

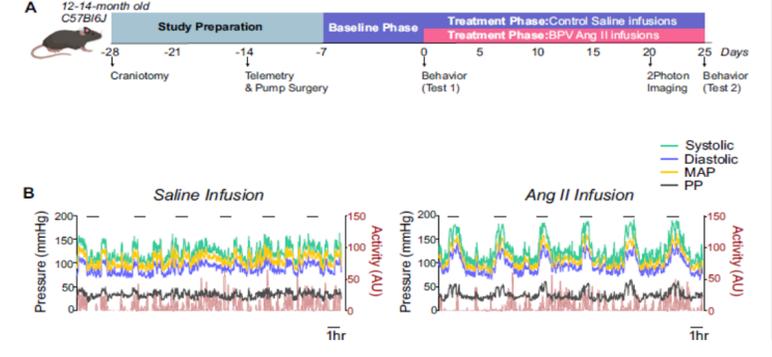
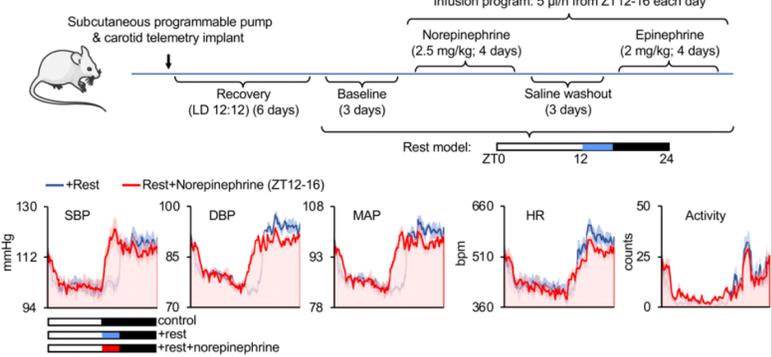
Tabular highlights gives a high level view of how iPRECIO pumps were used/programmed in selected scientific publications in Applications Examples eBook. For more detailed view, refer eBook and publications . In e-book for example, Research Application 1 (RA1) on page 5 & 6 of eBook is on row 1 of Tabular highlights – Chavan et al. The protocol is once a day infusion. RA2 on pages 7 & 8 (row 2 Kroon et al) has a 3 day stop prior to start of infusion of Nicotinic acid with the animal in the metabolic cage all of the time of the infusion protocol.

Research Application (RA), Author, doi:	Refillability of Pump		How pump programmed?			Administration Site	Key words /Subjects	Duration
	KVO/RCV	Vehicle and Drug(s)	Continuous	Intermittent or bolus	Circadian / Timed release			
RA 1 Chavan et al. doi:10.1038/ncomms10580 pgs 5-6 of eBook	1 week recovery	Pumps programmed to infuse saline (2ul/hr) or β OHB (2ul/hr) or sodium pyruvate (5ul/hr) or coconut oil (5ul/hr) prior to meal time (6h, ZT22-ZT) in Restricted Food (RF)	No	Yes	Yes	SC	Biological sciences-Neuroscience-Biochemistry Mice + SMP-300 iPRECIO Pump	< 3 weeks
RA 2 Kroon et al. doi: 10.1194/jlr.M058149 pgs 7-8 of eBook	Pump programmed to stop for 3 days	Nicotinic Acid (NiAc) or saline 5 days of continuous or intermittent (12 hr ON/OFF cycles, infusion on 13:00h)	Yes	Yes	Yes	SC	Adipose tissue-diabetes-drug therapy-Lipoyosis and fatty acid metabolism-GPR109A-Niacin-Tachyphylaxis Zucker rat + SMP-200 Pump	5 or 11 days infusion + 2 days recovery
RA 3 Suehiro et al. doi:10.1038/srep04972 pgs 9-10 of eBook	No	PKA and ATP - solution change every 2 days 1ul/hour	Yes	No	No	intrathecal	Neural-stem cells-spinal cord injury rat + SMP-200 Pump	14 days
RA 4 Mitchell et al. Developments in LifeSciences Vol. 14 No. 4 http://www.abstronline.com/Plan/ViewAbstract.aspx?mid=2964&key=87d8b951-316f-466a-9eb7-4b154d0bbd2c&ckey=b4b8338f-9bd2-44e2-bcf4-6e05a36cbcb&mkey=%7b70007181-01c9-4DE9-A0A2-EEBFA14CD9F1%7d pgs 11-12 of eBook	1ul/hr saline for 1 week for full recovery	Test articles infusing at 30ul/hr for 72 hours after 1ul/hr saline recovery after catheterization and pump implantation	Yes	No	No	intrathecal	Regulatory request, CNS end points (modified Irwin assessment) rat + SMP-200 Pump	10 days
RA 5 Asemu et al. DOI: 10.1152/ajpheart.00674.2012 pg 13 of eBook	No	Aldosterone (15% ethanol 50% DMSO and 35% water) was continuous infused	Yes	No	No	IV jugular	Cardiac, diastolic dysfunction, heart failure, metabolism dog + SMP-200 Pump	14 weeks
RA 6 Thisgaard et al. DOI: 10.7150/thno.15898 pg 14 of eBook	No	isotone saline, 0.1 mM MTX, then 0.3 μ g/ml 125 I-UdR, 127 I-UdR was continuously infused	Yes	No	No	Brain infusion	Glioblastoma, Auger-electron therapy, convection delivery, [125 I]5-Iodo-2'- deoxyuridine, temozolomide, SMP-200 Pump	10 days
RA 7 Devlin MacKeigan et al. https://doi.org/10.1016/j.eplepsyres.2023.107276 pg 15 of eBook	No	intermittent intra-subthalamic delivery of vigabatrin (VGB) or vehicle (aCSF, artificial cerebrospinal fluid)	No	Yes	Yes	Brain infusion (STN)	Basal ganglia, Epilepsy, GABA, transaminase Intracerebral, pharmacotherapy, Pentylentetrazole, Tolerance	3 weeks
RA 8 An, Le, et al. https://doi.org/10.3390/ph17020179 pg 16 of eBook	No	G7883 in the iPRECIO pump IV infusion study 20% Dimethyl Sulfoxide (DMSO): 80% Polyethylene glycol 400 (PEG400) at 3.3 mg/mL. 0.8 mg/kg/h with an infusion rate of 0.2 mL/h/kg (5 μ L/h). The pump was refilled every 24 h with a study duration of 7 days. G6893 in the iPRECIO pump IV infusion study was 100% PEG400 at pH 6 at 2.5 mg/mL. 0.5 mg/kg/h with an infusion rate of 0.2 mL/h/kg (5 μ L/h). The pump was refilled every 24 h with a study duration of 5 days.	Yes	No	No	IV jugular	Drug delivery; PO; IV infusion; IP; SC; small molecule; PK profile; exposure	5 days and 7 days
RA 9, Tenna Bering et al. https://doi.org/10.1159/000533151 pg 17 of eBook	No	The pump reservoir was filled with 12.5 mg/mL corticosterone. Dissolved in 10% dimethyl sulfoxide in polyethylene glycol 400. Pumps were programmed in 24 h repetitive loops to deliver corticosterone at 4 μ L/h from ZT6-ZT10, 6 μ L/h from ZT10-16, 4 μ L/h from ZT16-ZT18 and a maintenance dose of 1 μ L/h to avoid clotting in the outlet tubing for the remaining 12 h, ZT18-ZT6.	No	Yes	Yes	SC	Clock gene, Corticosterone, Hippocampus, Programmable pumps, Suprachiasmatic nucleus	7 to 9 days
RA10 Moghe et al. https://doi.org/10.1038/s41556-025-01618-9 pg 18 of eBook	No	human follicle-stimulating hormone was embedded subcutaneously under anesthesia and injected 7 μ L/hr for 10 days. Continuous infusion for 10 days.	Yes	No	No	SC	Embryonic patterning, Inner cell mass (ICM), Epiblast (EPI), Primitive endoderm (PrE), Apical polarity, Cell migration, Extracellular matrix (ECM), Surface tension, Blastocyst development, Robustness / tissue geometry	10 days

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	KVO/RCV	Vehicle and Drug(s)	Continuous	Intermittent or bolus	Circadian / Timed release			
RA11 Nakaya et al. https://doi.org/10.1038/s41467-025-57365-w pg 18 of eBook	No	human follicle-stimulating hormone was embedded subcutaneously under anesthesia and injected 7 µl/hr for 10 days. Continuous infusion for 10 days.	Yes	No	No	SC	Subjects Disease model Genetic engineering Genetic vectors Transgenic organisms	10 days
RA12 Atsou Kano et al. https://doi.org/10.1038/s41467-025-60628-1 pg 19 of eBook	Yes	For one week after cannula placement in the ventricle, PBS was ICV infused at a flow rate of 2.0 µL/h using a micro-infusion pump. Then, it was replaced with a micro-infusion pump filled with pathogenic #003-102 Ab (5,000 µg/mL), at a 2.0 µL/h (10 µg/h) flow rate. ICV administration of ART5803. After 14 days of continuous #003-102 Ab infusion, the micro-infusion pump was replaced by a mixture of pathogenic antibody and therapeutic antibody (ART5803, n=9) or control Ab (n = 3) in equal amounts for each (2500 µg/mL) and delivered at a flow rate of 4.0 µL/h (10 µg/h) for 14 days.	Yes	No	No	ICV	Anti-NMDA receptor encephalitis, Monoclonal antibody therapy, Humanized monovalent antibody, ART5803, GluN1 subunit (NTD), Pathogenic autoantibodies, NMDAR internalization, Precision immunotherapy	1 week recovery and then 28 days infusion
RA13 Gullledge M et al. https://doi.org/10.1371/journal.pone.0312794 pg 20 of eBook	Yes	After recovery, pumps infused saline for 5 days, the last 3 of which were used as baseline sleep recordings. Following saline infusions, pumps delivered escalating-dose oxycodone twice a day (ZT0-2 and ZT12-14) for 14 days (0.5–8.0 mg/kg/inf, 2 inf/d), resulting in 28 total infusions. Starting with 0.5 mg/kg, rats received the following: number of infusions at oxycodone dose: 4 at 0.5, 6 at 1.0, 6 at 2.0, 6 at 4.0, 6 at 8.0. The last infusion (8.0 mg/kg) occurred from ZT0-2 on withdrawal day 1 (W1).	No	Yes	Yes	SC	Oxycodone withdrawal, Opioid dependence, Sleep disruption, Diurnal rhythms, Electroencephalography (EEG), Non-REM (NREM) sleep, Rapid eye movement (REM) sleep, Aperiodic 1/f slope, Rat model	5 days recovery and then 14 days intermittent infusion
Author, doi:								
GLP Studies with iPRECIO Pumps (page 21 eBook)								
Patten et al pg 21 of eBook	1ul/hr artificial CSF	Treatment period 30ul/hour for 72 hours	No	Yes	Yes	intrathecal	CNS (modified Irwin assessment) rat + SMP-200 pump	3 days for TA
Perron et al pg 21 of eBook	No	Flow-rate and dosing validation studies on the bench	No	Yes	Yes	in-vitro	GLP validation	< 7 days
Ringer et al pg 21 of eBook	Saline when not infusing test article	2 hour baseline, 2 hour infusion (Milrinone or vehicle)	No	Yes	Yes	right jugular vein	GLP validation, jacketed, ambulatory, cardiovascular Dog + iPRECIO Dual	24 hours
Author, doi:								
Toxicology with iPRECIO pumps (page 21 eBook)								
Tsuboi et al. http://doi.org/10.2131/fts.3.1 pg 21 of eBook	No but full study saline infusion	Saline infusion for 4 weeks and 13 weeks 2 or 2.5ul/hour	Yes	No	No	IV jugular	Infusion pump, implantation, rat, iPRECIO, Physiological condition SMP-200 pump	4 or 13 weeks
Webinar (WE), Author, www or doi								
Webinar: Compound Delivery, PK-PD & Validation Studies in Oncology Studies. Schnell et al. http://www.insidescientific.com/webinars/item/384-gold-standard-physiological-measurements-and-novel-drug-delivery-methods-iprecio pg 22 of eBook	RCV or KVO not discussed	2 pumps (SMP-200 & SMP-310R) 3 tool compounds, 24 doses, 7 infusion rates (2.2ul/hr to 20 ul/hr)	Yes	No	No	iv, external jugular vein	PK/PD, oncology, tool compounds, validation, programmable pump	12-13 days
Weiss, Andreas, et al. https://doi.org/10.1158/2159-8290.CD-22-0158 pg.22 & 23 of eBook	RCV or KVO not discussed	For infusion, JDQ443 was dissolved in 30% PEG and 10% Kolliphor at a concentration of 3 and 10 mg/mL. The infusion rate of 4 µL/h was programmed with iPRECIO Management Software v1.0.4.0. Pumps were refilled with vehicle or JDQ443 daily.	Yes	No	No	iv, external jugular vein	PK/PD, oncology, programmable pump, Selective Covalent Oral Inhibitor of KRAS ^{G12C} , JDQ443	13 days
WE 1 Schnell http://www.insidescientific.com/webinars/item/384-gold-standard-physiological-measurements-and-novel-drug-delivery-methods-iprecio pg 23 of eBook	Saline infusion for tumor size to grow to a certain size (12th day)	On day 21 (tumor reached certain size), infusion of Compound A for 22 days. Behaviour and weight gain not impaired versus control without subcutaneous pump	Yes	No	No	Intra-cranial infusion	Cancer, orthotopic, glioblastoma, bioluminescence Nude rats, SMP-200	22 days

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WE 2 Doyle http://www.insidescientific.com/webinars/item/384-gold-standard-physiological-measurements-and-novel-drug-delivery-methods-iprecio pg 23 of eBook	7 days recovery Saline 5 days baseline Saline 5 day TA or 10 day TA	Vitamin B12 Conjugation of Peptide-YY3-36 or Native Peptide-YY3-36 or saline 5 pulses per day; three 1 hour pulses of 10 nmol.kg-1.h-1 (20 µl.h-1) with three hours between pulses and two 1 hour pulses of 5 nmol.kg-1.h-1 (10 µl.h-1) with five hours between pulses	No	Yes	Yes	subcutaneous	endocrinology vitamin B12, BBB, reduction of food intake, peptides rats, SMP-200 pumps	5 or 10 days
Henry et al. DOI: http://dx.doi.org/10.1210/en.2014-1825 (WE 2) pg 23 of eBook	7 days recovery Saline 5 days baseline Saline 5 day TA or 10 day TA	Vitamin B12 Conjugation of Peptide-YY3-36 or Native Peptide-YY3-36 or saline 5 pulses per day; three 1 hour pulses of 10 nmol.kg-1.h-1 (20 µl.h-1) with three hours between pulses and two 1 hour pulses of 5 nmol.kg-1.h-1 (10 µl.h-1) with five hours between pulses	No	Yes	Yes	subcutaneous	endocrinology vitamin B12, BBB, reduction of food intake, peptides rats, SMP-200 pumps	5 or 10 days
Webinar: Development of a Low-dose Percutaneous Delivery System of Lenalidomide for Hematologic Malignancies: The Journey from Ideation to Phase 2 https://www.labroots.com/webinar/development-low-dose-percutaneous-delivery-system-lenalidomide-hematologic-malignancies-journey-idea?campaign=eBook2025tabular pg 24 of eBook	No	See webinar more for details:- Study1 : 48 µg/day, 144 µg/day, 288 µg/day& 600 µg/day (continuous for 10 days) Study 2: 144 mcg (6 mcg/hr), 48 mcg (2 mcg/hr), 24 mcg (1 mcg/hr), 12 mcg (0.5 mcg/hr) (continuous for 14 days / 1 day off / continuous for 14 days) Study 3: 144 mcg, 216 mcg, 288,mcg (13/ 1 day off /13 pump refill)	Yes	No	No	subcutaneous	multiple myeloma, controlled lo dose, drug delivery	max 28 days
Cardiovascular Applications pg 32 of eBook								
Reitz, Cristine J., et al. "A brief morning rest period benefits cardiac repair in pressure overload hypertrophy and postmyocardial infarction." JCI insight 7.22 (2022). 10.1172/jci.insight.164700 Pg. 32 of eBook copyright of figure to authors referenced. Saline, sympathetic agonists norepinephrine and epinephrine.	Yes		No	Yes	Yes	subcutaneous	Rest Cardiac Remodeling, Circadian Rhythms, Heart Failure, Translational Medicine	20 days
Dey et al. DOI https://www.ahajournals.org/doi/10.1161/CIRCRESAHA.118.312708 Page 33 of eBook.	No	Daily bolus of Isoproterenol (ISO) was administered via implantation of a programmable iPRECIO® Pump in the peritoneal cavity. The iPRECIO pump enables reliable, timed delivery of pharmacological agents. The pump was programmed for 1 hour delivery of Isoproterenol at 30µl/hr, total dose of 2mg/kg/day, once a day at the same time (1 PM).	no	Yes	Yes	IP	ventricular fibrillation, phosphorylation, proteomics, heart failure, reactive oxygen species, mitochondria 300g hartley guinea pig, SMP-200	3 to 5 weeks
Joshi, Pooja, et al https://doi.org/10.7554/eLife.88638.3 Page 33 of eBook	No	Daily bolus of Isoproterenol (ISO) was administered via implantation of a programmable iPRECIO® Pump in the peritoneal cavity. The iPRECIO pump enables reliable, timed delivery of pharmacological agents. The pump was programmed for 1 hour delivery of Isoproterenol at 30µl/hr, total dose of 2mg/kg/day, once a day at the same time (1 PM).	no	Yes	Yes	IP	Sudden Cardiac Death (SCD) Heart Failure (HF) Ventricular Tachycardia/Fibrillation (VT/VF) Ryanodine Receptor 2 (RyR2) Dantrolene Calcium (Ca2+) Leak Repolarization Abnormalities Oxidative Stress Chronotropic Competence Cardiac Contractility	4 weeks

Research Application (RA), Author, doi:	Refillability of Pump		How pump programmed?			Administration Site	Key words /Subjects	Duration
	KVO/RCV	Vehicle and Drug(s)	Continuous	Intermittent or bolus	Circadian / Timed release			
For more details on applications, see bibliography section (https://www.iprecio.com/support/tabid/196/Default.aspx) and iPRECIO® Application and Technology Report (https://www.frontiersin.org/journals/pharmacology/articles/10.3389/fphar.2011.00044/full)								
https://www.iprecio.com/support/tabid/196/Default.aspx		https://www.frontiersin.org/journals/pharmacology/articles/10.3389/fphar.2011.00044/full						
<p>Discovery, Preclinical Characterization, and Early Clinical Activity of JDQ443, a Structurally Novel, Potent, and Selective Covalent Oral Inhibitor of KRASG12CMU6</p> <p>Mouse Update 1 (MU 1) Andreas Weiss et al. https://aacrjournals.org/cancerdiscovery/article/12/6/1500/699171/Discovery-Preclinical-Characterization-and-Early-Clinical-Activity-of-JDQ443,-a-Structurally-Novel,-Potent,-and-Selective-Covalent-Oral-Inhibitor-of-KRASG12C. "Discovery, Preclinical Characterization, and Early Clinical Activity of JDQ443, a Structurally Novel, Potent, and Selective Covalent Oral Inhibitor of KRASG12C." <i>Cancer Discovery</i> 12.6 (2022): 1500-1517. [Open Access]</p> <p>pg 23 of eBook</p>	Unknown (not described in detail)	<p>To assess the effect of continuous dosing on tumor growth, LU99 tumor-bearing nude mice were implanted subcutaneously with a programmable microinfusion pump (iPRECIO, SMP310R, Primetech Corporation) as previously described (56). For this purpose, the catheter connected to the microinfusion pump was inserted into the left external jugular vein via midcervical incision, and the body of the microinfusion pump was implanted subcutaneously on the flank of the mice opposite to the xenograft tumor. For infusion, JDQ443 was dissolved in 30% PEG and 10% Kolliphor at a concentration of 3 and 10 mg/mL. The infusion rate of 4 µL/h was programmed with iPRECIO Management Software v1.0.4.0. Pumps were refilled with vehicle or JDQ443 daily. At days 2 to 3, 9 to 10, and 12 to 13, the drug released was quantified in blood samples collected at the tail vein by LC-MS/MS. "excerpt without modification according to Attribution-Non Commercial-No Derivatives 4.0 International (CC BY-NC-ND4.0) https://creativecommons.org/licenses/by-nc-nd/4.0/</p>	Yes	No	No	IV external jugular vein	<p>Mice were kept under optimal hygiene conditions in individually ventilated cages under 12-hour dark/12-hour light conditions and had access to sterilized food and water ad libitum. Subcutaneous tumors were induced by injecting cells in HBSS containing 50% BD matrigel in the flank of female athymic Crl:NU(NCr)-Foxn1nu-homozygous nude mice (Charles River; MIA PaCa-2, NCI-H2122, NCI-H441 5 × 10⁶; LU99 2 × 10⁶) or female CB17.Cg-PrkdcscidLystbg-J mice (Charles River; KYSE410 10 × 10⁶). Subcutaneous NCI-H2030 and HCC44 tumors were induced by transplantation of tumor fragments in the flank of female C.B-Igh-1b/GbmsTac-Prkdcscid-Lystbg N7 mice (Taconic).</p>	13 days at least
<p>Mouse Update 2 (MU 2) Webinar: Development of a Low-dose Percutaneous Delivery System of Lenalidomide for Hematologic Malignancies: The Journey from Ideation to Phase 2 https://www.labroots.com/webinar/development-low-dose-percutaneous-delivery-system-lenalidomide-hematologic-malignancies-journey-idea?campaign=eBook2025tabular</p> <p>pg 24 of eBook</p>	No	<p>See webinar more for details:-</p> <p>Study1 : 48 µg/day, 144 µg/day, 288 µg/day& 600 µg/day (continuous for 10 days)</p> <p>Study 2: 144 mcg (6 mcg/hr), 48 mcg (2 mcg/hr), 24 mcg (1 mcg/hr), 12 mcg (0.5 mcg/hr) (continuous for 14 days / 1 day off / continuous for 14 days)</p> <p>Study 3: 144 mcg, 216 mcg, 288,mcg (13/ 1 day off /13 pump refill)</p>	Yes	No	No	subcutaneous	multiple myeloma, controlled lo dose, drug delivery	max 28 days
<p>MU 3 Di Francesco, Valentina, et al.</p> <p>Nose to Brain delivery</p> <p>Di Francesco, Valentina, et al. "Minimally invasive nasal infusion (MINI) approach for CNS delivery of protein therapeutics: A case study with ovalbumin." <i>Journal of Controlled Release</i> 372 (2024): 674-681 https://doi.org/10.1016/j.jconrel.2024.06.056</p> <p>pg 27 of eBook</p>	N/A	<p>ovalbumin (43 kDa) as a model protein to assesstrans-nasal delivery into the brains of CD-1 mice</p> <p>Minimally Invasive Nasal Infusion (MINI) delivery approach for administering ovalbumin, a model protein, utilizing a programmable infusion pump (iPRECIO SMP-310R) in a mouse model.</p>	Yes	No	No	Nose To Brain ICV for direct comparison	CD-1 mice (female and male, 25–30 g weight) Neurodegenerative diseases, Nose-to-brain delivery, Protein therapeutics, CNS delivery, Microfluidic infusion system	3 days

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<p>Pulsatile gnRH administration for treating cognitive disorders</p> <p>MU 4 PREVOT et al. International Publication Number WO 2020/221821 A1; https://patents.google.com/patent/WO2020221821A1/en?q=PULSATIVE+GNRH+ADMINISTRATION+FOR+TREATING+COGNITIVE+DISORDERS&oq=PU LSATIVE+GNRH+ADMINISTRATION+FOR+TREATING+COGNITIVE+DISORDER S pg 30 of eBook</p>	N/A	<p>Pulsatile GnRH infusion reverses both olfactory- and cognitive-related impairments in Ts65Dn mice. (A) Schematic diagram illustrating the pharmacological therapy performed in adult Ts65Dn mice with LUTRELEF®, a GnRH peptide of clinic use. Mice were implanted with osmotic pump, to receive a continuous infusion of vehicle or LUTRELEF® (0.25 pgr/ 3h); or with a programmable mini-pump (iPRECIO), to receive a pulsatile LUTRELEF® infusion (every 3 hours; a peak of 0.25 pg with peak duration of 10min). (B-F) Representative graphs for LH pulsatility assessment after 15 days of vehicle or LUTRELEF® subcutaneous administration. LUTRELEF® pulsatile infusion in Ts65Dn males significantly increased LH pulse frequency and LH pulse amplitude (G) compared to LUTRELEF® continuous infusion which prevented both LH pulse frequency and LH pulse amplitude both in WT and Ts65Dn mice(G). LUTRELEF® pulsatile infusion rescued the capacity to discriminate between different odors (H) and cognitive deficits (I) in Ts65Dn mice. *p < 0.05; ** p < 0.01; *** p < 0.001.</p>	No	Yes	Yes	SC	<p>mouse model of Down syndrome (DS - Ts65Dn mice)</p> <p>a mouse model of Alzheimer disease (AD) THY::TAU22 mice.</p>	2 weeks
<p>Blood pressure variability compromises vascular function in middle-aged mice</p> <p>MU 5 Mendiola, Perenkita J., et al. "Blood pressure variability compromises vascular function in middle-aged mice." <i>Elife</i> 14 (2025): RP104082. https://elifesciences.org/articles/104082 Page 31 of eBook. copyright to authors reference. © 2025, Mendiola et al. https://creativecommons.org/licenses/by/4.0/</p>	N/A		No	Yes	Yes	SC	<p>middle-aged mice (12–15 month-old male C57BL/6 mice (Jackson Laboratories))</p>	25 days
<p>Repeated to highlight mouse</p> <p>MU 6 Reitz, Cristine J., et al. Reitz, Cristine J., et al. "A brief morning rest period benefits cardiac repair in pressure overload hypertrophy and postmyocardial infarction." <i>JCI insight</i> 7.22 (2022). 10.1172/jci.insight.164700 Pg. 32 of eBook copyright of figure to authors referenced. Saline, sympathetic agonists norepinephrine and epinephrine.</p>	Yes		No	Yes	Yes	subcutaneous	<p>Rest Cardiac Remodeling, Circadian Rhythms, Heart Failure, Translational Medicine</p>	20 days
<p>An adipokine feedback regulating diurnal food intake rhythms in mice</p> <p>MU 7 Tsang et al. Tsang et al. <i>eLife</i> 2020;9:e55388. DOI: https://doi.org/10.7554/eLife.55388 Cite as: <i>eLife</i> 2020;9:e55388 DOI: 10.7554/eLife.55388 https://elifesciences.org/articles/55388 pg 35 of eBook</p>	2 weeks recovery 0.5ul/hr	<p>After 2 weeks of recovery (MT experiment; Figure 4) or after 6 weeks of HFD (WT HFD experiment; Figure 6), infusion of AdipoRon (1 mg/ml) or vehicle (DMSO/aCSF/PEG-400) was started, either cyclically with infusions starting at ZT13 for 10 hr followed by 14 hr of inactivity or constantly with a maximal flow of 0.5 ul/hr (for treatment regimens see Figures 4A and 8A).</p> <p>Pumps were re-freshed every 7-8 days and 3-4 days after re-freshing, feeding data taken at the appropriate time - ZT4-6.</p>	Yes	Yes	Yes	ICV	<p>8-week-old Adipoq^{-/-} or WT mice.</p> <p>Circadian rhythms, Adipoq-deficient mice or wild-type mice - 8 weeks of age</p>	3 weeks of rhythmic or constant icv

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	KVO/RCV	Vehicle and Drug(s)	Continuous	Intermittent or bolus	Circadian / Timed release			
<p>A combination of two human monoclonal antibodies cures symptomatic rabies</p> <p>MU 8 Dias de Melo et al. https://doi.org/10.15252/emmm.202012628 pg 35 of eBook</p>	<p>(i) a flow rate of 0.1 l/h, to keep the pump delivering PBS from the day of surgery on; (ii) a flow rate of 1.0 ul/h, 2 days before the treatment, to allow flow stability and dead volume elimination from the tubing (27.4 ul)</p>	<p>The pumps were activated the day before the surgery using three infusion programs: (i) a flow rate of 0.1 l/h, to keep the pump delivering PBS from the day of surgery on; (ii) a flow rate of 1.0 l/h, 2 days before the treatment, to allow flow stability and dead volume elimination from the tubing (27.4 l); and (iii) a flow rate of 1.0 l/h during 20 days to deliver the treatment.</p>	yes	No	Yes, precise timing with respect to clinical signs.	icv	Eight-week-old female SPF Balb/cJRj mice	20 days delivery of antibody cocktail following saline infusion for 2-3 days.
<p>Sympathetic Overactivity in CKD Disrupts Buffering of Neurotransmission by Endothelium-Derived Hyperpolarizing Factor and Enhances Vasoconstriction</p> <p>MU 9 Cao et al. DOI: https://doi.org/10.1681/ASN.2020030234 https://jasn.asnjournals.org/content/31/10/2312 pg 35 of eBook</p>	N/A	<p>Clonidine (5.76 mg/kg per day) To study the effects of inhibiting central sympathetic outflow, groups of 5/6Nx mice received continuous intracerebroventricular (i.c.v.) infusions of clonidine (5.76 mg/kg per day; Sigma, St. Louis, MO) or artificial cerebral spinal fluid (Sigma) from the first day after operation for 4 weeks, using Micro Infusion Pumps (iPrecio SMP/IMS-310R model, Durect Corporation, Cupertino, CA). Micro Infusion Pumps were implanted in mice under anesthesia 7 days before the 5/6Nx operation, and were programmed wirelessly using proprietary iPrecio pump software (Durect Corporation). The accuracy of the i.c.v. infusion was confirmed by the tracer Evans blue.</p>	Yes	No	No	icv	Male CD1 mice, 6 week old Male CD-1 mice (6 weeks old) weighing 20–24 g were obtained from the Institutional Animal Experiment Center.	4 weeks
<p>Vagus nerve stimulation mediates protection from kidney ischemia-reperfusion injury through α7nAChR+ splenocytes</p> <p>MU 10 Inoue et al. https://doi.org/10.1172/JCI83658 https://www.jci.org/articles/view/83658 pg 35 of eBook</p>	<p>During the recovery period, normal saline was continuously infused at the rate of 1 μl/h for 4 days.</p>	<p>Saline in the microinfusion pump was changed to the LPS solution (10 μg/ml) The catheter part of the microinfusion pump was inserted into the left external jugular vein via a midcervical incision. The main body of the microinfusion pump was implanted s.c. in the lumbar region. One day before LPS infusion, mice were anesthetized (ketamine [120mg/kg] and xylazine [12 mg/kg]) and the left cervical vagus nerve (uncut) was electrically stimulated (50 μA, 5 Hz, 1 ms) for 10 minutes as described above. At the infusion start time, normal saline in the microinfusion pump was changed to the LPS solution (10 μg/ml) under isoflurane anesthesia. LPS was infused at the rate of 10 μl/h for 3 hours. At the end of infusion, mice were anesthetized (ketamine [120 mg/kg] and xylazine [12 mg/kg]) and blood was collected from the periorbital sinus. Plasma TNF-α was measured with a commercially available ELISA kit (Affymetrix).</p>	Yes	No	No	IV jugular	C57BL/6J male mice Mice. Male mice (8–12 weeks of age, 20–25 g) were used for all experiments. WT C57BL/6 mice were purchased from the National Cancer Institute, Chrna7 $^{-/-}$ (referred to as α 7KO) mice (B6.129S7-Chrna7tm1Bay/J) were obtained from Jackson Laboratories, and WT (Chrna7+/+) progeny were used as controls in experiments depicted in Figures 8 and 10.	10ul/hr for 3 hours LPS
<p>Time of Day Drives Angiotensin II–Dependent Hypertension.</p> <p>MU 11 Benson, Lance N., et al. "Time of Day Drives Angiotensin II–Dependent Hypertension." Hypertension 83.2 (2026): e25906. https://www.ahajournals.org/doi/abs/10.1161/HYPERTENSIONAHA.125.25906 pg 35 of eBook</p>	<p>Continuous infusion of AngII (490 ng/kg*min, Sigma-Aldrich #A9525) was initiated 32 hours later at ZT14–16</p>	<p>C) Experimental design schematic to determine whether the time of surgery was a confounding factor in the blood pressure outcomes. Mice were implanted with telemetry devices at 10 weeks of age at ZT1–7. Ten days later a programmable minipump (iPrecio SMP-310R) was implanted at ZT5–6. Continuous infusion of AngII (490 ng/kg*min, Sigma-Aldrich #A9525) was initiated 32 hours later at ZT14–16 (red squares). In a separate group of telemetry and programmable minipump implanted mice, AngII infusion was initiated after 44 hours later at ZT2–4 (blue circles). Presented as mean arterial pressure (MAP) in 1-hour and 24-hour averages show a significantly higher response in mice that received AngII infusion initiated at ZT2–4 compared to initiation at ZT14–16. Analyzed via mixed effects analysis (24-hour averages) and unpaired two-tailed t test (change from baseline).</p>	Yes	No	No	SC	12 weeks of age, male C57Bl/6J mice	Continuous infusion of AngII (490 ng/kg*min, Sigma-Aldrich #A9525) was initiated 32 hours later at ZT14–16

Research Application (RA), Author, doi:	Refillability of Pump		How pump programmed?			Administration Site	Key words /Subjects	Duration
	KVO/RCV	Vehicle and Drug(s)	Continuous	Intermittent or bolus	Circadian / Timed release			
More Translational Preclinical Models eBook pg 36								
Repeated to highlight Clinical Regimen to mimic human use in animals. Giri, Tusar, et al. "Labor induction with oxytocin in pregnant rats is not associated with oxidative stress in the fetal brain." [Open Access] Scientific reports 12.1 (2022): 3143. https://www.nature.com/articles/s41598-022-07236-x Keywords: Neonatal opioid withdrawal syndrome, Morphine	N/A	Saline and oxytocin 50 µg/mL. The pumps were initially filled with saline and programmed to infuse at a rate of 10 µl/h for 72 hours. The saline served to maintain patency of the tubing until the switch to oxytocin. The oxytocin regimen was programmed as follows: Phase 1: 5 µl/h for 4 hours Phase 2: 10 µl/h for 4 hours Phase 3: 20 µl/h for 4 hours Phase 4: 30 µl/h for 12 hours The oxytocin solution used had a concentration of 50 µg/mL.	No	Yes	no	SC	Oxytocin Labor induction Animal model Pregnant rat iPRECIO pump Oxidative stress Fetal brain Neurodevelopment	3 days, with oxytocin infusion lasting about 8–12 hours within this period
[2] Harder, Hannah J., et al. "Perinatal opioid exposure leads to decreased social play in adolescent male and female rats: Potential role of oxytocin signaling in brain regions associated with social reward." Hormones and Behavior 153 (2023): 105384. https://www.sciencedirect.com/science/article/abs/pii/S0018506X2300082X Keywords: Neonatal opioid withdrawal syndrome, Juvenile play, Social play, Morphine	N/A	Morphine The iPRECIO pumps in the Harder et al. (2023) study were programmed to deliver escalating doses of morphine to female rats. The pumps were initially set to deliver 10 mg/kg of morphine three times a day. The morphine dose was then increased weekly by 2 mg/kg until it reached 16 mg/kg. At E18, the pumps were reprogrammed to deliver the morphine dose twice a day instead of three times a day. Finally, from P5 to P7, the morphine dose was decreased by 2 mg/kg daily until the dams received 0 mg/kg morphine on P7.	No	Yes	No	SC	Neonatal opioid withdrawal syndrome Juvenile play Social play Morphine	28 days
[3] Warn, Peter, et al. "Intermittent micafungin for prophylaxis in a rat model of chronic Candida albicans gut colonization." [Open Access] Journal of Antimicrobial Chemotherapy 75.10 (2020): 2919-2924 https://academic.oup.com/jac/article/75/10/2919/5877001 Topic: candida albicans, feces, rats, micafungin, microbial colonization, prevention	N/A	Micafungin was diluted in 0.9% saline for injection (SFI) and administered as a subcutaneous (SC) bolus dose of 10mL/kg or by iPrecio infusion pump	No	Yes	No	SC	Micafungin, Invasive candidiasis Prophylaxis, Intermittent dosing Rat model, Candida albicans Gastrointestinal colonization Systemic dissemination Humanized dosing iPrecio pump	3 days
[4] Rodrigues, Marinelle, et al. "Susceptible bacteria "can" survive antibiotic treatment in the mammalian gastrointestinal tract without evolving resistance." Cell Host & Microbe (2024). https://www.cell.com/cell-host-microbe/abstract/S1931-3128(24)00016-7 Keywords: antibiotic resistance, antibiotic persistence, antibiotic tolerance, mammalian GI tract, bacterial survival, Escherichia coli, bacterial virulence	N/A	Cefepime. The study also explored the impact of different cefepime concentrations (20, 40, and 60 mg/mL) loaded into the pumps on plasma and tissue drug levels. The article by Rodrigues et al. (2024) employed iPRECIO pumps to deliver cefepime to mice subcutaneously, aiming to mimic the antibiotic's pharmacokinetics in humans. The pumps were filled with a solution of 20 mg/mL cefepime and set to dispense at a rate of 5 mL/h, resulting in a near-constant cefepime plasma concentration of 5 mg/mL over time. The pumps were refilled daily to maintain consistent drug delivery. The study also explored the impact of different cefepime concentrations (20, 40, and 60 mg/mL) loaded into the pumps on plasma and tissue drug levels. They found that higher pump concentrations led to proportionally higher cefepime levels in plasma, feces, small intestine, and colon tissues.	Yes	No	No	SC	Antibiotic evasion Gastrointestinal tract Escherichia coli Cefepime Persistence Intracellular invasion wbaP gene Capsule synthesis Antibiotic pharmacokinetics Murine model	7 days
Withey, Sarah L., Jack Bergman, and Carol A. Paronis. "The effects of chronic naltrexone on reinstatement of opioid-induced drug-seeking behavior and antinociception." Journal of Pharmacology and Experimental Therapeutics 389.1 (2024): 5-14. https://jpet.aspetjournals.org/content/389/1/5.abstract	N/A	Naltrexone To mimic the extended-release formulation, iPrecio programmable minipumps (SMP-200) delivered a constant infusion of 8.33 µg/h naltrexone via an indwelling subcutaneous hydrophilic coated polyurethane catheter (0.55 mm inside diameter) that previously was inserted and secured to the latissimus dorsi muscle under isoflurane anesthesia and in aseptic conditions. The catheter exited the subject's back in the scapular region on the side opposite the intravenous catheter exit site (described above). A 22G stainless steel connector was used to attach the externalized portion of the SC catheter to the iPrecio pump, which was protected in an inside pocket of a nylon jacket worn by the subject at all times. The pump was refilled every third day and replaced when the battery expired. Daily treatment with 0.2 mg/kg/d naltrexone lasted for 5 months for reinstatement studies and for 3 months for antinociception studies.	Yes	No	No	Secured to the latissimus dorsi muscle	Naltrexone Opioid addiction Relapse Reinstatement Squirrel monkeys Oxycodone Antinociception Efficacy Priming Drug-seeking behavior	3 months or 5 months