Table S1: Adrenocortical expression and limitations of Cre mouse strains available to study adrenal cortex development and maintenance

Mouse strains	Expression in the adrenal gland	Recombination	Usage	Limitations*
CAG-CreER	- Expression in all cells of the adrenal	- Tamoxifen injection dependent	- Varying (depending on the cell type expressing the gene of interest)	- Timing of tamoxifen injection should be carefully selected - Global gene inactivation: Potential indirect effect on the adrenal, might lead to rapid embryonic death if used to study development
Osr1$^{eGFP\text{-}CreERt2}$	- Coelomic Epithelium	- Tamoxifen injection dependent (injection of dams at e8.5)	- Study of coelomic epithelium and early stages of AGP development	- Timing of tamoxifen injection should be carefully selected (*Osr1* is not expressed in the AGP/AP) - Variable efficiency, might need to use this strain in combination with the *Wt1*$^{CreERt2/+}$ strain - Expressed in intermediate and dorsal lateral plate mesoderms and their descendants (heart, kidney, gonad, muscle connective tissue, fibro-adipogenic progenitors)
Wt1$^{CreERt2/+}$	- Coelomic epithelium/AGP	- Tamoxifen injection dependent (injection of dams at e8.5)	- Study of coelomic epithelium and early stages of AGP development	- Timing of tamoxifen injection should be carefully selected (*Wt1* is not expressed in the AP) - Variable efficiency, might need to use this strain in combination with the *Osr1*$^{eGFP\text{-}CreERt2}$ strain to study coelomic epithelium development - Expressed in intermediate mesoderm and its descendants (heart, kidney, wolffian duct, gonads…) both in the embryos and postnatally. Also

	- Subpopulation of capsular cells (from e13.5 to adult)	- Injection of dams at e13.5 or postnatally to study capsular cell population	- Tracing *Wt1+* cell population -study development of subcapsular hyperplastic lesion following gonadectomy	expressed in spleen, breast and smooth muscle - *Wt1+* cells are not the main capsular stem cell population
Gata4^{CreERt2} **(Not characterized except in the digestive tract epithelium, expected results)**	- Coelomic epithelium/AGP	- Tamoxifen injection dependent (injection of dams at e8.5)	- Study of coelomic epithelium and early stages of AGP development	- Timing of tamoxifen injection should be carefully selected (*Gata4* is not expressed in the AP) - Potential expression in gonads, neural crest, heart, vasculature, placenta, pancreas, digestive tract (only verified for the digestive tract epithelium)
*Tbx*18^{Cre}	- Anterior coelomic epithelium/ AP	- e10-e10.5	- Study of late AGP and AP development	- Expression in the anterior GP, heart, limb buds, urogenital tract, bladder, inner ear mesenchyme, adipocytes, smooth muscle… - Expression in the definitive cortex has not been evaluated
FAdE/Nr5a1-Cre *FAdE/Nr5a1-CreERT2*	- Fetal adrenocortical cells and their descendants (adrenocortical cells of the definitive cortex and some capsular stem cells) - Fetal adrenal cortex and their descendants forming the definitive cortex	- e10 .5 - Tamoxifen injection dependent - Injection of dams between e11.5-e13.5 (recombination in the fetal cortex and definitive cortex) - Injection of dams at e14.5 (recombination	- Tracing studies of fetal adrenocortical cells - Could potentially be used to study fetal cortex (and definitive cortex) development - Could be used to the fetal cortex (without affecting the definitive cortex) - Useful to confirm if a phenotype observed in other models (*Nr5a1-Cre*, *Cyp11b2*^{Cre}) is solely associated with the definitive cortex	- Expression in gonads and some cells in the thoracic region -Stochastic recombination in the definitive cortex (percentage of recombined cells not evaluated) - Timing of tamoxifen injection should be carefully selected - Expressed in rare gonadal cells - Stochastic recombination in the definitive adrenal cortex

		in the fetal cortex only)		
Nr5a1-Cre^{high} (from Keith Parker lab) and *Nr5a1-Cre* (from Bradford Lowell)	- AGP/AP, fetal adrenal cortex, definitive adrenal cortex (including subcapsular progenitor cells)	-e10.5 (exact recombination onset has not been evaluated for the strain from Lowell group)	- Most used models, best characterized models - Study of the development of the fetal cortex and development/maintenance/function of the definitive cortex	- Expressed in the gonads (Leydig/Sertoli/Theca/Granulosa), gonadotropes of the pituitary, VMH, subpopulation of dermal fibroblast progenitor, spleen - Potential indirect effect of sex hormones due to the inactivation of the targeted genes in testis/ovary/pituitary; Should measure circulating testosterone, oestrogen, LH and FSH levels - Inactivation of the targeted gene in the VMH could affect corticosterone/ACTH diurnal feedback.
Nr5a1-Cre^{low} (from Keith Parker lab)	- Same as *Nr5a1*-Cre^{high} but in fewer cells	-e10.5	- Interesting to evaluate gain-of-function mutation in proto-oncogene or mutation in tumor suppressor genes (more representative of tumor formation. i.e clonal expansion of few mutated cells)	- Not as useful to study the development of the fetal cortex (recombination in fewer cells)
Nr5a1$^{eGFP\text{-}CreERt2}$ **(not characterized in the adrenal gland, expected results)**	- Potentially AGP/AP, fetal adrenal cortex, definitive adrenal cortex (including subcapsular progenitor cells)	- Tamoxifen injection dependent	- Study of the development of the fetal cortex and development/maintenance/function of the definitive cortex	- Similar limitations to the postnatal characterization of *Nr5a1*-Cre models
hCyp11a1-iCre *mCyp11a1-iCre*	- Adrenal gland cortex (fetal and definitive), Expression should be limited to steroidogenic cells (expression at	- *hCyp11a1-iCre* (e10.5)	- Study of the development of the fetal cortex and development/maintenance/function of the definitive cortex	- Expressed in fetal and adult Leydig cells, theca cells and corpus luteum of the postnatal ovaries, brain (*hCyp11a1-iCre* and *Cyp11a1*$^{Gfp,Cre/+}$; not evaluated

Cyp11a1$^{Gfp,Cre/+}$	e10.5 in the *hCyp11a1-iCre* suggests it might not be the case)	- *mCyp11a1-iCre* (not evaluated before e14.5) - *Cyp11a1*$^{Gfp,Cre/+}$ (not evaluated before e17.5)		in *mCyp11a1-iCre*), fetal ovaries (*hCyp11a1-iCre*) - Potential indirect effect of sex hormones due to the inactivation of the targeted genes in testis/ovary. Should measure circulating testosterone, oestrogen, LH and FSH levels.
Akr1b7-Cre	- Steroidogenic cells of the fetal and definitive adrenal cortex	- e14.5 (stochastic recombination, 80% the cells) - Not expressed in fetal adrenocortical cells that differentiate into cells of the definitive cortex	- Useful to study function of the definitive adrenal cortex (independently of the fetal cortex) - Expression is more specific than *Nr5a1-Cre* and *Cyp11a1-Cre*	- Expressed in the kidney (developing and adult) - Recombination less efficient than *Nr5a1*-Cre/ *Cyp11a1-Cre* strains (but more specific)
Cyp11b2^{Cre}	- Steroidogenic zG cells and their descendants (zF cells)	- Rare cells from e16.5 to 1dpp (all zG cells at 6 weeks) - Recombination in all zF cells at 3 months in females and approximately 9 months in male	- Best model to study zG morphogenesis and functions (no recombination in fetal/definitive cortex before zG formation) - Useful to study zG to zF centripetal transdifferentiation/adrenal maintenance and perform tracing studies	-Mosaic of recombined and not recombined zG cells (rapid transdifferentiation of stem and progenitor cells population to restore zG functions) - zF cell maintenance can become independent of zG cell transdifferentiation in some models
Cyp11b1$^{eGFP-Cre}$ **(not fully characterized)**	- zF cells (double marking/higher magnification images needed to determine if some zG cells are recombined or not)	- Unknown (not evaluated in the embryo)	- Potentially useful to study maintenance/functions of the zF.	- Model not well characterized (expression in the fetal adrenal cortex, and potential expression in the fetal gonads not evaluated), only one article published in Chinese
Gli1^{CreERt2}	- Subpopulation of capsular (stem cells) (and their descendants)	- Tamoxifen injection dependent	- Useful to target capsular stem cells - Study of adrenal cortex maintenance	- Expressed in kidney, brain, astrocytes, fibroblast, chondrocytes, adipocytes, hair follicle, prostate, perisoteal cells, Leydig cell, theca cells…

			- Tracing experiment to study centripetal transdifferentiation	- Capsular stem cells do not normally contribute to adrenal maintenance in adult males - Potential indirect effect of sex hormones due to inactivation of the targeted genes in Leydig and theca cells. Should measure circulating testosterone, oestrogen, LH and FSH levels
Shh^{Cre} *Shh* ^{CreERt2}	- Cortex periphery in the forming definitive cortex, subcapsular progenitor cells of the zG (and their descendants) - Subcapsular progenitor cells of the definitive cortex in the zG (and their descendants)	-e11.5 -Tamoxifen injection dependent	-Tracing experiment of progenitor cells - Mostly used for tracing experiment of progenitor cells	- Expressed in developing limb buds, heart, ventral neural tube, lung epithelium, stomach endoderm, intestinal epithelium, external genitalia, neurons, prostate, secondary heart field… - Expressed in bladder epithelial stem cells, papillary collecting duct, uritheric epithelium, hair follicle, brain astrocytes, epithelial taste bud progenitors, spleen, gastric parietal cells…
Axin2^{CreERt2} and *Wnt4*^{CreERt2}	- Cortex periphery in the forming definitive cortex (and their descendants) - Postnatally, Adrenal zG cells (including the subcapsular progenitors and their descendants)	- Tamoxifen injection dependent	- Mostly used for tracing experiment of zG cells (including subcapsular progenitors)	- Expressed in intestinal epithelium stem cells, mammary gland, neural stem cells, ovaries, liver, kidney… (*Axin2*) -Expressed in kidney, oesophagus, ovary, skin, small intestine… (*Wnt4*)
Nes-CreERt2	- Stress induced progenitor cell populations of	- Tamoxifen injection dependent	- Tracing and purification of stress-induced progenitor cells	- Expressed in glial progenitor cells, astrocytes, oligodendrocytes

	steroidogenic cells of the adrenal cortex and of chromaffin cells (and their descendants)		- Evaluation of stress adaptation	- Should consider the contribution of other adrenocortical stem/progenitor cells to stress response

* Postnatal phenotypes should be evaluated in males and females as the adrenal cortex is sexually dimorphic