

**Table S1.** SARS-CoV-2 nucleoprotein and RNA expression in mice infected with the beta variant with different infectious doses at 2, 3 or 4 days post infection. **Legend:** Ag – antigen; BG – Bowman’s glands; BLN – bronchial lymph node; DC – dendritic cells; EC – epithelial cells; NB – nerve bundles; NE – not examined; neg – negative; OEC – olfactory epithelial cells; pos – positive; REC – respiratory epithelial cells; RdRp PCR:  $Ct_{RdRp}-Ct_{actin} \leq 3 = ++, > 3 = +$ , no Ct = -; subE PCR:  $Ct_{subE}-Ct_{actin} \leq 4.5 = ++, > 4.5 = +$ , no Ct = -; E PCR:  $Ct_E-Ct_{actin} \leq -1 = ++, -1 \leq Ct_E < 10 = +, > 10 = -$ .

Dose [Animal no]	DPI	Viral Ag	Viral RNA in lung (RT-qPCR)		
			RdRp	subE	E
2 x 10 <sup>5</sup> PFU [1]	2	Nose: individual pos REC/OEC, patches of pos REC/OEC; pos EC in BG Brain: neg (incl olfactory bulb) Trachea: several individual pos EC Lung: bronchus, bronchioles: individual and patches of pos EC, viral Ag covering luminal surface; some adjacent small patches of alveoli with pos type I and II pneumocytes BLN: several pos macrophages/DC	++	+	+
		Nose: individual pos REC/OEC, patches of pos REC Brain: neg (incl olfactory bulb) Trachea: NE Lung: several bronchioles with individual to abundant pos EC, viral Ag covering luminal surface; some individual adjacent pos type I and II pneumocytes BLN: NE	+	+	+
2 x 10 <sup>5</sup> PFU [3]	2	Nose: some individual pos REC/OEC, patches of pos REC Brain: neg (incl olfactory bulb) Trachea: several individual pos EC Lung: bronchioles with several individual and patches of pos EC; viral Ag covering luminal surface; areas with degenerate EC and leukocyte infiltration with viral Ag also in infiltrating macrophages; patches of alveoli with pos type I and II pneumocytes BLN: neg	++	+	+
		Nose: some individual pos REC/OEC, patches of pos REC Brain: neg (incl olfactory bulb) Trachea: NE Lung: bronchioles with several individual and patches of pos EC and some degenerate pos cells in lumen; viral Ag covering luminal surface; areas with degenerate EC and leukocyte infiltration with viral Ag also in infiltrating macrophages; patches of alveoli with pos type I and II pneumocytes BLN: a few pos macrophages/DC	++	+	+
2 x 10 <sup>5</sup> PFU [4]	2	Nose: some individual pos REC/OEC, large stretch of pos REC Brain: neg (incl olfactory bulb) Trachea: a few pos EC Lung: most bronchioles with several individual and patches of pos EC; viral Ag covering luminal surface; areas with degenerate EC and leukocyte infiltration with viral Ag also in infiltrating macrophages; patches of alveoli with pos type I and II pneumocytes BLN: several pos macrophages/DC	++	++	+
		Nose: large patches of pos REC/OEC Brain: neg (incl olfactory bulb) Trachea: rare individual pos EC Lung: bronchus and bronchioles with individual and patches of pos EC; abundant viral Ag covering luminal surface; adjacent several patches of alveoli with pos type I and II pneumocytes, sloughed off pos alveolar	++	++	++

			macrophages/type II pneumocytes, and cell free viral Ag in alveolar lumen <b>BLN:</b> numerous pos macrophages/DC			
$2 \times 10^5$ PFU [2]	3		<b>Nose:</b> patches of pos REC; large area of pos OEC; some pos cells in BG and NB layer <b>Brain:</b> neg (incl olfactory bulb) <b>Trachea:</b> rare individual pos EC <b>Lung:</b> bronchus and bronchioles with individual and patches of pos EC; abundant viral Ag covering luminal surface; rare small patches of alveoli with pos type I and II pneumocytes, sloughed off pos alveolar macrophages/type II pneumocytes, and cell free viral Ag in alveolar lumen <b>BLN:</b> several pos macrophages/DC	+	-	+
$2 \times 10^5$ PFU [3]	3		<b>Nose:</b> large patches of pos REC <b>Brain:</b> neg (incl olfactory bulb) <b>Trachea:</b> rare individual pos EC <b>Lung:</b> bronchus with rare pos EC, bronchioles often with abundant viral Ag covering luminal surface; adjacent a few patches of alveoli with pos type I and II pneumocytes, sloughed off pos alveolar macrophages/type II pneumocytes, and cell free viral Ag in alveolar lumen <b>BLN:</b> numerous pos macrophages/DC	+	-	++
$2 \times 10^5$ PFU [4]	3		<b>Nose:</b> large patches of pos REC <b>Brain:</b> neg (incl olfactory bulb) <b>Trachea:</b> a few individual pos EC <b>Lung:</b> bronchus and some bronchioles with few individual and patches of pos EC; abundant viral Ag covering luminal surface; adjacent large patch of alveoli with pos type I and II pneumocytes, sloughed off pos alveolar macrophages/type II pneumocytes, and cell free viral Ag in alveolar lumen <b>BLN:</b> several pos macrophages/DC	+	-	++
$2 \times 10^5$ PFU [5]	3		<b>Nose:</b> a few individual pos REC; a few patches of pos REC <b>Brain:</b> neg (incl olfactory bulb) <b>Trachea:</b> rare individual pos EC <b>Lung:</b> bronchus and bronchioles with individual and patches of pos EC; abundant viral Ag covering luminal surface; adjacent several patches of alveoli with pos type I and II pneumocytes, sloughed off pos alveolar macrophages/type II pneumocytes, and cell free viral Ag in alveolar lumen <b>BLN:</b> numerous pos macrophages/DC	++	++	-
$2 \times 10^5$ PFU [6]	3		<b>Nose:</b> patches of pos REC; large area of pos OEC; some pos cells in BG and NB layer and olfactory nerves <b>Brain:</b> neg (incl olfactory bulb) <b>Trachea:</b> rare individual pos EC, a few pos degenerate cells in lumen <b>Lung:</b> bronchus with rare pos EC, abundant viral Ag covering luminal surface; adjacent a few patches of alveoli with pos type I and II pneumocytes, sloughed off pos alveolar macrophages/type II pneumocytes, and cell free viral Ag in alveolar lumen <b>BLN:</b> numerous pos macrophages/DC	+	++	+
$6 \times 10^4$ PFU [1]	2		<b>Nose:</b> several patches of and individual pos REC and OEC; some viral Ag attached to epithelial surface <b>Olfactory bulb:</b> neg <b>Trachea:</b> patches of pos EC <b>Lung:</b> abundant viral Ag deposition covering luminal surface of several bronchioles	-	-	-

$6 \times 10^4$ PFU [2]	2	<b>Nose:</b> some patches of and several individual pos REC <b>Olfactory bulb:</b> neg <b>Trachea:</b> one patch of pos EC <b>Lung:</b> neg	-	-	-
$6 \times 10^4$ PFU [3]	2	<b>Nose:</b> abundant patches of and individual pos REC; some cell free viral Ag in mucus <b>Olfactory bulb:</b> neg <b>Trachea:</b> neg <b>Lung:</b> neg	-	-	-
$6 \times 10^4$ PFU [4]	2	<b>Nose:</b> abundant patches of and individual pos REC, occasional pos OEC; cell free viral Ag in mucus <b>Trachea:</b> neg <b>Lung:</b> neg	-	-	-
$6 \times 10^4$ PFU [1]	4	<b>Nose:</b> individual and groups of pos REC and OEC; some cell free viral Ag in mucus <b>Olfactory bulb:</b> neg <b>Trachea:</b> neg <b>Lung:</b> neg	-	-	-
$6 \times 10^4$ PFU [2]	4	<b>Nose:</b> individual and groups of pos REC, a few pos OEC <b>Lung:</b> one bronchiole and one bronchio-alveolar transition with a few pos EC <b>BLN:</b> several pos macrophages/DC	-	-	-
$6 \times 10^4$ PFU [3]	4	<b>Nose:</b> numerous pos OEC; cell free viral Ag in mucus <b>Olfactory bulb:</b> neg <b>Lung:</b> one pos EC in one bronchiole <b>BLN:</b> several pos macrophages/DC	-	-	-
$6 \times 10^3$ PFU [1]	2	<b>Nose:</b> several patches of and individual pos REC; some cell free viral Ag in mucus <b>Olfactory bulb:</b> neg <b>Trachea:</b> neg <b>Lung:</b> neg	-	-	-
$6 \times 10^3$ PFU [2]	2	<b>Nose:</b> several patches of and individual pos REC and OEC; cell free viral Ag in mucus <b>Olfactory bulb:</b> neg <b>Trachea:</b> several patches of pos EC <b>Lungs:</b> viral Ag covering luminal surface of bronchioles <b>BLN:</b> neg	-	-	-
$6 \times 10^3$ PFU [3]	2	<b>Nose:</b> abundant patches of and individual pos REC; some cell free viral Ag in mucus <b>Olfactory bulb:</b> neg <b>Trachea:</b> neg <b>Lung:</b> neg	+	+	+
$6 \times 10^3$ PFU [4]	2	<b>Nose:</b> large patches of and individual pos REC; some cell free viral Ag in mucus <b>Olfactory bulb:</b> neg <b>Trachea:</b> neg <b>Lung:</b> neg	++	+	++