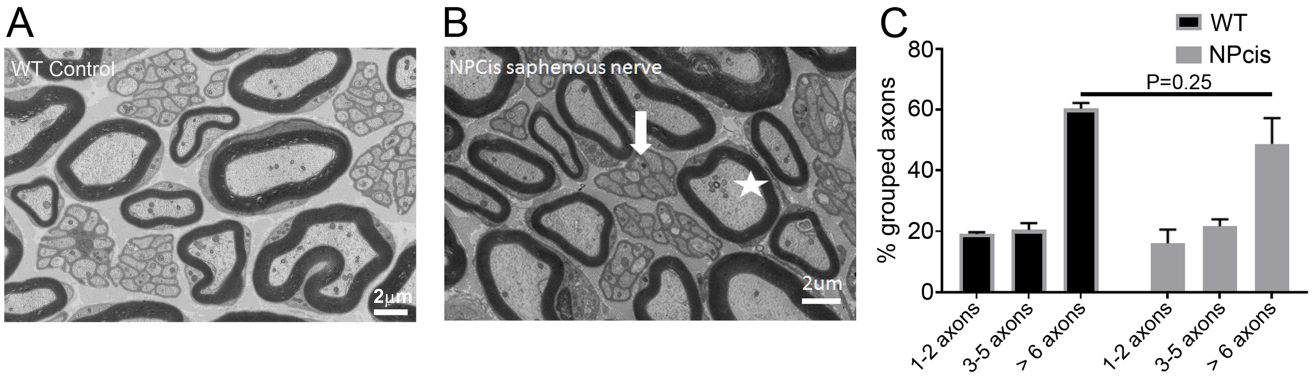


**Figure S1.** NPCis (*Nf1+/-;p53+/-*) peripheral nerves show normal nerve Remak bundle ultrastructure. **(a)** Representative electron micrograph showing wild type saphenous nerve with Remak bundles and myelinated axons. **(b)** NPCis saphenous nerve. White arrow points to normal Remak bundles; white star points to normal myelinated axon. All mice were analyzed at 4 months of age; n=3 per genotype. **(c)** Quantification of small axons per Schwann cell in Remak bundles was performed as described (37). 100-150 Remak bundles were analyzed per animal.

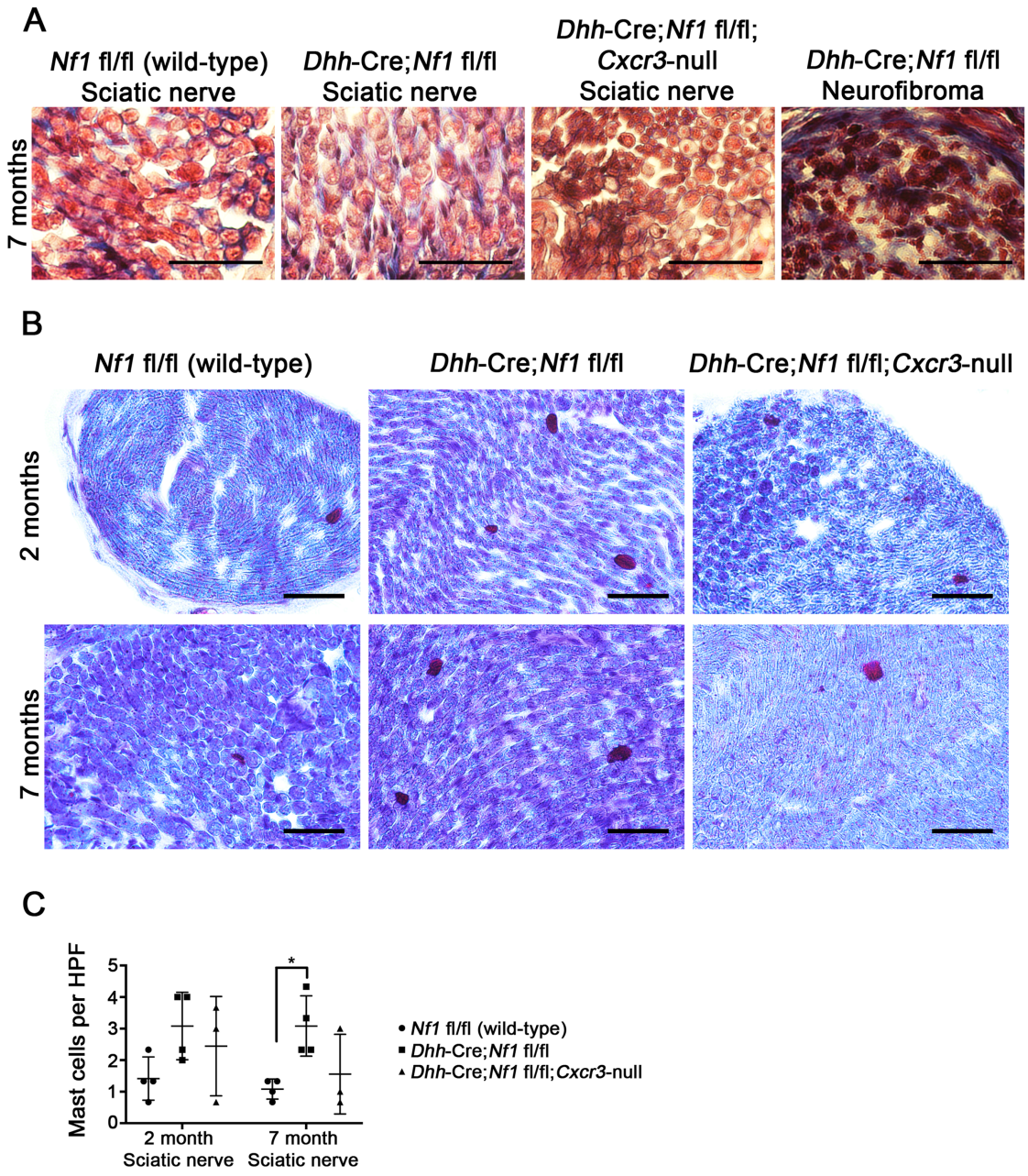


**Figure S2.** Additional characterization of *Dhh*-Cre;*Nf1* fl/fl;*Cxcr3*-null mice. **(a)** Changes in collagen deposition in 7-month sciatic nerves are not evident by trichrome staining (40x objective, 50μm scale bar). Fibrosis is evident in neurofibroma. **(b)** Leder staining for mast cells in 2 and 7 month *Nf1* fl/fl control, *Dhh*-Cre;*Nf1* fl/fl, and *Dhh*-Cre;*Nf1* fl/fl;*Cxcr3*-null sciatic nerves. (40x objective, 50μm scale bar). **(c)** Consistent with toluidine blue staining, loss of *Cxcr3* did not significantly reduce sciatic nerve mast cells

at 2 or 7 months. However, the difference in mast cells between control and *Dhh*-Cre;*Nf1* fl/fl sciatic nerves was significant at 7 months (two-way ANOVA, $p < 0.05$ Sidak's MCT).

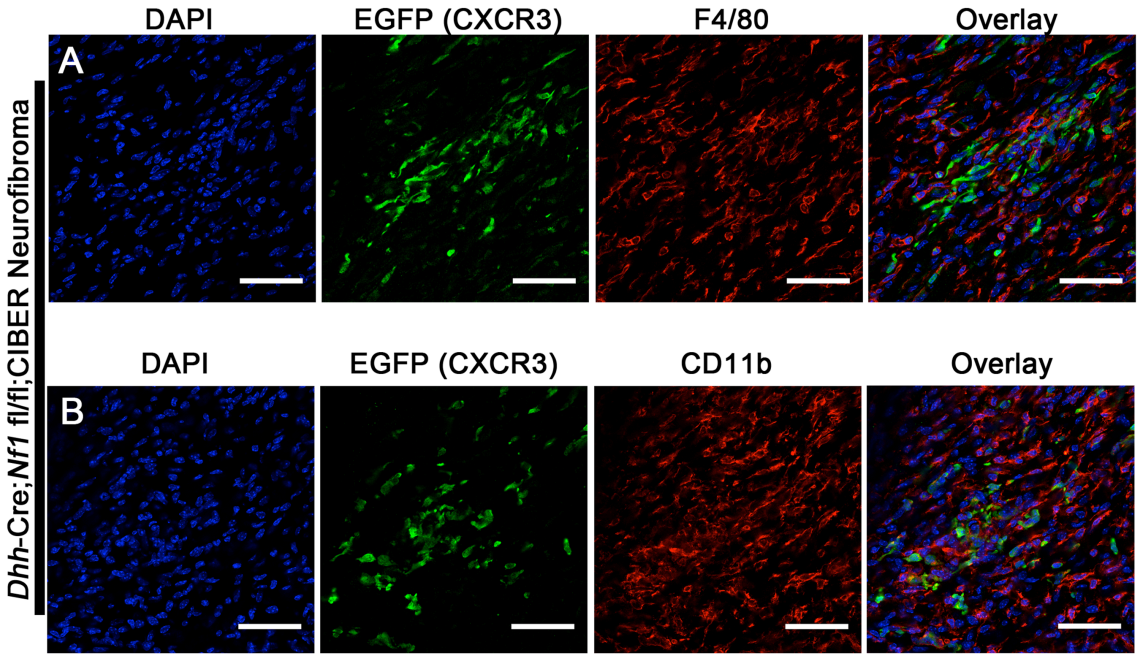


**Figure S3.** Immunofluorescence staining for CXCR3 with additional macrophage markers. *Cxcr3* expression did not co-localize with either **(a)** F4/80 (red, top; 60x objective, 50μm scale bar) or **(b)** CD11b (red, bottom; 60x objective, 50μm scale bar).

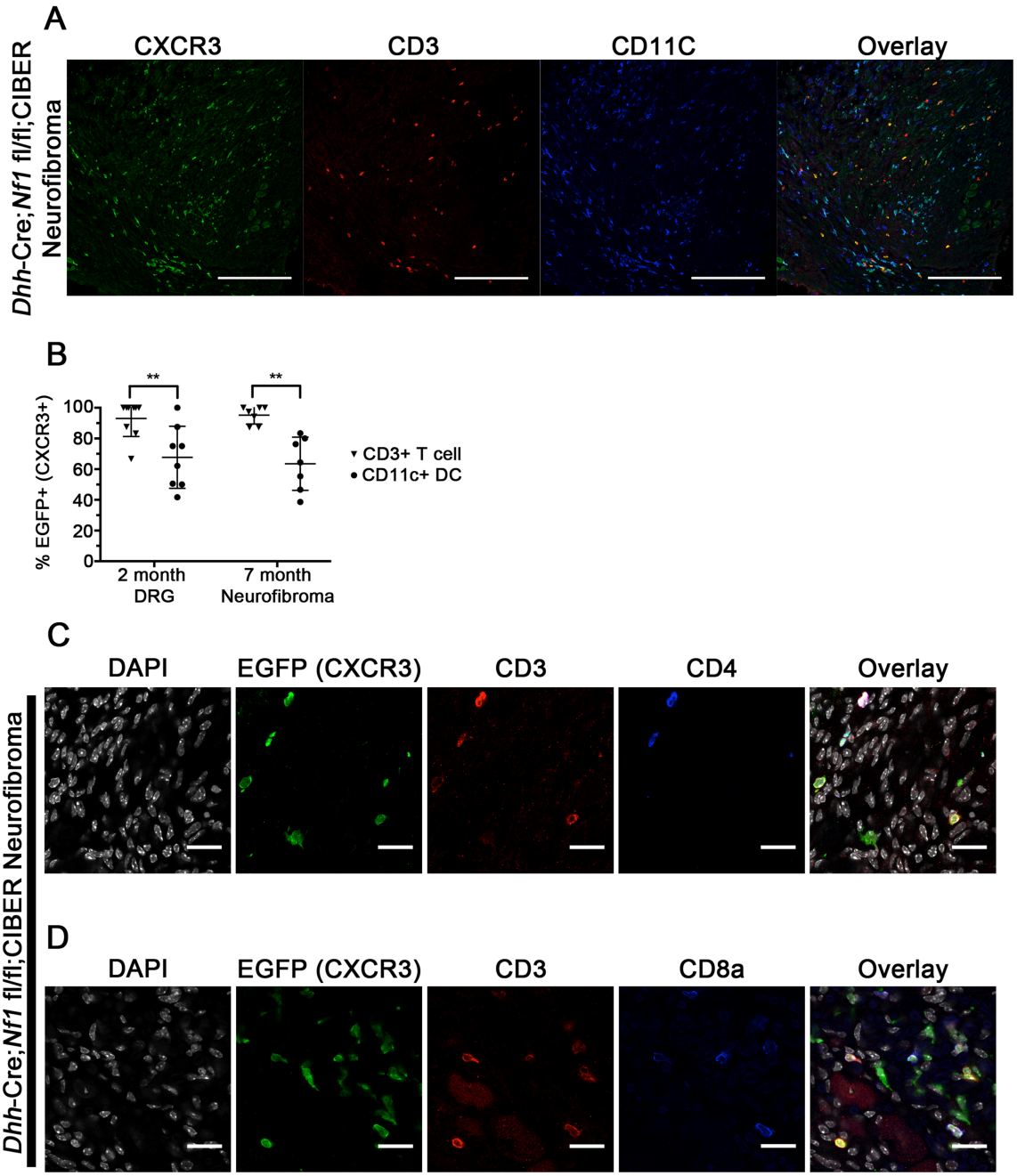


**Figure S4.** Additional characterization of *Cxcr3* expression in T cells and DCs.
**(a)** Foci of *Cxcr3* expressing T cells and DCs in neurofibroma (20x objective, 200μm scale bar). **(b)** A significantly higher proportion of T cells (>90%) express *Cxcr3* than do DCs (~65%) in 2-month DRG and neurofibroma (** $p < 0.01$, Tukey's MCT). **(c-d)** CD3+ T cells in neurofibroma are an admixture of CD4+ and CD8a+ cells (60x objective, 20μm scale bar).

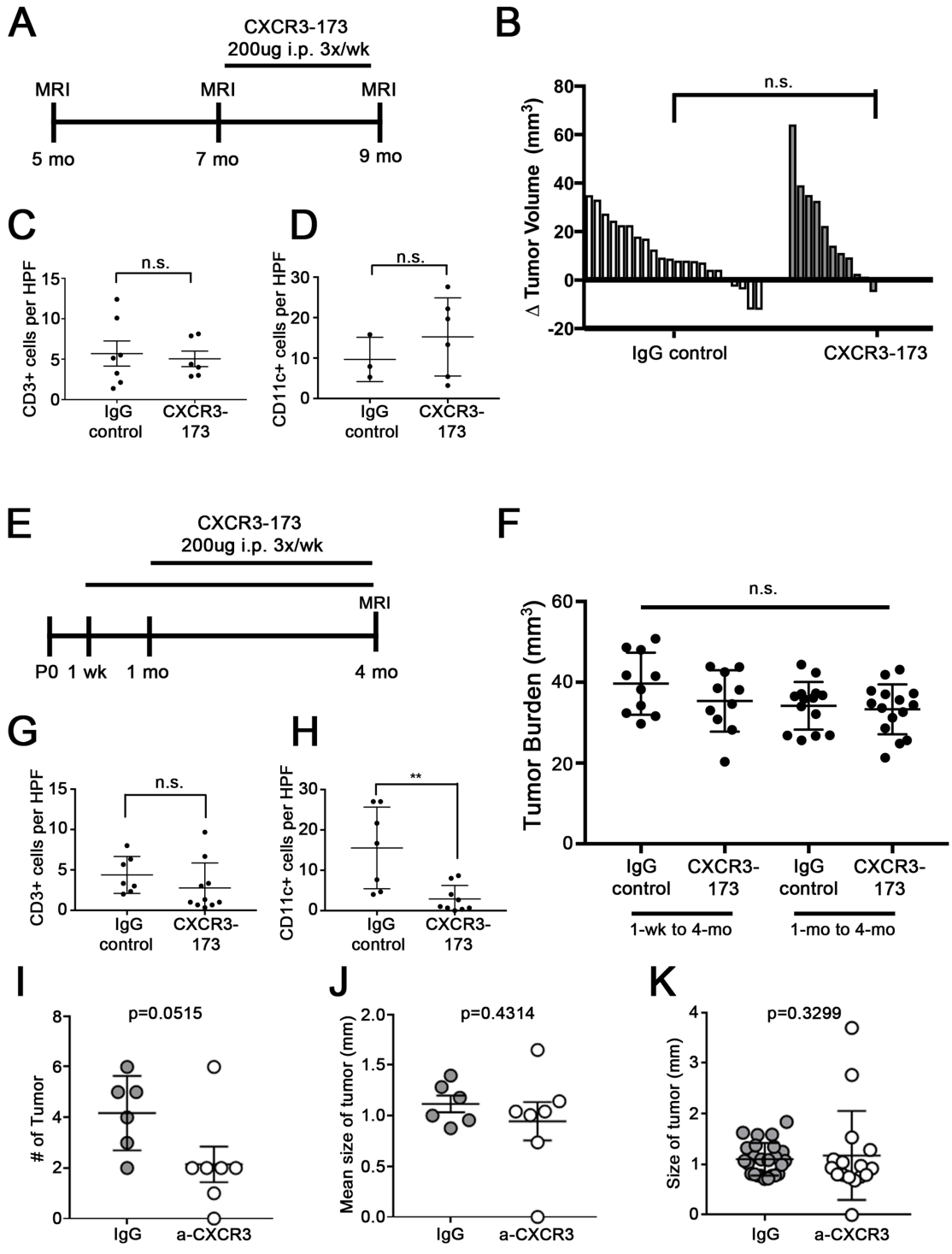
A
CXCR3-173
200ug i.p. 3x/wk
MRI
MRI
MRI
5 mo
7 mo
9 mo
B
n.s.
Δ Tumor Volume (mm3)
80
60
40
20
0
-20
IgG control
CXCR3-173
C
n.s.
CD3+ cells per HPF
15
10
5
0
IgG control
CXCR3-173
D
n.s.
CD11c+ cells per HPF
30
20
10
0
IgG control
CXCR3-173
E
CXCR3-173
200ug i.p. 3x/wk
MRI
P0
1 wk
1 mo
4 mo
F
n.s.
Tumor Burden (mm3)
60
40
20
0
IgG control
CXCR3-173
IgG control
CXCR3-173
1-wk to 4-mo
1-mo to 4-mo
G
n.s.
CD3+ cells per HPF
15
10
5
0
IgG control
CXCR3-173
H
**
CD11c+ cells per HPF
30
20
10
0
IgG control
CXCR3-173
I
p=0.0515
# of Tumor
8
6
4
2
0
IgG
a-CXCR3
J
p=0.4314
Mean size of tumor (mm)
2.0
1.5
1.0
0.5
0.0
IgG
a-CXCR3
K
p=0.3299
Size of tumor (mm)
4
3
2
1
0
IgG
a-CXCR3

**Figure S5.** Therapeutic and preventive drug trials with anti-CXCR3 neutralizing antibody CXCR3-173. **(a)** For testing the therapeutic effect of CXCR3-173 in plexiform neurofibroma, volumetric MRI was performed at 5 and 7 months in *Dhh*-Cre;*Nf1* fl/fl mice to establish baseline tumor volumes and growth kinetics. Mice were then treated with 200μg i.p. CXCR3-173 3x/week for 2 months before a final MRI. **(b)** CXCR3-173 treatment did not significantly alter neurofibroma growth kinetics (n = 22 IgG control, n = 11 CXCR3-173, random effects model analysis on log transformed tumor volume data, see Methods). **(c-d)** CXCR3-173 treatment did not reduce CD3+ T cell (n = 7 IgG control, n = 6 CXCR3-173) or CD11c+ DC numbers (n = 3 IgG control, n = 6 CXCR-173 in established neurofibromas (unpaired t-tests). **(e)** Neutralizing antibody administration was initiated at time-points prior to a detectable increase of *Cxcr3* expressing T cells and DCs in *Dhh*-Cre;*Nf1* fl/fl DRGs relative to control DRGs (1 week and 1 month), and continued until a time-point (4 months) at which untreated *Dhh*-Cre;*Nf1* fl/fl mice invariably develop MRI-detectable neurofibroma. **(f)** MRI-detectable tumor burden was not significantly different between CXCR3-173 and IgG control treated *Dhh*-Cre;*Nf1* fl/fl mice at 4 months (n = 10 1-week IgG Control and 1-week CXCR3-173, n = 14 1-month IgG control, n = 15 1-month CXCR3-173, p = 0.13 ANOVA). **(g)** Preventative CXCR3-173 treatment did not significantly reduce the number of CD3+ T cells in neurofibroma relative to IgG control (n = 7 IgG control, n = 10 CXCR3-173, unpaired t-test. **(h)** CD11c+ DC numbers were significantly decreased in by preventative CXCR3-173 treatment relative to IgG control (** $p < 0.01$, unpaired t-test, n = 7 IgG control, n = 10 CXCR3-173). **(i-j)** Gross dissections of spinal cord and associated DRGs (n = 6 IgG control, n = 7 CXCR3-173). **(i)** Tumor number per animal showed a trend toward

reduction in CXCR3-173- treated mice. Neither the average size of tumors **(j)** nor the mean size of individual tumors differed between groups **(k)**. In **(j)** a parametric *t*-test with Welch's correction and in **(l,k)** a non-parametric *t*-test with Welch's correction were used for statistical analysis, with p=0.05 denoting significance.