

**Figure 5 – Supplement 1:   
Development of neuropathic pain phenotype after tibial nerve transection and analgesic profile of chemogenetic activation of LC:SC vs LC:PFC**(A) Progression of mechanical sensitivity, cold sensitivity and incapacitance before and for 7 weeks after nerve injury (**LC:SC** N=8, **LC:PFC** N=7, sham N=6, 2-way repeated measures ANOVA with Bonferroni’s multiple comparison, \* P<0.05 , \*\* P<0.01, \*\*\* P<0.001, \*\*\*\* P<0.0001, red stars: **LC:SC** vs Sham, blue stars: **LC:PFC** vs Sham, black star **LC:SC** vs **LC:PFC**)   
(B) PSEM308 (10 mg/kg) alleviates ipsilateral hypersensitivity and improves incapacitance only in the **LC:SC** group 4 weeks after nerve injury (2-way repeated measures ANOVA with Bonferroni’s multiple comparison PSEM308 vs saline, \* P<0.05, \*\*\*\* P<0.0001, **LC:SC** N=8, **LC:PFC** N=7, sham N=6)  
(C) Timeline of sensory testing and representative image of an intrathecal injection of pontamine sky blue 5 minutes before trans-cardiac perfusion (N=3). Dye was restricted to the caudal region of the spinal cord.  
(D) Ipsilateral chemogenetic analgesia was blocked by pre-treatment with yohimbine (repeated measures ANOVA with Bonferroni’s multiple comparison, \* P<0.05, \*\* P<0.01, \*\*\* P<0.001). Note also that Intrathecal yohimbine (60ng i.t) lowered the mechanical and cold thresholds contralateral to nerve injury in the presence or absence of PSEM308 (10 mg/kg i.p) (2-way repeated measures ANOVA with Bonferroni’s multiple comparison, \* P<0.05, \*\* P<0.01). Unmasking of contralateral sensitization was used as a positive control for successful intrathecal delivery of yohimbine (Hughes et al 2013).  
Data are presented as mean ±SEM