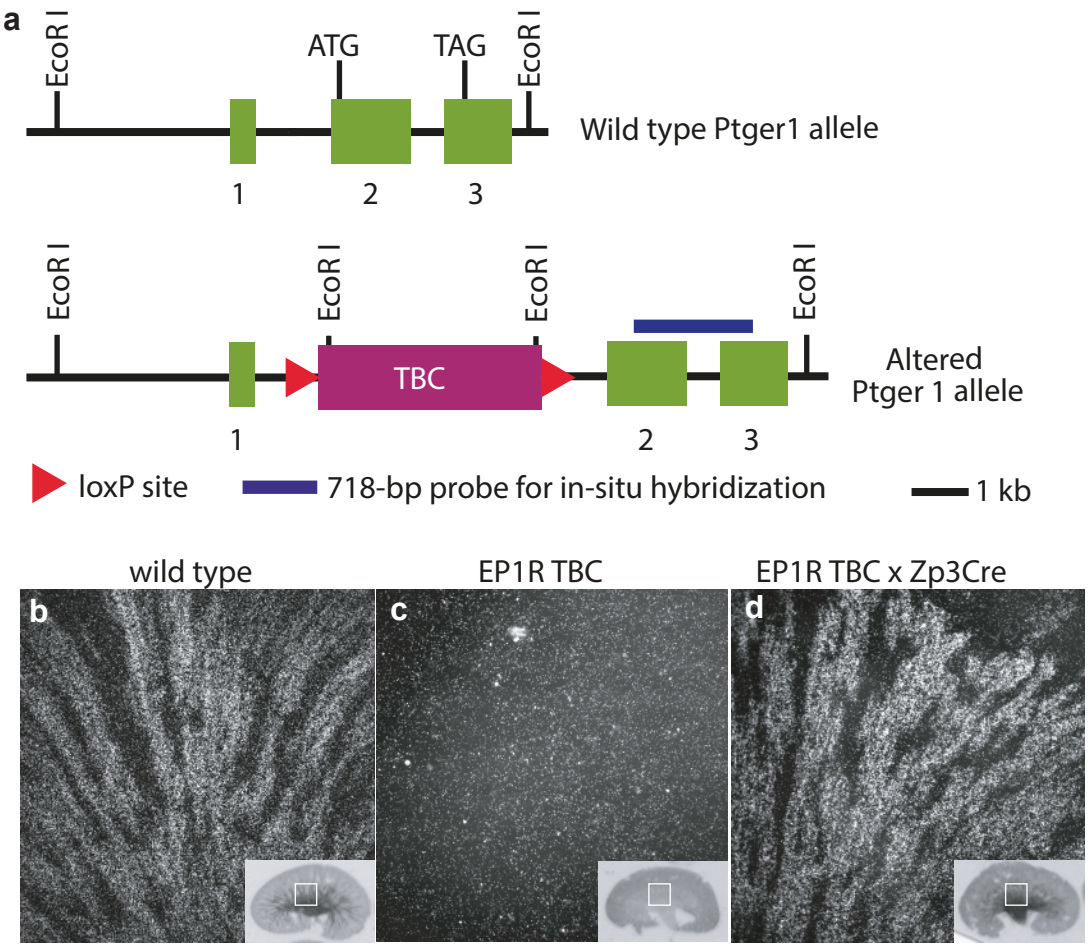
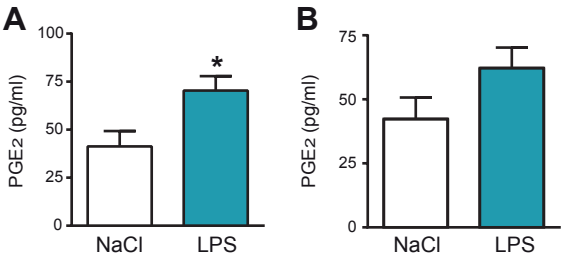
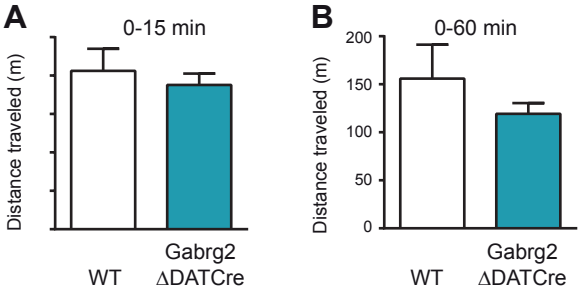
Supplementary Figure 1



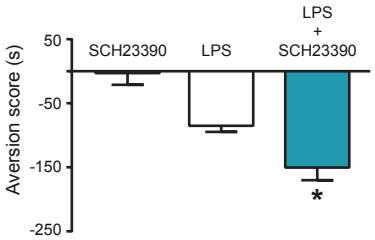
Supplementary Figure 2



Supplementary Figure 3



Supplementary Figure 4



Supplementary Fig. 1: Generation of conditional EP1R knock-in mice. A, loxP-flanked transcriptional blocking cassette (TBC) was inserted in the first intron of the Ptger1 gene. This allele was bred to homozygosity to generate EP1R TBC mice. The Cre-mediated removal of TBC allows the expression of a functional EP1R. Care of all mice followed Institutional Animal Care and Use Committee (IACUC) guidelines, and all procedures were approved by the Standing Committee on Animals at Harvard University. **B-D**, The EP1R is known to be strongly expressed in the collecting ducts of kidneys. Dark field photomicrographs of emulsion-coated sections of kidneys from a wild-type and EP1R TBC mouse show silver grains marking EP1R mRNA hybridization signals in the collecting ducts of kidneys of wild-type (B) but not EP1R TBC (C) mice. **D**, To restore EP1R expression throughout the animal, we crossed EP1R TBC mice with Zp3-Cre mice (Jackson Laboratory), which express Cre recombinase in the female germline. The offspring lacked the entire TBC and showed expression of EP1R mRNA in the collecting ducts of kidneys that is essentially identical wild-type mice.

Supplementary Fig. 2: Inflammation-induced cerebral PGE2 induction. A, PGE2 levels in a section of the forebrain at the striatal level (n = 6 + 6), 1h after injection of LPS (10 µg/kg, i.p.). **B**, PGE2 levels in the cortex dissected from sections as those in A (n = 8 + 8).

Supplementary Fig. 3: Locomotor activity in Gabrg2ΔDATCre mice. **A**, Distance travelled during the first 15 minutes after introduction to the locomotion arena (n = 8 + 8). This time window corresponds to the pretest and posttest sessions. **B**, Distance traveled during the entire hour spent in the arena. This corresponds to the duration of the training sessions.

Supplementary Fig. 4: The D1R antagonist SCH23390 is not aversive and mildly potentiates LPS CPA. WT mice do not develop a negative conditioning score, i.e. place aversion, after injections of SCH23390 (0.2 mg/kg) i.p. (n=6). However, SCH23390 slightly increases LPS CPA (average 75 sec) in WT mice when administered prior to training-sessions (n = 9 + 11).