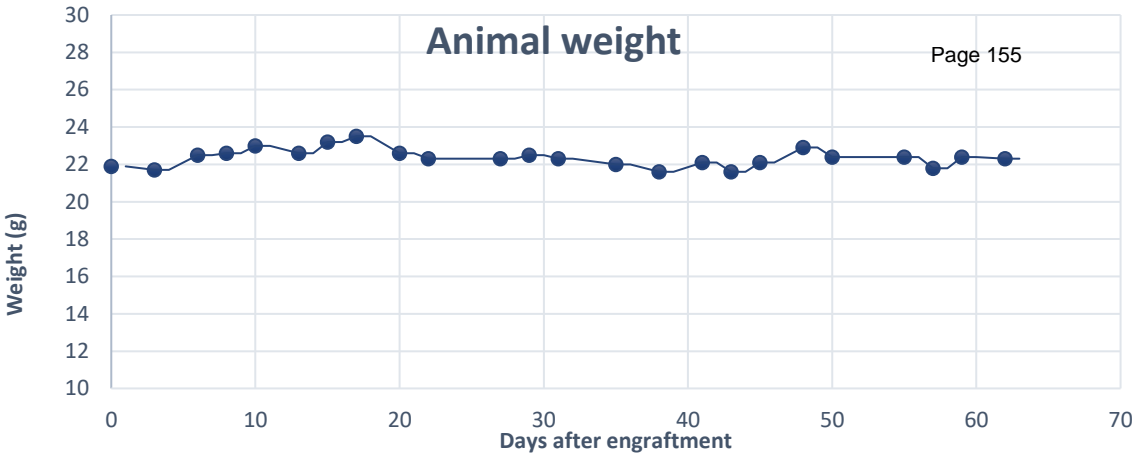
Parameter	State	Assessment scale	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date	Date
General appearance	Normal	0	2/10	23/10	28/10	30/10	1/11	4/11					
	Reduced grooming	1											
	Minor distention of abdomen, rough hair coat	3											
	Hunchback or distended abdomen, inactive	18											
Behaviour (Level of activity)	Normal	0											
	Slightly reduced	1											
	Moderately reduced	3											
	Distressed behaviour due to growing tumour	3											
	Obviously reduced	5											
Body weight (Compared to body weight before experiment)	Isolated, inactive, lethargic	18											
	Body weight:		22.9	22.4	22.4	21.8	22.4	22.3					
	No loss	0											
	Loss < 5%	1											
	Loss 5-9%	3											
Clinical signs (Infection, bleeding, discoloration)	Loss 10-14%	5											
	Loss ≥ 15%	18											
	Normal	0											
	Minor irritation around surgical wound	1											
	Moderate irritation/infected surgical wound	3											

Comments, treatments etc:

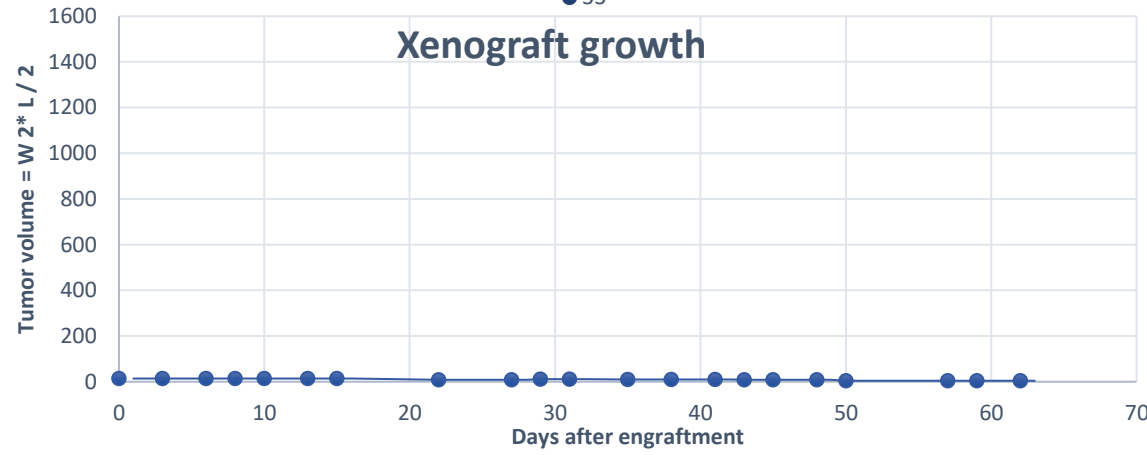
6-3: Normal
4-9: Pay attention to health state and consider treatment
10-13: Pay close attention to health state, consider treatment or euthanasia
14-18: Euthanasia *Start treatment with antibiotics. If no effect within 3 days, euthanize the animal

Supplementary figure 1-33-5.
Mouse, xenograft and secondary
tumor growth curves

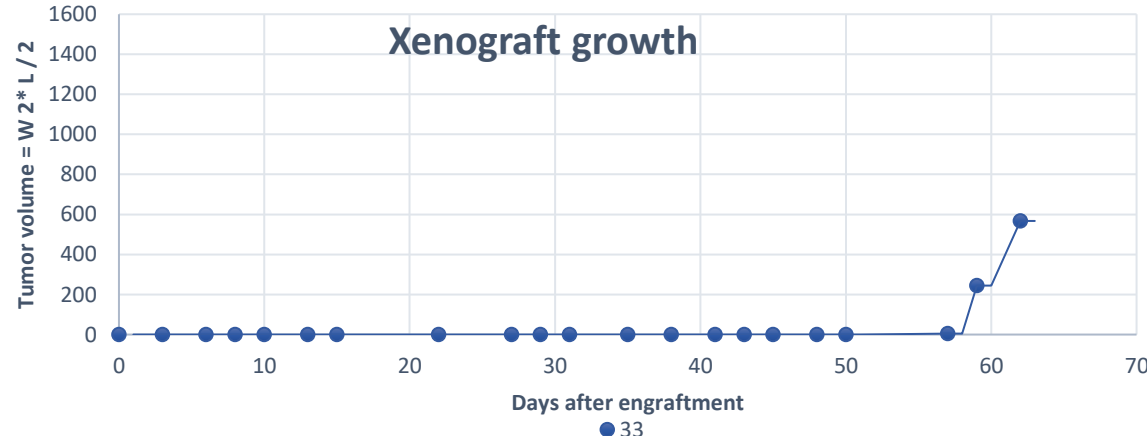
Weight curve

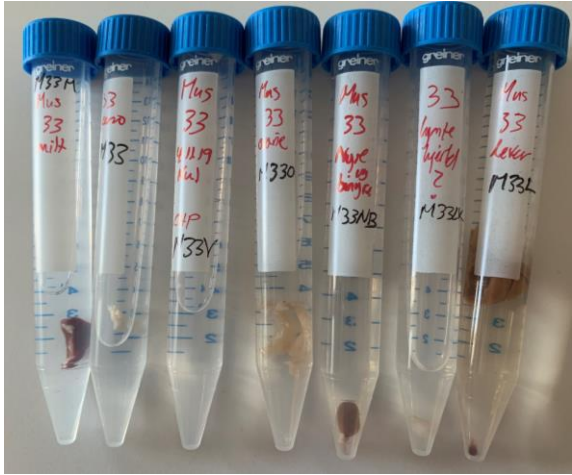
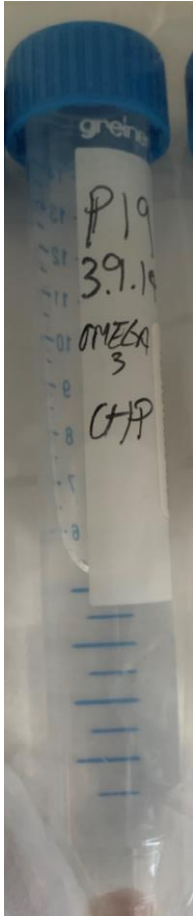


Xenograft growth curve



Secondary tumor growth curve





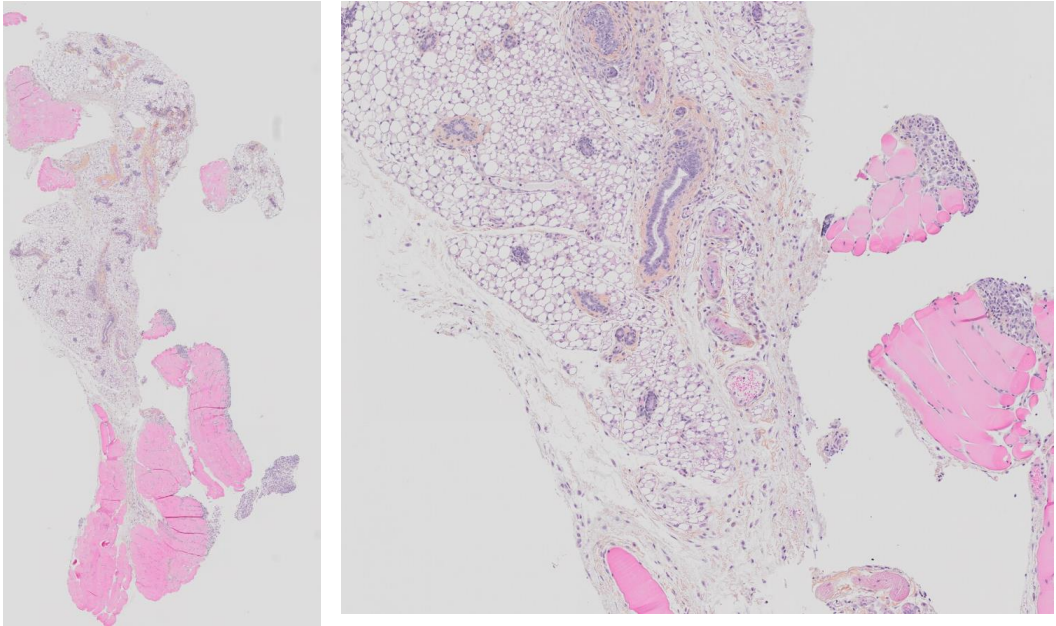
Histology samples

Mus 33		
Mus 33	xenograft 4.11	M33
Mus 33	4.11.19 Milt	M33M
Mus 33	4.11.19 Kulvenstre	M33V
- -	ovarie	M330
- -	nyreog binyre	M33NB
- -	lymfelysterel ?	M33LK
- -	lever	M33L

- Xenograft
- Spleen
- Tumor left
- Ovary
- Kidney
- Lymph node?
- Liver

Naming of histology samples

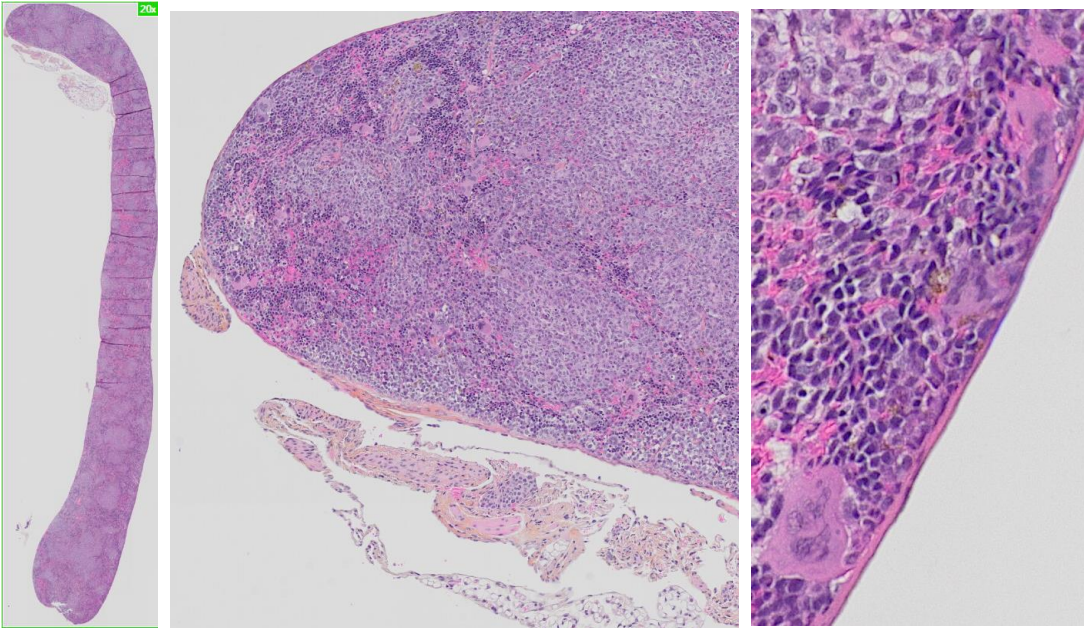
M33X



•Probably not the xenograft due to most muscle cells surrounded by muscle and connective tissue and lymphoid tumor cells, but not epithelial cells as in the colon

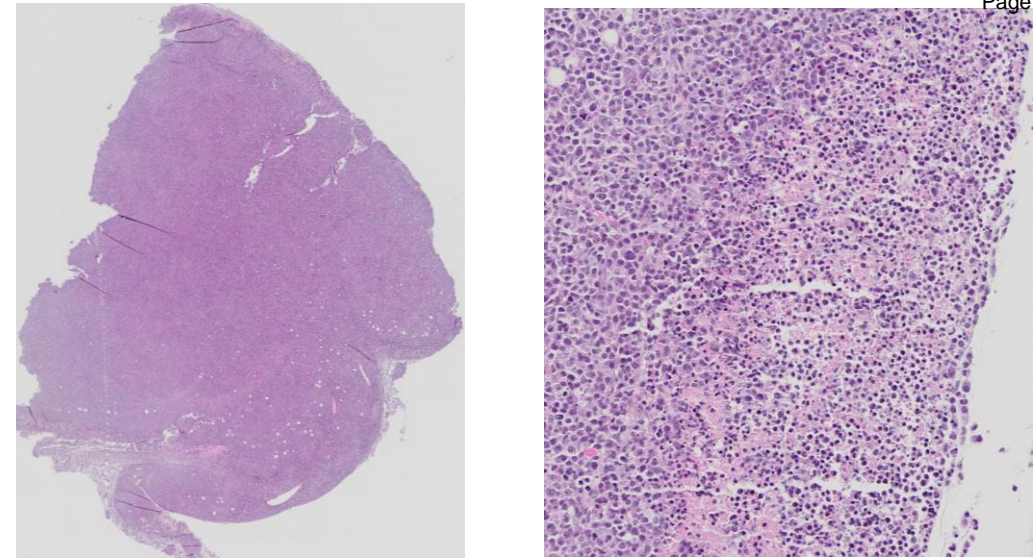
Supplementary figure 1-33-6. Histology pictures

M33M (spleen)



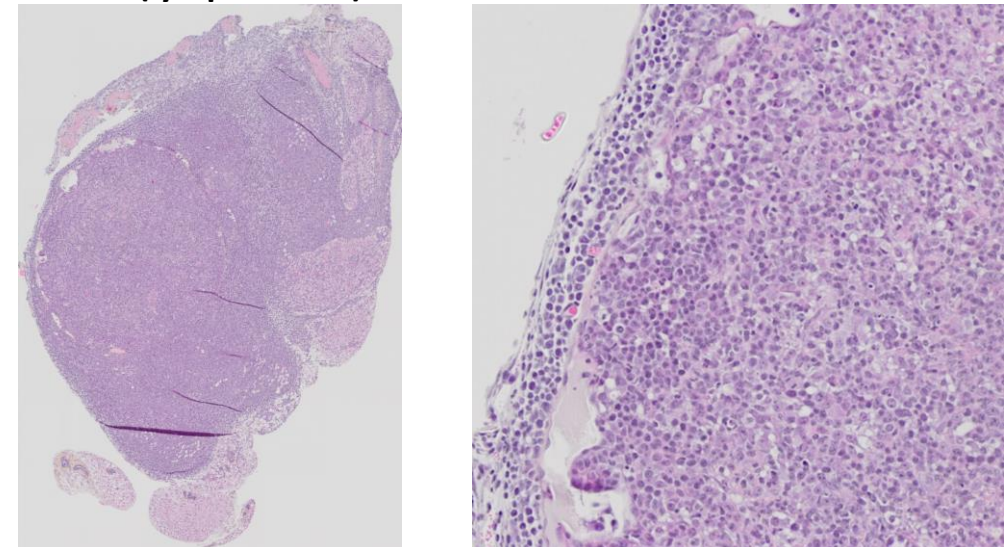
- Plenty lymphoid tumor cells in the spleen
- Measured on 1.3 cm on the slide, 2.56 cm calculated from picture of spleen in petri dish after euthanization
- Red areas with possible bleedings
- Can see macrophages, giant cells/ghost cells

M33V (tumor left shoulder)



- Plenty lymphoid tumor cells packed dense together
- Smaller areas with necrosis

M33LK (lymph node?)



- Plenty lymphoid tumor cells densely packed together

Supplementary figure 1-33-7. Histology and immunohistochemistry pictures

Page 158

M33V (tumor left shoulder)

-IHC staining for Ki67 and CD45

-EBER-ISH staining for EBV

Mouse

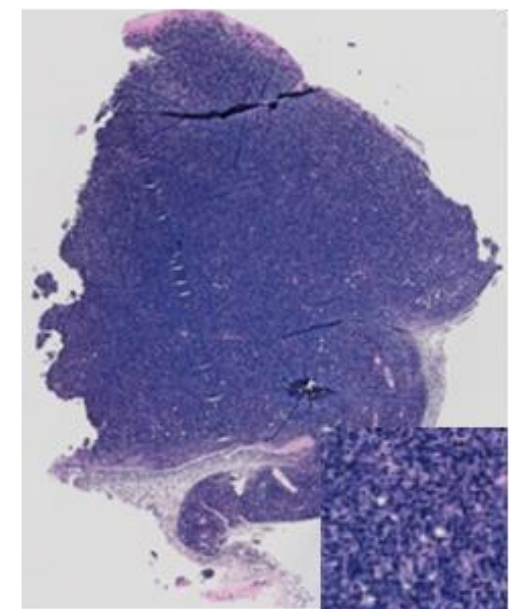
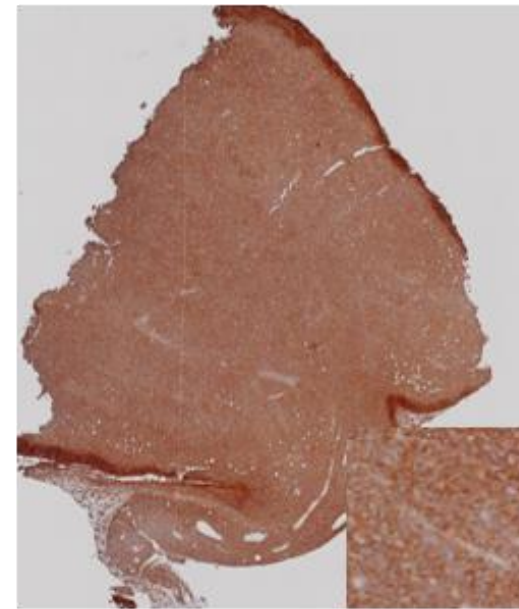
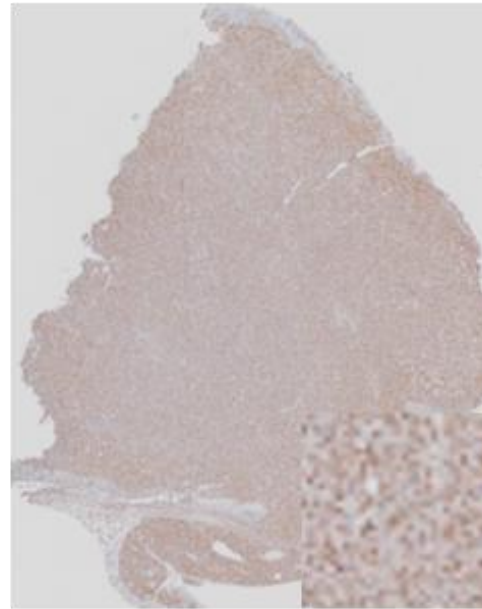
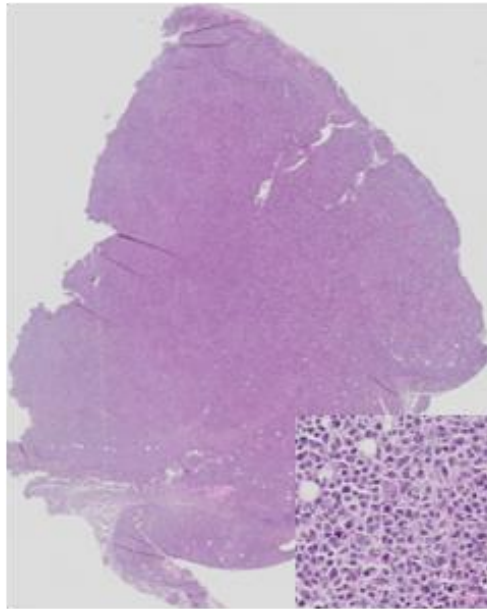
HES

Ki67

CD45

EBER-ISH

#33



Supplementary file 2

Date:	Mouse nr:	Tumor:	Patient:
Heating chamber 37°C		HiBiscrub, Klorhexidin, 4xNaCl	
Wash surface areas with ethanol			
Heating pad 37°C			
Weight			
Anasthesia chamber		N ₂ O ₂ 60 % - O ₂ 40 % - Isofluran 2%	
Anasthesia mask		N ₂ O ₂ 60 % - O ₂ 20 % - Isofluran 1.5-2%	
Eye gel			
Ear mark			
Shaving			
Change surgery tissue			
Fixate feet with tape			
Metacam – systemic anesthesia (~0.1 ml)		Orange canyle	
Wash surgery area: HiBiscrub			
Wash surgery area: Chlorhexidine			
Marcain – local anesthesia (~0.08 ml)		Yellow canyle	
Pinch foot with forceps			
Make a cut with scalpel			
Use sizzors to make a pocket under the skin			
Flush tumor fragment with NaCl			
Stich the wound			
Take a picture of the mouse/surgery area			
Exuipment: Eye gel Heating pad 2 x Sterile surgery tissues HiBiscrub Chlorhexidine Autoclaved surgery instruments (2 x forceps, 2 x sizzors, Suture instruments) 2 x Scalpels 4 x sutures (nr 5) 8 x 1 ml syringe + 8 x yellow canyle 2 x white plastic dish for HiBiscrub and ethanolS Sterilizer for surgery instruments between animals Sterile q tips Tape Ear mark instrument NaCl Metacam Marcain		Comments:	
Performed by: _____			

Supplementary figure 2-1. Bullet point form for surgery

Sample: Surgery/Anesthetic Log

Date	Client ID	Animal ID	Species & Breed	Age	Sex	Weight (kg)	Patient Status	Anesthetic Regimes (Name/Dose/Route)			Procedure	Time (min.)		Veterinarian
								Pre-Op	Post-Op	Maintenance		Anes.	Sx	
11/3		1	CIEANOS		F	20g				metacam 0.1ml morgain 0.008ml isoflurane 2%				Knut
12/3		1	CIEANOS		F	20g				metacam 0.1ml morgain 0.008ml isoflurane 2%				Knut
25/3		1	CIEANOS		F	ca 20g				metacam 0.1ml morgain 0.008ml isoflurane 2%				Knut
25/3		1	CIEANOS		F	ca 20g				metacam 0.1ml morgain 0.008ml isoflurane 2%				Knut
26/3		1	CIEANOS		F	ca 20g				metacam 0.1ml morgain 0.008ml isoflurane 2%				Knut
26/3		1	CIEANOS		F	ca 20g				metacam 0.1ml morgain 0.008ml isoflurane 2%				Knut
1/4-19		12	CIEANOS		F	20.5g				metacam 0.1ml morgain 0.008ml isoflurane 2%				Knut/Helle
1/4-19		2	CIEANOS		F	18.5g				metacam 0.1ml morgain 0.008ml isoflurane 2%				Knut/Helle
1/4-19		3	CIEANOS		F	18.15g				metacam 0.1ml morgain 0.008ml isoflurane 2%				Knut/Helle
1/4-19		4	CIEANOS		F	18.35g				metacam 0.1ml morgain 0.008ml isoflurane 2%				Knut/Helle
1/4-19		19 (1)	CIEANOS		F	20.62g				metacam 0.1ml morgain 0.008ml isoflurane 2%				Caroline
"		20 (2)	CIEANOS		F	24.63				metacam 0.1ml morgain 0.008ml isoflurane 2%				Helle
"		21 (3)	CIEANOS		F	20.3				metacam 0.1ml morgain 0.008ml isoflurane 2%				Helle
"		22 (4)	CIEANOS		F	21.2				metacam 0.1ml morgain 0.008ml isoflurane 2%				Caroline
"		21 (3)	CIEANOS		F					metacam 0.1ml morgain 0.008ml isoflurane 2%				Caroline
"		22 (4)	CIEANOS		F					metacam 0.1ml morgain 0.008ml isoflurane 2%				Caroline
"		19 (1)	CIEANOS		F					metacam 0.1ml morgain 0.008ml isoflurane 2%				Caroline

Sample: Surgery/Anesthetic Log

Date	Client ID	Animal ID	Species & Breed	Age	Sex	Weight (kg)	Patient Status	Anesthetic Regimes (Name/Dose/Route)			Procedure	Time (min.)		Veterinarian
								Pre-Op	Post-Op	Maintenance		Anes.	Sx	
20/8/19		23 (1)	CIEANOS	7m	F	24g	pinpoint	metacam 0.1ml morgain 0.008ml isoflurane 2%		post-op 24h	PDX	ca 20min		Helle/Karoline
"		24 (2)	CIEANOS	"	"	"	OK	metacam 0.1ml morgain 0.008ml isoflurane 2%		post-op 24h	PDX	"	"	"
"		25 (3)	CIEANOS	"	"	"	"	metacam 0.1ml morgain 0.008ml isoflurane 2%		post-op 24h	PDX	"	"	"
"		26 (4)	CIEANOS	"	"	"	"	metacam 0.1ml morgain 0.008ml isoflurane 2%		post-op 24h	PDX	"	"	"
21/8/19		27 (1)	CIEANOS	"	"	"	"	metacam 0.1ml morgain 0.008ml isoflurane 2%		post-op 24h	PDX	"	"	"
"		28 (2)	CIEANOS	"	"	"	"	metacam 0.1ml morgain 0.008ml isoflurane 2%		post-op 24h	PDX	"	"	"
"		29 (3)	CIEANOS	"	"	"	"	metacam 0.1ml morgain 0.008ml isoflurane 2%		post-op 24h	PDX	"	"	"
"		30 (4)	CIEANOS	"	"	"	"	metacam 0.1ml morgain 0.008ml isoflurane 2%		post-op 24h	PDX	"	"	"
3/9/19		31 (1)	CIEANOS	"	"	"	"	metacam 0.1ml morgain 0.008ml isoflurane 2%		post-op 24h	PDX	"	"	"
"		32 (2)	CIEANOS	"	"	"	"	metacam 0.1ml morgain 0.008ml isoflurane 2%		post-op 24h	PDX	"	"	"
"		33 (3)	CIEANOS	"	"	"	"	metacam 0.1ml morgain 0.008ml isoflurane 2%		post-op 24h	PDX	"	"	"
"		18 (4)	CIEANOS	"	"	"	"	metacam 0.1ml morgain 0.008ml isoflurane 2%		post-op 24h	PDX	"	"	"

Supplementary figure 2-2. Picture of anesthesia logs

Supplementary file 3

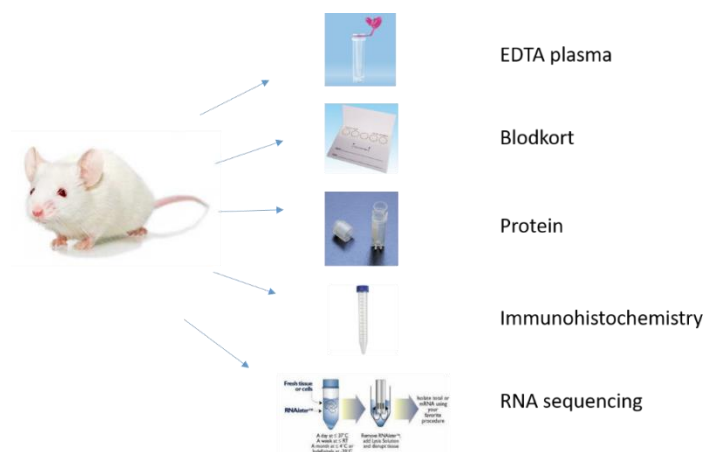
Procedure for euthanization, blood- and tissue sampling of CIA NOG mice

Human endpoints:

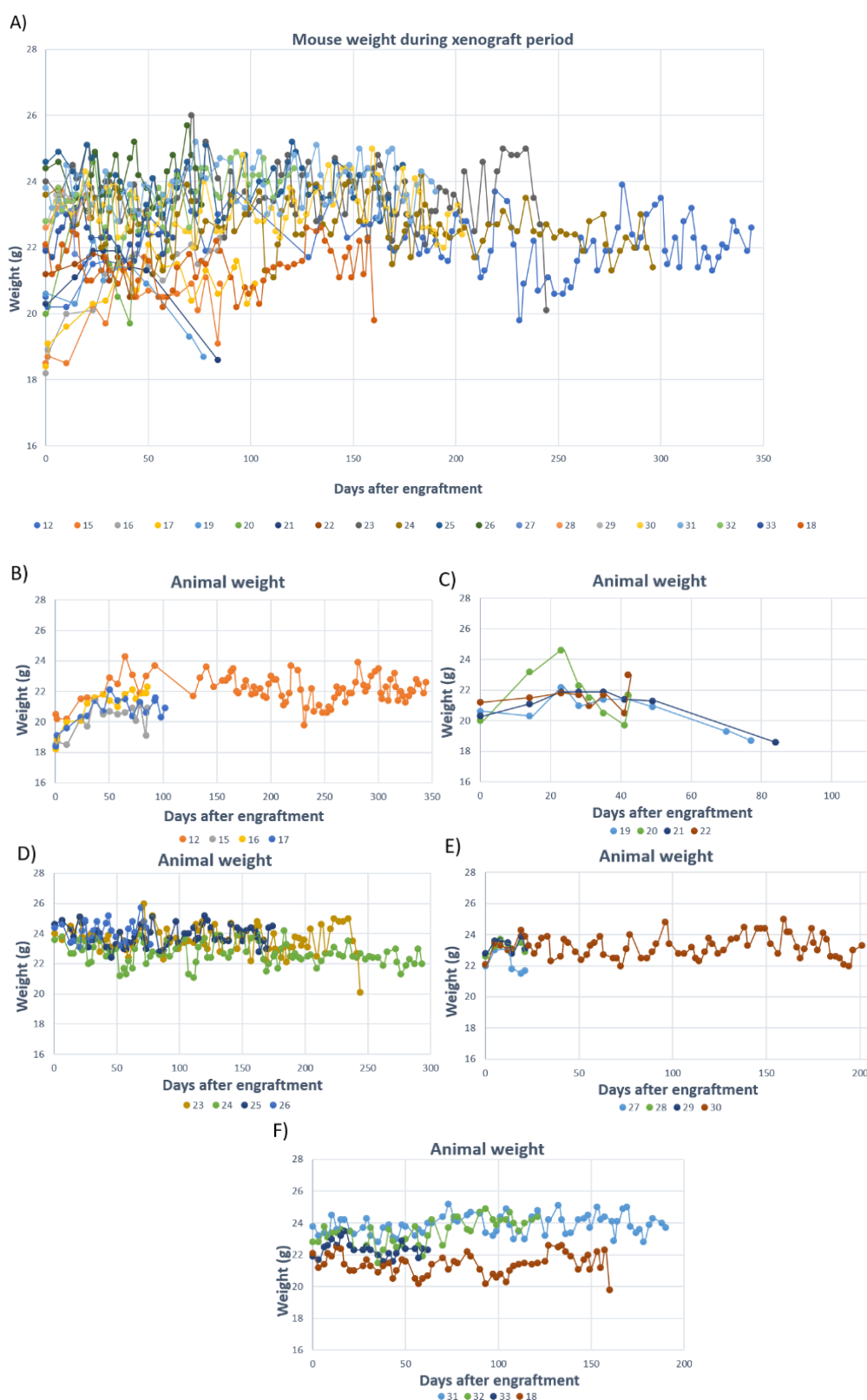
- 8 weeks treatment with Smartfish Remune with fishoil or placebo
- Tumor volume ~1500 mm³ or >10 % loss of body weight

Procedure:

1. Register mouse weight
2. Put mouse into anesthesia chamber with isoflurane 2% (O₂, N₂O)
3. Place the mouse on the back on a heating pad with surgery tissue and anesthesia mask
4. Take blood sample by heart punctation
 - a. Collect full blood in a EDTA tube
 - b. Spot 50 µl full blood onto a Whatman filtercard (dry 2 h at RT, freeze -80°C)
 - c. Mark blood cards with mouse name and date
5. Centrifuge EDTA tube to prepare blood plasma (4°C, 3000 rpm, 10 min)
6. Measure tumor size
7. Shave and wash (EtOH) the tumor area
8. Cut out the PDX using a scalpel
 - a. Remove necrotic tissue/connective tissue
 - b. Take 4 samples from the tumor (Histology prioritized if small PDX)
 - i. 4x4x4 mm for **histology** in a tube with 4% NBF
 - ii. 4x4x4 mm for **RNA-sekvensering** in a cryotube (snapfreeze N₂, then -80°C)
 - iii. 4x4x4 for **protein** isolation in cryotubes (snapfreeze in N₂, then -80°C)
 - iv. The rest of the PDX is frozen in fragments in cryotube (snapfreeze N₂, -80°C)
9. Wash (EtOH) and open the abdomen
10. Cut the aorta
11. Shut of the anastesia gas
12. Perform necroscopy
 - a. Organs are sampled on tubes with 4% NBF
13. Fill out autopsy card
14. Pipett the blood plasma into a sterile tube and freeze at -80°C
15. Mark plasma tubes (mouse ID, plasma, date and initials)



Supplementary material 4: Mice weight curves



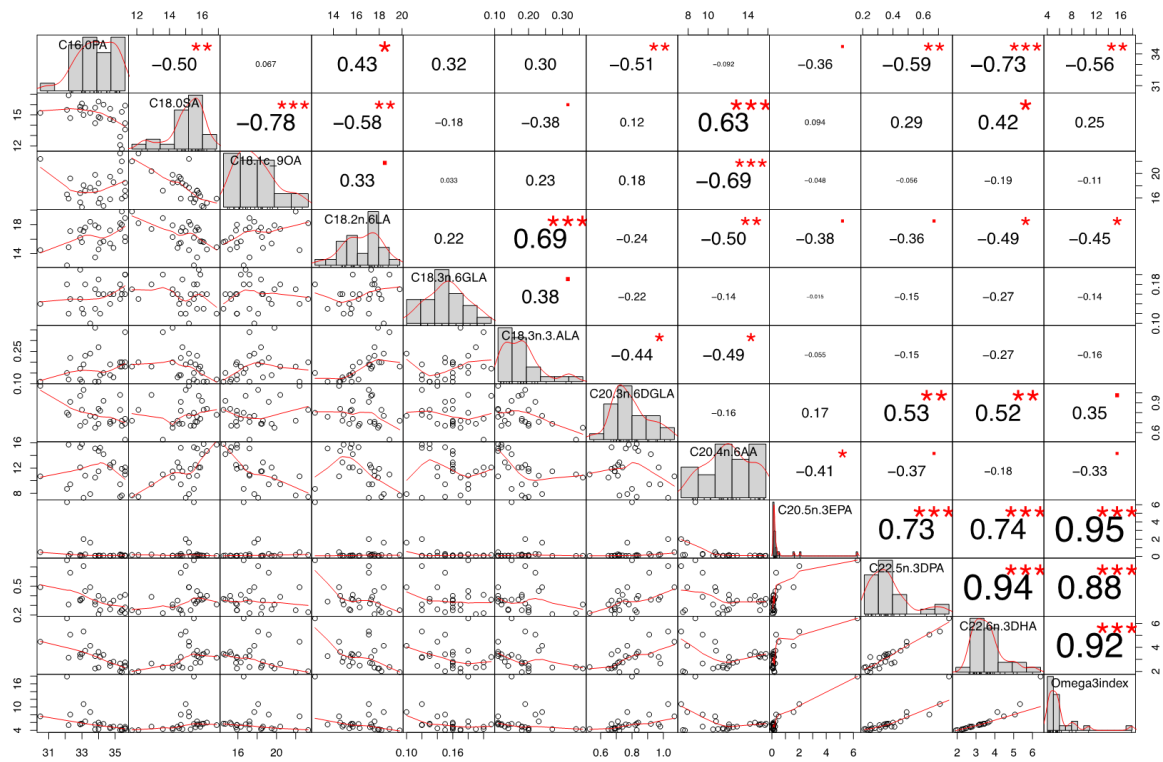
Supplementary figure 4-1. Animal weight curves for A) all mice B) mouse #12, 15, 16 and 17 (tumor fragments from patient 3), C) mouse #19, 20, 21 and 22 (tumor fragments from patient 11), D) mouse #23, 24, 25 and 26 (tumor fragments from patient 17), E) mouse #27, 28, 29 and 30 (tumor fragments from patient 18), and F) mouse #31, 32, 33 and 18 (tumor fragments from patient 19).

Supplementary file 5

Supplementary Table 5-1. Fatty acid profiling of patient and mouse whole blood

Sample ID	Tumor fragment	Treatment status	Fatty acid methyl ester content (g FAME / 100 g FAME)											Omega-3 index
			C16:0 PA	C18:0 SA	C18:1 c-9 OA	C18:2 n-6 LA	C18:3 n-6 GLA	C18:3 n-3 ALA	C20:3 n-6 DGLA	C20:4 n-6 AA	C20:5 n-3 EPA	C22:5 n-3 DPA	C22:6 n-3 DHA	
P3			25.7	16.2	23.7	19.7	0.08	0.39	1.17	8.13	0.85	1.05	2.89	6.12
P11			29.0	12.9	24.6	22.0	0.10	0.60	1.18	5.97	0.91	0.80	1.90	4.99
P17			31.3	13.0	24.1	19.0	0.28	0.44	0.97	4.89	2.02	0.92	3.07	8.00
P18			26.7	15.8	24.3	19.1	0.20	0.30	1.28	8.15	0.83	1.13	2.29	5.35
P19			29.6	14.8	26.2	17.4	0.19	0.33	1.58	6.88	0.47	0.89	1.64	4.06
M12	P3-1a	No	34.9	14.5	18.6	14.8	0.16	0.13	0.72	12.9	0.10	0.35	2.81	4.98
M15	P3-1b	Start	35.4	15.3	15.9	18.0	0.16	0.20	0.67	11.9	0.07	0.25	2.25	4.24
M15	P3-1b	PLACEBO	35.3	12.9	20.4	17.4	0.18	0.18	0.98	9.45	0.24	0.39	2.66	4.99
M16	P3-2a	Start	34.7	15.6	15.8	17.2	0.16	0.19	0.71	12.5	0.08	0.32	2.71	4.98
M16	P3-2a	OMEGA-3	33.1	15.0	18.1	17.1	0.12	0.19	1.03	7.30	2.02	0.71	5.34	10.80
M17	P3-2b	Start	33.8	14.2	19.8	17.9	0.17	0.36	0.65	10.5	0.09	0.31	2.24	4.26
M18	P19-2b	No	35.6	13.6	17.2	18.9	0.20	0.34	0.53	11.0	0.07	0.22	2.36	4.37
M19	P11-1a	OMEGA-3	32.1	15.5	16.6	12.4	0.18	0.15	0.80	8.72	6.30	0.77	6.43	17.9
M20	P11-1b	Start	32.9	15.5	15.3	16.2	0.15	0.12	0.67	15.3	0.06	0.35	3.43	5.66
M20	P11-1b	PLACEBO	35.4	11.7	22.0	19.8	0.17	0.18	0.72	7.68	0.19	0.25	1.93	4.01
M22	P11-2b	Start	33.0	16.1	14.5	15.6	0.13	0.11	0.83	15.8	0.09	0.37	3.47	5.75
M22	P11-2b	OMEGA-3	35.3	12.1	23.3	18.2	0.15	0.20	0.83	7.47	0.17	0.23	2.01	4.09
M23	P17-1a	Start	34.7	14.6	19.5	15.4	0.14	0.14	0.69	12.1	0.09	0.26	2.46	4.53
M23	P17-1a	PLACEBO	30.5	15.2	22.4	14.5	0.14	0.11	1.07	10.7	0.50	0.49	4.48	7.62
M24	P17-1b	No	34.1	14.7	15.9	15.5	0.12	0.14	0.82	15.2	0.10	0.25	3.20	5.43
M25	P17-2a	No	35.6	15.9	16.3	15.7	0.20	0.18	0.74	12.1	0.12	0.41	2.75	4.93
M26	P17-2b	Start	35.6	14.2	18.5	16.3	0.16	0.20	0.69	11.5	0.10	0.28	2.48	4.57
M26	P17-2b	OMEGA-3	32.3	14.7	19.2	17.1	0.15	0.22	0.91	9.45	0.31	0.64	5.07	8.09
M27	P18-1a	Start	34.3	16.0	14.7	15.7	0.16	0.15	0.92	14.2	0.11	0.36	3.38	5.68
M27	P18-1a	OMEGA-3	32.9	15.8	16.8	17.3	0.21	0.17	0.97	12.1	0.17	0.36	3.20	5.56
M28	P18-1b	Start	34.0	16.3	15.2	14.6	0.16	0.11	0.84	14.7	0.11	0.40	3.63	6.00
M28	P18-1b	PLACEBO	33.2	15.7	17.2	17.6	0.18	0.23	0.71	10.8	0.26	0.45	3.73	6.33
M29	P18-2a	OMEGA-3	33.5	15.2	17.7	18.4	0.10	0.24	0.77	7.91	1.60	0.49	4.14	8.72
M30	P18-2b	No	32.2	16.9	15.9	14.9	0.12	0.12	0.78	15.7	0.08	0.31	3.14	5.35
M31	P19-1a	No	33.8	15.7	17.2	13.5	0.13	0.11	0.76	15.1	0.07	0.34	3.28	5.51
M33	P19-2a	No	34.0	14.8	18.4	17.6	0.19	0.27	0.69	11.5	0.07	0.21	2.32	4.33
Average untreated mice			34.29	15.24	16.79	16.11	0.16	0.18	0.73	13.25	0.09	0.31	2.87	5.03
Standard deviation			1.02	0.91	1.70	1.46	0.03	0.08	0.09	1.84	0.02	0.06	0.49	0.60
Average Smartfish treated			33.20	14.72	18.62	16.75	0.15	0.20	0.89	8.83	1.76	0.53	4.37	9.19
Standard deviation			1.15	1.34	2.48	2.20	0.04	0.03	0.10	1.80	2.36	0.21	1.59	4.88
Average Placebo treated			33.60	13.88	20.50	17.33	0.17	0.18	0.87	9.66	0.30	0.40	3.20	5.74
Standard deviation			2.30	1.89	2.36	2.17	0.02	0.05	0.18	1.45	0.14	0.11	1.13	1.57

P=patient, M=mouse, FAME=fatty acid methyl ester, No=no treatment given, OMEGA-3=Smartfish Remune with fish oil, PLACEBO=Smartfish Remune Placebo with rapeseed oil



Supplementary figure 5-1. Correlation in values for different fatty acids measured in mouse whole blood.