

Supplementary Table 2. DNIC expression after systemic drug application. Listed by the drug.

PMID	CONDITION	DRUG	INJECTION SITE	ANAESTHESIA	READOUT	DNIC EXPRESSION BEFORE DRUG	DNIC EXPRESSION AFTER DRUG	PHARMACOLOGY
6260285	Naïve	Naloxone	Systemic (i.v.)	N/A	Beh	Expressed	Not expressed	Opioid receptor antagonist
6257327	Naïve	Naloxone	Systemic (i.v.)	Halothane	Eph	Expressed	Not expressed	Opioid receptor antagonist
2247225	Naïve	Naloxone	Systemic (i.v.)	Halothane	Eph	Expressed	Not expressed	Opioid receptor antagonist
27178898	Naïve	Naloxone	Systemic (i.p.)	N/A	Beh	Expressed	Not expressed	Opioid receptor antagonist
20302612	Naïve	Naloxone	Systemic (i.p.)	Halothane	Beh	Expressed	Not expressed	Opioid receptor antagonist
21330219	Muscle inflammation	Naloxone	Systemic (s.c.)	N/A	Beh	Expressed	Not expressed	Opioid receptor antagonist
27178898	Naïve	Naloxone	Intracerebroventricular (i.c.v.)	N/A	Beh	Expressed	Not expressed	Opioid receptor antagonist
7260590	Naïve	Morphine + Naloxone	Systemic (i.v.) + Systemic (i.v.)	Halothane	Eph	Expressed	Expressed	MOR-DOR agonist + opioid receptor antagonist
3171978	Naïve	Morphine + Naloxone	i.c.v. + Systemic (i.v.)	Halothane	Eph	Expressed	Expressed	MOR-DOR agonist + opioid receptor antagonist
3378576	Naïve	Morphine + Naloxone	i.c.v. + Systemic (i.v.)	Halothane	Eph	Expressed	Expressed	MOR-DOR agonist + opioid receptor antagonist
1397003	Naïve	Morphine + Naloxone	Systemic (i.v.) + Systemic (i.v.)	Halothane	Eph	Expressed	Expressed	MOR-DOR agonist + opioid receptor antagonist
23843537	Naïve	Naloxone + DAMGO	Systemic (i.v.) + i.th.	Halothane	Eph	Expressed	Expressed	Opioid receptor antagonist + MOR agonist
23843537	Naïve	Naltrindole + Deltorphin II	Systemic (i.v.) + i.th.	Halothane	Eph	Expressed	Expressed	DOR antagonist + DOR agonist
7260590	Naïve	Morphine	Systemic (i.v.)	Halothane	Eph	Expressed	Not expressed	MOR-DOR agonist
1397003	Naïve	Morphine	Systemic (i.v.)	Halothane	Eph	Expressed	Not expressed	MOR-DOR agonist
1397003	PAG lesion	Morphine	Systemic (i.v.)	Halothane	Eph	Expressed	Expressed	MOR-DOR agonist
20016098	Naïve	Morphine sulfate	Subcutaneous pellets	Urethane	Eph	Expressed	Not expressed	MOR-DOR agonist
20016098	Naïve	Morphine sulfate	Subcutaneous osmotic minipumps	Urethane	Eph	Expressed	Not expressed	MOR-DOR agonist
21929659	Naïve	Morphine sulfate	Subcutaneous pellets	Urethane	IHC	Expressed	Not expressed	MOR-DOR agonist
29369967	Naïve	Morphine sulfate	Subcutaneous osmotic minipumps	N/A	Beh	Expressed	Expressed	MOR-DOR agonist
30286616	Naïve	Morphine sulfate	Subcutaneous osmotic minipumps	N/A	Beh	Expressed	Not expressed	MOR-DOR agonist
3171978	Naïve	Morphine sulphate	Intracerebroventricular (i.c.v.)	Halothane	Eph	Expressed	Not expressed	MOR-DOR agonist
3378576	Naïve	Morphine base	Intracerebroventricular (i.c.v.)	Halothane	Eph	Expressed	Not expressed	MOR-DOR agonist
29369967	BLS	nor-binaltorphimine	Systemic (s.c.)	N/A	Beh	Not expressed	Expressed	MOR agonist
30870321	SNL	Nor-binaltorphimine	Systemic (s.c.)	N/A	Beh	Not expressed	Expressed	KOR antagonist
2986769	Naïve	ES 52	Systemic (i.v.)	Halothane	Eph	Expressed	Expressed	Inhibitor of enkephalinase (derivative of Thiorphan)
8750730	Naïve	Buprenorphine hydrochloride	Systemic (i.v.)	Halothane	EMG	Expressed	Not expressed	Partial MOR agonist
26010460	SNL	Tapentadol	Systemic (s.c.)	Isoflurane	Eph	Not expressed	Expressed	NRI and MOR agonist
30821870	OA-MIA (late stage)	Tapentadol	Systemic (s.c.)	Isoflurane	Eph	Not expressed	Expressed	NRI and MOR agonist
30461363	OA-MIA (late stage)	Tapentadol	Systemic (s.c.)	Isoflurane	Eph	Not expressed	Expressed	NRI and MOR agonist
30821870	OA-MIA (late stage)	Tapentadol + Pregabalin	Systemic (s.c.)	Isoflurane	Eph	Not expressed	Expressed	NRI and MOR agonist + See below
30821870	OA-MIA (late stage)	Pregabalin	Systemic (s.c.)	Isoflurane	Eph	Not expressed	Not expressed	Blocker of voltage-gated calcium channels (VGCCs) that inhibits neurotransmitter release
32315711	PSNL	Pregabalin	Orally administered (p.o.)	N/A	Beh	Not expressed	Not expressed	
32315711	OA-MIA (late stage)	Pregabalin	Orally administered (p.o.)	N/A	Beh	Not expressed	Not expressed	
26010460	SNL	Yohimbine	Systemic (s.c.)	Isoflurane	Eph	Not expressed	Not expressed	α_2 -adrenoceptor antagonist
32745472	Naïve	Atipamezole hydrochloride	Systemic (s.c.)	N/A	Beh	Expressed	Not expressed	α_2 -adrenoceptor antagonist
19697515	Naïve	Atipamezole hydrochloride + Dexmedetomidine hydrochloride	Systemic (i.m.) + Systemic (i.v.)	Sevoflurane	EMG	Expressed	Expressed	α_2 -adrenoceptor antagonist + α_2 -adrenoceptor agonist
19697515	Naïve	Phentolamine mesylate + Phenylephrine	Contralateral biceps femoris (i.m.)	Sevoflurane	EMG	Expressed	Expressed	$\alpha_{1/2}$ -adrenoceptor antagonist + α_1 -adrenoceptor agonist
28700539	Migraine model	Propranolol	Oral gavage	Halothane	Eph	Not expressed	Expressed	Non-selective β -adrenoceptor antagonist
19697515	Naïve	Dexmedetomidine hydrochloride	Systemic (i.v.)	Sevoflurane	EMG	Expressed	Not expressed	α_2 -adrenoceptor agonist
19697515	Naïve	Phenylephrine	Systemic (i.v.)	Sevoflurane	EMG	Expressed	Not expressed	α_1 -adrenoceptor agonist
6978166	Naïve	Metergoline	Systemic (i.v.)	Halothane	Eph	Expressed	Not expressed	5-HT ₂ , 5-HT _{2c} and 5-HT _{2b} receptor antagonist
6976820	Naïve	Cinanserin	Systemic (i.p.)	N/A	Beh	Expressed	Expressed	5-HT _{2a} and 5-HT _{2c} receptor antagonist
6978166	Naïve	Cinanserin	Systemic (i.v.)	Halothane	Eph	Expressed	Not expressed	5-HT _{2a} and 5-HT _{2c} receptor antagonist
6976820	Naïve	5-hydroxytryptophan + cinanserin	Systemic (i.p.)	N/A	Beh	Expressed	Expressed	Serotonin precursor + 5-HT _{2a} and 5-HT _{2c} receptor antagonist
6978166	Naïve	5-hydroxytryptophan	Systemic (i.v.)	Halothane	Eph	Expressed	Expressed	Serotonin precursor
6976820	Naïve	5-hydroxytryptophan	Systemic (i.p.)	N/A	Beh	Expressed	Expressed	Serotonin precursor
27891703	SNL	Citalopram	Systemic (s.c.)	Isoflurane	Eph	Not expressed	Not expressed	SSRI
27891703	SNL	Fluoxetine	Systemic (s.c.)	Isoflurane	Eph	Not expressed	Not expressed	SSRI
32315711	OA MIA (late stage)	Duloxetine	Systemic (s.c.)	N/A	Beh	Not expressed	Expressed	SNRI
32315711	PSNL	Duloxetine	Systemic (s.c.)	N/A	Beh	Not expressed	Expressed	SNRI
32745472	TBI	Duloxetine hydrochloride	Systemic (s.c.)	N/A	Beh	Not expressed	Expressed	SNRI
32745472	TBI	Reboxetine mesylate	Systemic (i.p.)	N/A	Beh	Not expressed	Not expressed	NRI
32745472	TBI	5,7-dihydroxytryptamine + Desipramine hydrochloride	Intrathecal (i.t.) + Systemic (i.p.)	N/A	Beh	Not expressed	Not expressed	Neurotoxin depleting serotonergic fibers + TCA
32745472	TBI	Escitalopram hydrochloride	Systemic (s.c.)	N/A	Beh	Not expressed	Expressed	SSRI
32745472	TBI	Escitalopram + Atipamezole	Systemic (i.p.) + Systemic (s.c.)	N/A	Beh	Not expressed	Expressed	SSRI + α_2 -adrenoceptor antagonist
32745472	TBI	5,7-dihydroxytryptamine + Desipramine hydrochloride + Escitalopram	Systemic (i.t.) + Systemic (i.p.) + Systemic (s.c.)	N/A	Beh	Not expressed	Not expressed	Neurotoxin depleting serotonergic fibers + TCA + SSRI
30286616	Naïve	Sumatriptan succinate	Subcutaneous osmotic minipumps	N/A	Beh	Expressed	Not expressed	5-HT ₁ receptor agonist
32315711	PSNL	Celecoxib	Orally administered (p.o.)	N/A	Beh	Not expressed	Not expressed	COX-2 inhibitor
32315711	OA MIA (late stage)	Celecoxib	Orally administered (p.o.)	N/A	Beh	Not expressed	Not expressed	COX-2 inhibitor
12818952	Naïve	Isoflurane	Gaseous (inhaled)	Isoflurane	Eph	Expressed	Not expressed for isoflurane above 1.2 MAC	General anaesthetic

Abbreviations: SNL - spinal nerve ligation model; TBI - traumatic brain injury; OA MIA - monoiodoacetate model of osteoarthritis; PSNL - partial sciatic nerve ligation; BLS - bright light stress; PAG - periaqueductal grey; i.p. - intraperitoneal; i.th. - intrathecal (L4/L5 - lumbar 4/5); Beh - behaviour; Eph - *in vivo* electrophysiology; EMG - electromyography; IHC - immunohistochemistry; MAC - minimum alveolar anesthetic concentration; TCA - tricyclic antidepressant; SSRI - selective serotonin reuptake inhibitor; NRI - selective noradrenaline reuptake inhibitor; SNRI - selective serotonin-noradrenaline reuptake inhibitor; MOR - μ -opioid receptor; KOR - κ -opioid receptor; DOR - δ -opioid receptor; COX2 - cyclooxygenase 2.