

## Co-expression of DCX with BMP-4 and Noggin in the hippocampus/dentate gyrus

Immunofluorescent analyses confirmed higher co-expression of BMP-4 with DCX in the hippocampus/dentate gyrus in male control rats and at PIA peak in regard to female control rats (Figure S1:  $p=0.000$ ,  $p < 0.001$ ). DCX and Noggin co-expression was confirmed at higher levels in male control rats (Figure S1:  $p < 0.001$ ). These results may imply a higher level of protection for adult neurogenesis in general in male rats.

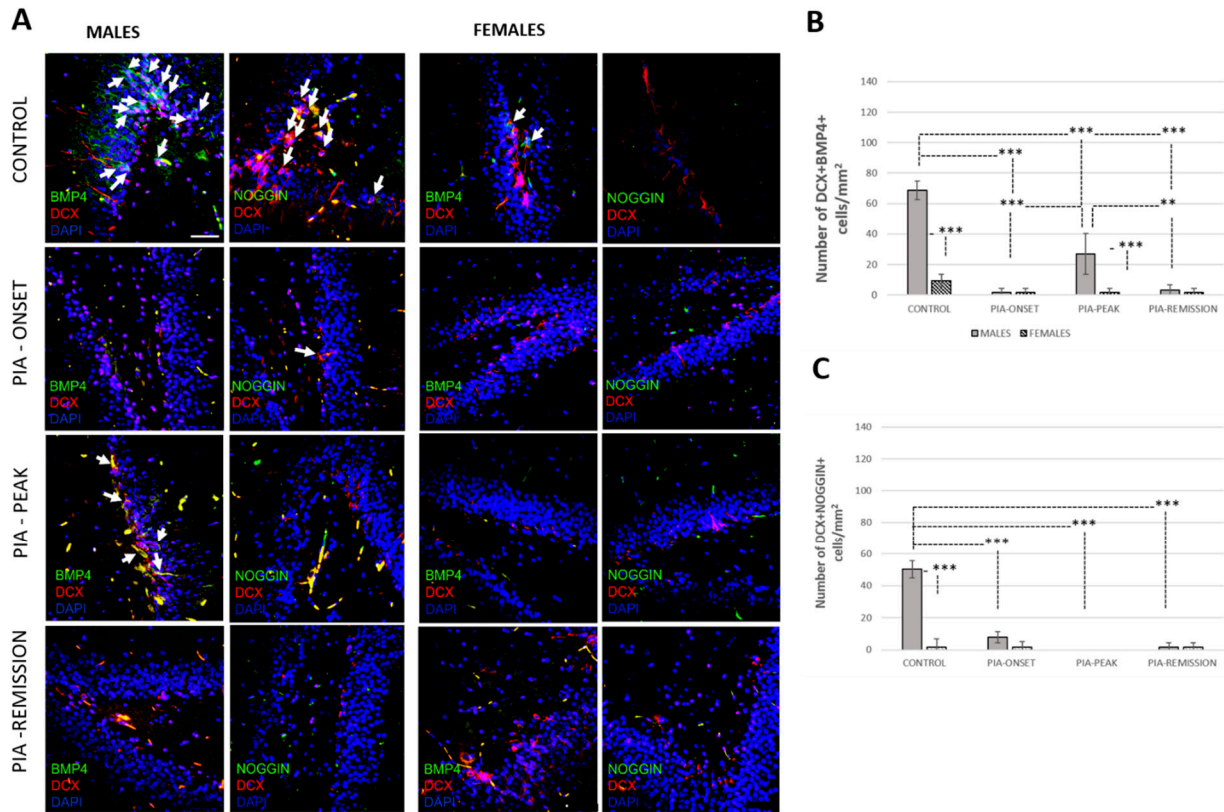


Figure S1. Co-expression of DCX with BMP-4 and Noggin in the hippocampus/dentate gyrus. (A) Representative immunofluorescent pictures show co-expression of DCX with BMP-4 and Noggin in paraffin-embedded sections of brain tissue obtained from male and female DA rats: control (treated with saline); PIA onset (between 9<sup>th</sup> and 12<sup>th</sup> day after induction); PIA peak (between 16<sup>th</sup> and 20<sup>th</sup> day after induction), PIA remission (between 20<sup>th</sup> and 25<sup>th</sup> day after induction). (B,C) The number of DCX<sup>+</sup> BMP-4<sup>+</sup> cells, and DCX<sup>+</sup> Noggin<sup>+</sup> cells per mm<sup>2</sup> were manually counted in regions of interest (8 ROI/4  $\mu$ m slide x 3 slides/rat x 6 rats/group; N = 24). One-way ANOVA followed by the post hoc Scheffé test: \*\*  $p < 0.01$  and \*\*\*  $p < 0.001$ . Scale bars indicate 50  $\mu$ m.

## Co-expression of DCX with BMP-7 and Gremlin in the hippocampus/dentate gyrus

Immunofluorescent analyses confirmed higher co-expression of BMP-7 with DCX in the hippocampus/dentate gyrus in male control rats and at PIA peak in regard to female control rats (Figure S2:  $p < 0.001$ ,  $p=0.04$ ). Rats of both genders show an increase in BMP-7 expression in the remission phase (Figure S2B). Furthermore, co-expression of Gremlin with DCX was confirmed at higher levels at PIA peak in male rats (Figure S2:  $p < 0.001$ ), which could provide better protection for adult neurogenesis.

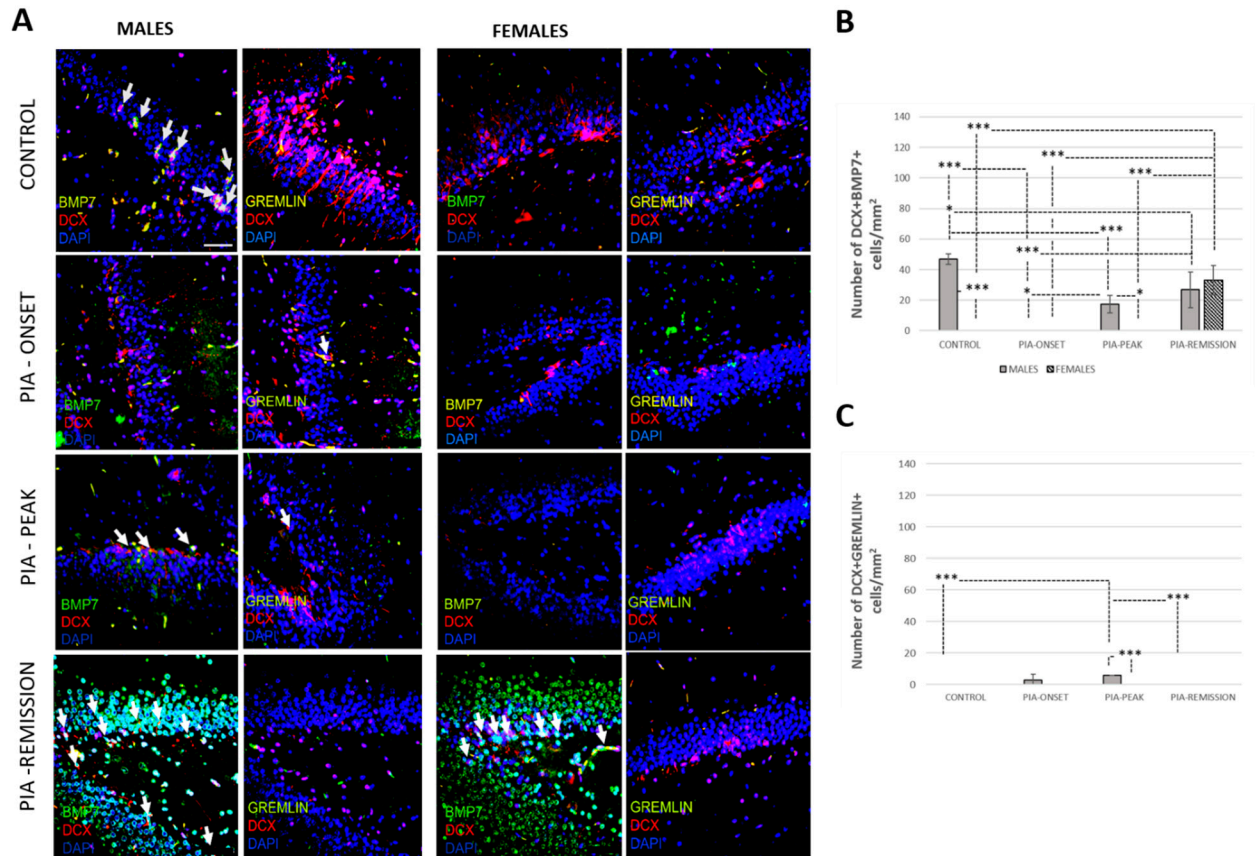


Figure S2. Co-expression of DCX with BMP-7 and Gremlin in the hippocampus/dentate gyrus. (A) Representative immunofluorescent pictures show co-expression of DCX with BMP-7 and Gremlin in paraffin-embedded sections of brain tissue obtained from male and female DA rats: control (treated with saline); PIA onset (between 9<sup>th</sup> and 12<sup>th</sup> day after induction); PIA peak (between 16<sup>th</sup> and 20<sup>th</sup> day after induction), PIA remission (between 20<sup>th</sup> and 25<sup>th</sup> day after induction). (B,C) The number of DCX<sup>+</sup> BMP-7<sup>+</sup> cells, and DCX<sup>+</sup> Gremlin<sup>+</sup> cells per mm<sup>2</sup> were manually counted in regions of interest (8 ROI/4  $\mu$ m slide x 3 slides/rat x 6 rats/group; N = 24). One-way ANOVA followed by the post hoc Scheffé test: \*  $p < 0.05$  and \*\*\*  $p < 0.001$ . Scale bars indicate 50  $\mu$ m.

Male rats express a higher level of hippocampal/dentate gyrus BMP-4 than female rats

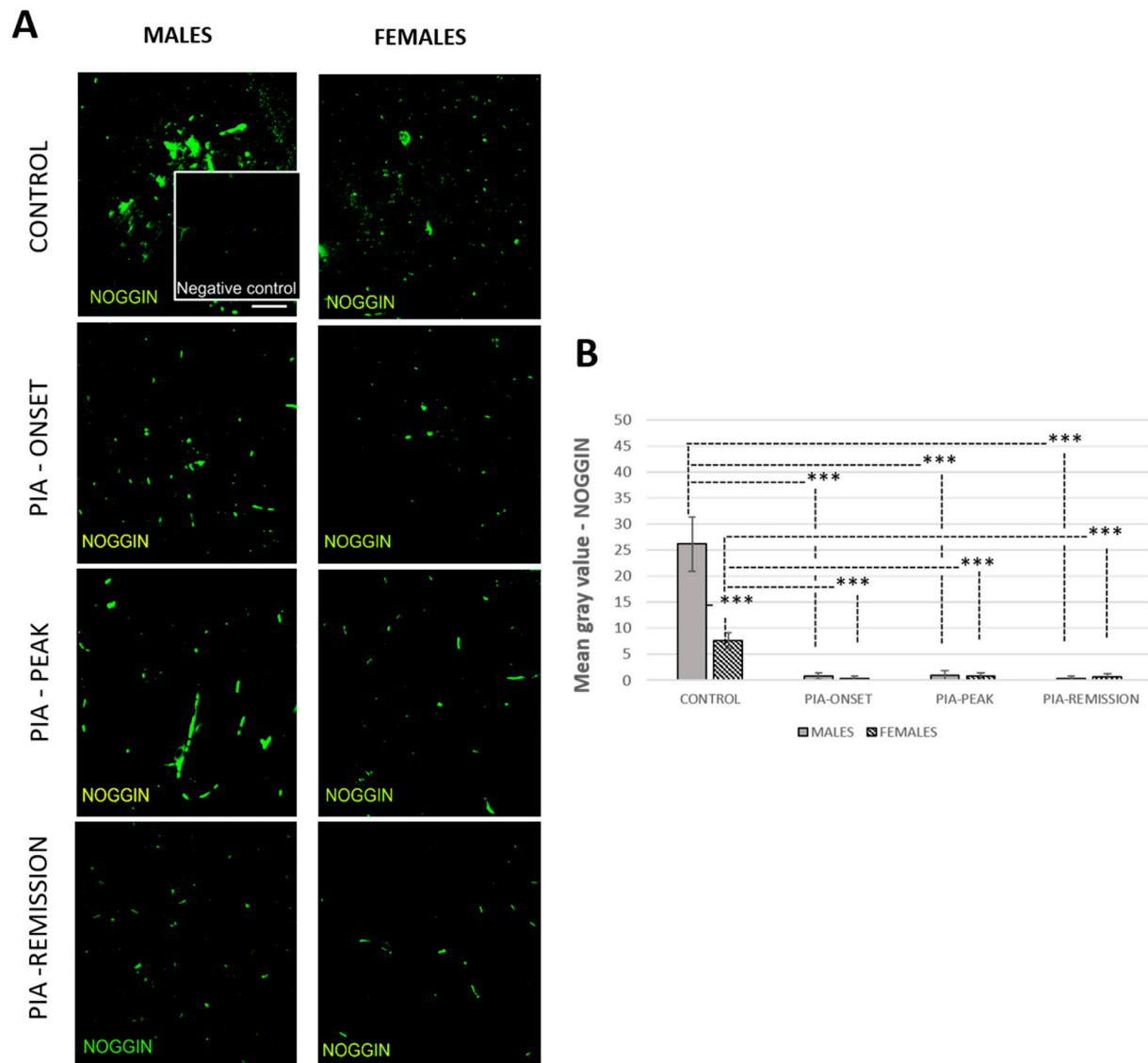


Figure S3. Pristane-induced arthritis downregulates Noggin expression in the hippocampus/dentate gyrus in DA rats. (A) Representative immunofluorescent pictures show staining with anti-Noggin antibody in paraffin-embedded sections of brain tissue obtained from male and female DA rats: control (treated with saline); PIA onset (between 9<sup>th</sup> and 12<sup>th</sup> day after induction); PIA peak (between 16<sup>th</sup> and 20<sup>th</sup> day after induction); PIA remission (between 20<sup>th</sup> and 25<sup>th</sup> day after induction). (B) Noggin immunoreactivity in the hippocampus/dentate gyrus. The immunofluorescent signal quantification was performed using Cell F v3.1 software analysis on 12 regions of interest (3 slides/rat × 6 animals/group). Values are expressed as mean grey value ± SD (N = 24). One-way ANOVA followed by the post hoc Scheffé test: \*\*\*  $p < 0.001$ . Insert shows staining in a slide incubated without primary anti-Noggin antibody (negative control). Scale bars indicate 50  $\mu$ m.

Male rats express a higher level of hippocampal/dentate gyrus Gremlin than female rats

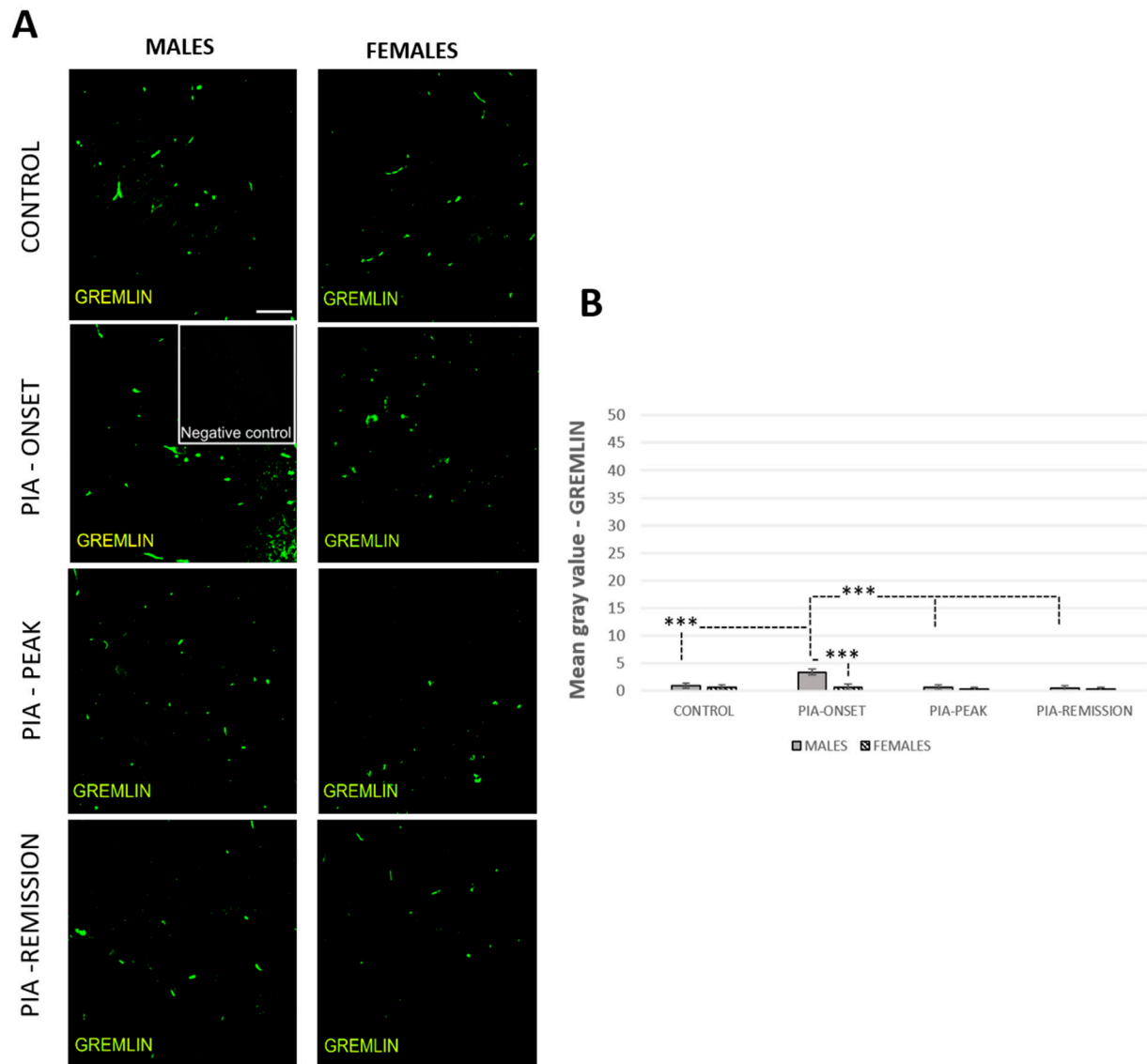


Figure S4. Pristane-induced arthritis upregulates Gremlin expression in the hippocampus/dentate gyrus in male rats. (A) Representative immunofluorescent pictures show staining with anti-Gremlin antibody in paraffin-embedded sections of brain tissue obtained from male and female DA rats: control (treated with saline); PIA onset (between 9<sup>th</sup> and 12<sup>th</sup> day after induction); PIA peak (between 16<sup>th</sup> and 20<sup>th</sup> day after induction); PIA remission (between 20<sup>th</sup> and 25<sup>th</sup> day after induction). (B) Gremlin immunoreactivity in the hippocampus/dentate gyrus. The immunofluorescent signal quantification was performed using Cell F v3.1 software analysis on 12 regions of interest (3 slides/rat × 6 animals/group). Values are expressed as mean grey value ± SD (N = 24). One-way ANOVA followed by the post hoc Scheffé test: \*\*\* p < 0.001. Insert shows staining in a slide incubated without primary anti-Gremlin antibody (negative control). Scale bars indicate 50 µm.