



Supplementary figure 1. ClustalW alignment of *Nipa1*, *Nipa2*, *Npal1*, *Npal2* and *Npal3* sequences from different species. *Nipa1* builds a separate branch; *Nipa2* and *Npal1* are closely related. *Npal2* and *Npal3* are building separate branches common for different species. *h-Homo sapiens*, *r-Rattus norvegicus*, *m-Mus musculus*, *g-Gallus gallus*, *p-Pan troglodytes*, *b-Bos Taurus*, *c-Canis familiaris*, *ma-Macaca mulatta*, *d-Danio rerio*, *e-Equus caballus*, *po-Pongo abelii*, *x-Xenopus tropicalis*, *o-Ornithorhynchus anatinus*.

Supplementary figure 2. ClustalW alignment of NPAL3 protein sequences from different species. Asterisks mark conserved amino acids in NPAL3 sequences.

Supplementary table 1. Behavioral analysis in the modified hole board test.

Parameter	<i>Npal3</i> ^{+/+} (A)		<i>Npal3</i> ^{-/-} (B)			
	male (N=10)	female (N=15)	male (N=8)	female (N=15)	male <i>p</i>	female <i>p</i>
Line crossing (frequency)	109.2±6.37	82.13±13.18	101.63±63	84.93±9.68	n. s.	n. s.
Line crossing (latency)	2.02±0.29	3.81±0.97	2.24±0.49	4.05±1.83	n. s.	n. s.
Rearings in box (frequency)	7.7±1.69	7.53±1.77	6.75±1.97	10.67±1.89	n. s.	n. s.
Rearings in box (latency)	107.87±18.0 5	117.89±22.5 2	104.94±10.0 6	63.39±11.4 9	n. s.	n. s.
Hole visit (frequency)	0±0	0±0	0±0	0±0	n. s.	n. s.
Hole visit (latency)	300±0	300±0	300±0	300±0	n. s.	n. s.
Board entry (frequency)	7.2±1	5.73±1.08	4.13±1.33	4.07±1.14	n. s.	n. s.
Board entry (latency)	81.65±18.52	103.11±27.5 6	135.73±37.4 8	142.35±28.6 9	n. s.	n. s.
Board entry (total duration %)	9.83±1.64	11.37±2.95	7.7±3.06	5.93±1.33	n. s.	n. s.
Rearing on board (frequency)	0.1±0.1	0±0	0.38±0.26	0±0	n. s.	n. s.
Rearing on board (latency)	299.92±0.08	300±0	273.51±22.2 7	300±0	n. s.	n. s.
Risk assessment (frequency)	0±0	0.93±0.33	0.13±0.13	0.6±0.25	n. s.	n. s.
Risk assessment (latency)	300±0	201.97±32.9 7	300±0	209.53±34.2 3	n. s.	n. s.
Group contact (frequency)	12.4±1.24	11.33±1.24	14±1.51	16.47±1.16	n. s.	p<0.01
Group contact (latency)	20.96±5.65	45.45±18.53	27.31±5.82	19.03±4.66	n. s.	p=0.05
Group contact (total duration %)	21.76±3.02	29.81±3.7	25.36±3.99	38.37±4.1	n. s.	n. s.
Hole exploration (frequency)	25.8±2.9	23.6±3.35	19.5±5.1	19±3.39	n. s.	n. s.
Hole exploration (latency)	41.29±15.64	24.33±5.06	11.29±3.33	75.79±26.18	p<0.05	n. s.
Grooming (frequency)	1.5±0.43	1.13±0.38	2.38±0.8	0.8±0.3	n. s.	n. s.
Grooming (latency)	212.82±25.5 3	206.87±26.3 7	170.13±0	247.41±15.8	n. s.	n. s.
Grooming (total duration %)	1.16±0.46	1.26±0.47	1.74±0.61	0.74±0.25	n. s.	n. s.
Defecation (frequency)	1.2±0.29	1.67±0.37	1.25±0.31	1.53±0.31	n. s.	n. s.
Defecation (latency)	153.3±33.58	90.7±28.77	136.06±46.5 7	116.23±29.7 9	n. s.	n. s.

Unfamiliar object exploration (frequency)	4.6±0.43	2.27±0.42	4.38±0.75	2.33±0.47	n. s.	n. s.
Familiar object exploration (frequency)	4.9±0.67	3.13±0.71	5.38±0.92	2.53±0.72	n. s.	n. s.
Unfamiliar object exploration (latency)	29.52±7.76	115.12±28.2	51.36±30.16	144.02±28.2	n. s.	n. s.
Familiar object exploration (latency)	48.41±22.25	121.45±30.3 6	31.41±8.05	159.51±34.5 9	n. s.	n. s.
Unfamiliar object exploration (total duration %)	0.84±0.14	0.58±0.1	1.15±0.27	0.59±0.14	n. s.	n. s.
Familiar object exploration (total duration %)	0.91±0.18	0.64±0.17	0.95±0.14	0.52±0.15	n. s.	n. s.
Object index	-0.02±0.11	0.06±0.13	0.05±0.07	0.14±0.1	n. s.	n. s.

The data is given as a mean ± standard deviation. For the significant differences the *p* value is given, n. s. – not significant, N – number of tested animals.

Supplementary table 2. Immunology screen.

Parameter	<i>Npal3</i> ^{+/+} (A)		<i>Npal3</i> ^{-/-} (B)			
	male (N=10)	female (N=15)	male (N=14)	female (N=15)	male	female
					<i>p</i>	<i>p</i>
CD19 ⁺ (%)	8.9±0.7	23.3±1.0	8.9±0.5	22.7±0.8	n. s.	n. s.
CD19 ⁺ CD5 ⁻ (%)	97.9±0.3	89.8±0.7	98.1±0.3	88.5±0.8	n. s.	n. s.
CD19 ⁺ CD5 ⁺ (%)	2.1±0.3	10.2±0.7	1.9±0.3	11.5±0.8	n. s.	n. s.
CD3 ⁺ (%)	45.6±1.2	59.6±1.0	47.6±0.9	59.7±0.8	n. s.	n. s.
γ/δ TCR ⁺ (%)	0.03±0.01	NA	0.04±0.01	NA	n. s.	NA
GR-1 ⁺ (%)	15.2±1.1	8.0±0.6	13.5±1.0	7.2±0.4	n. s.	n. s.
CD49b ⁺ (%)	11.3±0.8	10.3±1.0	8.5±0.7	6.5±0.7	P<0.02	p<0.01
CD4 ⁺ (%)	38.1±1.1	45.8±0.8	39.6±0.7	45.3±0.7	n. s.	n. s.
CD8β ⁺ (%)	11.9±0.3	13.9±0.3	12.3±0.3	14.3±0.3	n. s.	n. s.
IgG ₁ (μg/ml)	78.2±19.0	272.1±16.0	62.6±5.6	289.6±27.4	n. s.	n. s.
IgG _{2a} (μg/ml)	NA	995.4±126	NA	1603.5±173	NA	P<0.05
IgG _{2b} (μg/ml)	145.6±14.6	202.1±10.8	128.6±5.9	215.9±10.4	n. s.	n. s.
IgG ₃ (μg/ml)	NA	75.4±7.2	NA	66.9±4.6	n. s.	NA
IgM (μg/ml)	692.8±67.1	515.1±39.0	492.3±66.2	657.7±47.3	p<0.05	p<0.05
IgA (μg/ml)	30.7±6.0	166.1±28.2	55.7±9.7	117.2±18.5	p<0.05	n. s.
Anti-DNA Ab (%)	0	0	0	0	n. s.	n. s.
Rheumatoid factor (%)	0	0	0	0	n. s.	n. s.

The data is given as a mean \pm standard deviation. For the significant differences the *p* value is given, n. s. – not significant, NA – not analyzed, N – number of tested animals.

Supplementary table 3. Spontaneous breathing pattern during the time of rest and activity.

Parameter	<i>Npal3</i> ^{+/+} (A)		<i>Npal3</i> ^{-/-} (B)			
	male (N=10)	female (N=15)	male (N=8)	female (N=15)	male	female
					<i>p</i>	<i>p</i>
Rest						
f (1/min)	265.7 \pm 12.9	329.4 \pm 8.5	313.3 \pm 22.3	300.5 \pm 10.5	n. s.	n. s.
TV (ml)	0.27 \pm 0.01	0.25 \pm 0.02	0.3 \pm 0.01	0.24 \pm 0.01	n. s.	n. s.
sTV (μ g/g)	9.3 \pm 0.3	11.2 \pm 0.7	11.6 \pm 0.3	10.7 \pm 0.2	p<0.01	n. s.
MV (ml/min)	70.5 \pm 4.0	81.3 \pm 4.7	91.1 \pm 4.0	71.1 \pm 3.2	p<0.01	n. s.
sMV (ml/min/g)	2.4 \pm 0.1	3.6 \pm 0.2	3.5 \pm 0.3	3.2 \pm 0.1	p<0.01	n. s.
Ti (ms)	75.6 \pm 4.3	56.2 \pm 1.7	69.3 \pm 5.1	63.9 \pm 4.2	n. s.	n. s.
Te (ms)	151.8 \pm 8.0	126.4 \pm 4.4	126.3 \pm 9.3	136.7 \pm 4.0	n. s.	n. s.
Ti/TT	0.33 \pm 0.01	0.31 \pm 0.01	0.35 \pm 0.01	0.32 \pm 0.01	n. s.	n. s.
PIF (ml/s)	6.2 \pm 0.3	7.7 \pm 0.5	7.4 \pm 0.4	6.5 \pm 0.4	n. s.	n. s.
PEF (ml/s)	3.5 \pm 0.3	3.9 \pm 0.3	4.5 \pm 0.2	3.2 \pm 0.3	p<0.02	n. s.
MIF (ml/s)	3.6 \pm 0.2	4.5 \pm 0.3	4.4 \pm 0.2	3.8 \pm 0.2	n. s.	n. s.
MEF (ml/s)	1.8 \pm 0.1	2.0 \pm 0.1	2.4 \pm 0.1	1.8 \pm 0.1	p<0.02	n. s.
Activity						
f (1/min)	412.5 \pm 6.8	445.9 \pm 8.4	433.5 \pm 18.1	427.9 \pm 6.9	n. s.	n. s.
TV (ml)	0.25 \pm 0.01	0.25 \pm 0.01	0.29 \pm 0.01	0.24 \pm 0.01	p<0.02	n. s.
sTV (μ l/g)	8.5 \pm 0.2	10.9 \pm 0.6	11.2 \pm 0.4	10.5 \pm 0.3	p<0.01	n. s.
MV (ml/min)	101 \pm 2.6	109.3 \pm 6	123.5 \pm 5.5	101.1 \pm 5.7	p<0.02	n. s.
sMV (ml/min/g)	3.4 \pm 0.1	4.8 \pm 0.3	4.8 \pm 0.3	4.5 \pm 0.2	p<0.01	n. s.
Ti (ms)	51.0 \pm 0.4	45.5 \pm 1.1	50.7 \pm 2.0	47.9 \pm 1.7	n. s.	n. s.
Te (ms)	94.6 \pm 2.5	89.2 \pm 2.1	88.7 \pm 3.9	92.5 \pm 0.9	n. s.	n. s.
Ti/TT	0.35 \pm 0.01	0.34 \pm 0.01	0.36 \pm 0.4	8.3 \pm 0.4	n. s.	n. s.
PIF (ml/s)	8.3 \pm 0.2	9.2 \pm 0.6	9.7 \pm 0.4	8.3 \pm 0.4	n. s.	n. s.
PEF (ml/s)	5.1 \pm 0.3	5.3 \pm 0.4	6.3 \pm 0.4	4.7 \pm 0.4	n. s.	n. s.
MIF (ml/s)	4.9 \pm 0.1	5.4 \pm 0.4	5.8 \pm 0.2	4.9 \pm 0.2	n. s.	n. s.
MEF (ml/s)	2.6 \pm 0.1	2.8 \pm 0.1	3.3 \pm 0.1	2.6 \pm 0.1	p<0.01	n. s.

The data is given as a mean \pm standard deviation. For the significant differences the *p* value is given, n. s. – not significant, NA – not analyzed, N – number of tested animals.