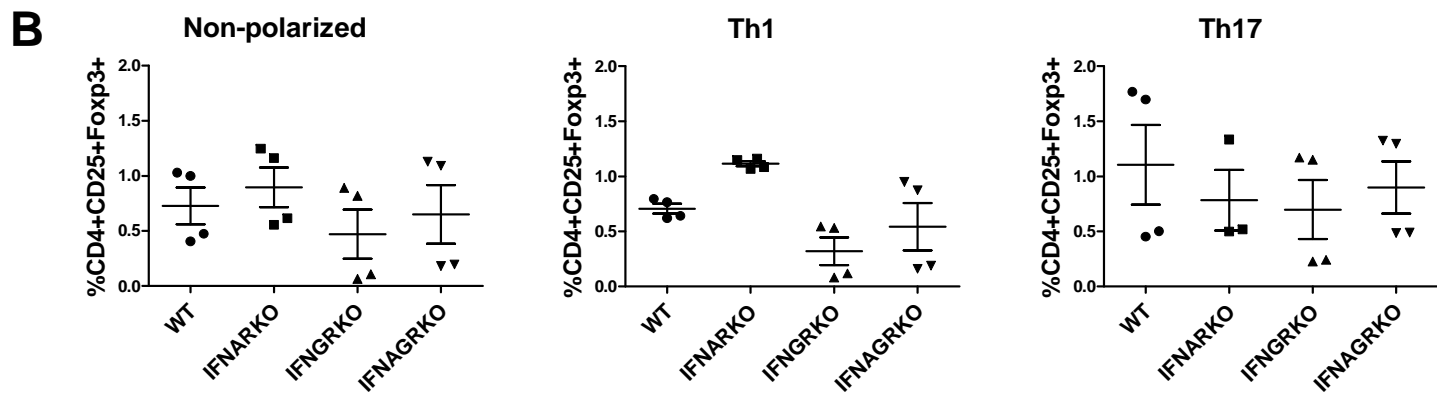
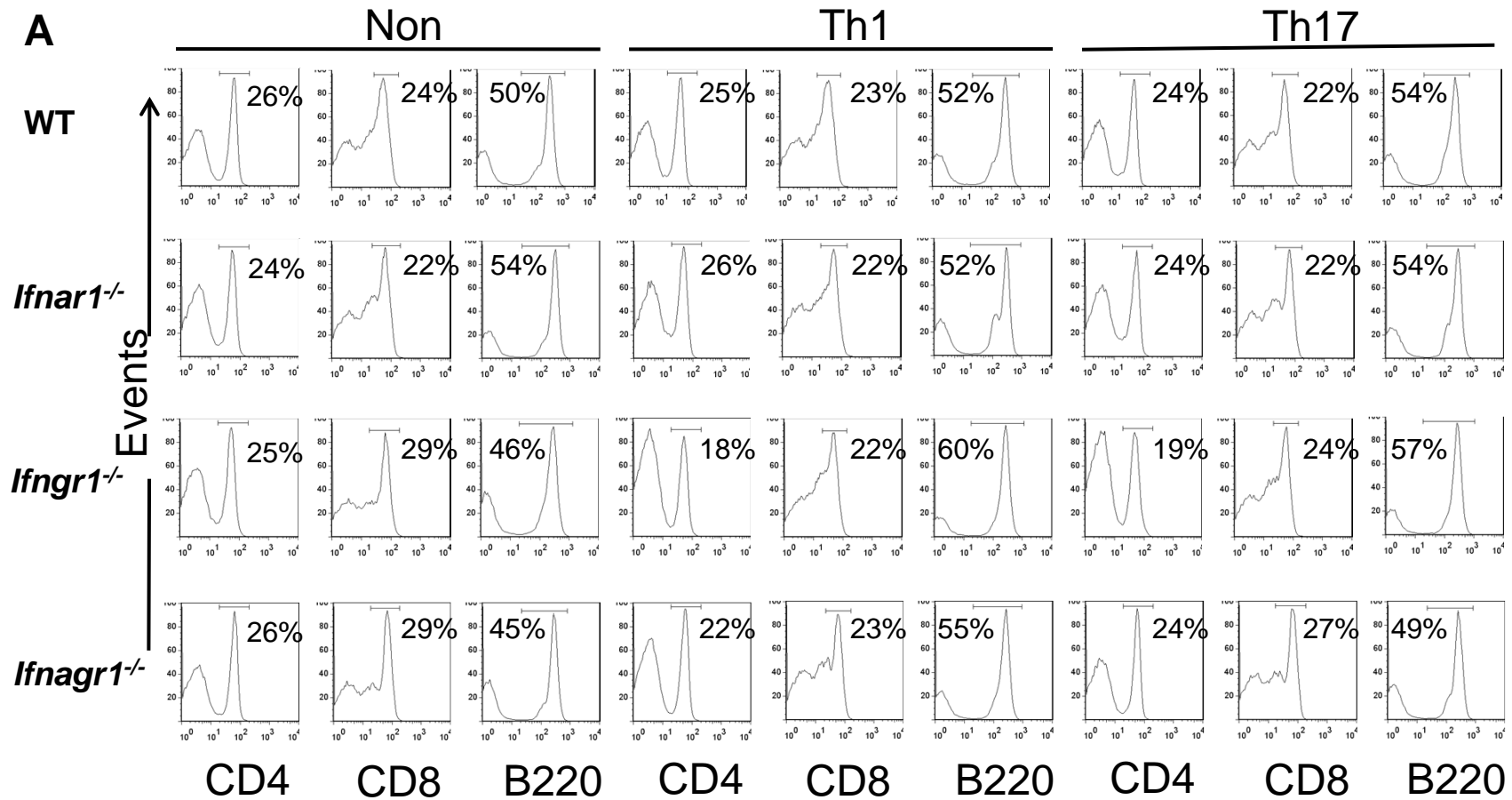


Supplemental Figure 1. Phenotypic composition of the donor population. Spleen and lymph node cells isolated from WT, *Ifnar1*^{-/-}, *Ifngr1*^{-/-} and *Ifnagr1*^{-/-} at 11 days after EAE induction were re-stimulated *in vitro* with MOGp under non-polarized (Non), Th1 polarizing (Th1) or Th17 polarizing (Th17) conditions. After 3 days of culture, the donor population was analyzed before transfer for (A) cells expressing CD4, CD8, B220, CD11b or CD11c by flow cytometry and (B) cells coexpressing CD4, CD25 and FoxP3 (Treg). Donor population did not contain CD11b⁺ and CD11c⁺ cells (data not shown). Percentage for each population is indicated in the histograms.

Supplemental Figure 2. Type I and type II IFNs set activation thresholds in the immune response. Classical EAE data shown in Fig. 1A and Fig. 8 re-analyzed to compare EAE induced by the different MOGp immunization dose in within each mouse line. Data are mean clinical scores \pm SEM, n=8-14 mice. Low dose is 50 μ g MOGp, standard dose is 150 μ g MOGp and high dose is 300 μ g MOGp. ***p<0.001 for standard dose vs low dose and standard dose vs high dose (WT) and **p<0.01 for high dose vs standard dose and high dose vs low dose (*Ifngr1*^{-/-}), one way Anova (Kruskall-Wallis) non-parametric test.

Supplemental Figure 3. The contribution of type I IFN signals to atypical EAE in IFNGR-deficient mice is dependent on MOGp immunization dose. Atypical EAE in mice immunized with 300 μ g MOGp – high dose (A) and 50 μ g MOGp – low dose (B). Data are mean clinical scores \pm SEM, n=8-14 mice. **p<0.01 for low dose MOGp immunized *Ifngr1*^{-/-} vs *Ifnagr1*^{-/-}, non-parametric student's t-test (Mann-Whitney non-parametric t-test).



Supplemental Fig. 1

Supplemental table I – Statistical analysis of cytokine and chemokine levels in spinal cord (SC) and brain (cerebellum and brain stem)^a

Cytokine	SC				Brain	
			p	Significant ^b	p	Significant ^b
IFN- γ	WT	unimm	0.036	Yes	0.089	
		<i>Ifnar1</i> ^{-/-}	0.252		0.295	
		<i>Ifngr1</i> ^{-/-}	0.017	Yes	0.027	Yes
		<i>Ifnagr1</i> ^{-/-}	0.028	Yes	0.032	Yes
	<i>Ifnar1</i> ^{-/-}	unimm	0.036	Yes	0.056	
		<i>Ifngr1</i> ^{-/-}	0.013	Yes	0.049	Yes
		<i>Ifnagr1</i> ^{-/-}	0.018	Yes	0.016	Yes
	<i>Ifngr1</i> ^{-/-}	unimm	0.005	Yes	0.045	Yes
		<i>Ifnagr1</i> ^{-/-}	0.490		0.302	
		unimm	0.005	Yes	0.006	Yes
IL-17	WT	unimm	<0.001	Yes	<0.001	Yes
		<i>Ifnar1</i> ^{-/-}	0.014	Yes	0.164	
		<i>Ifngr1</i> ^{-/-}	0.006	Yes	0.010	Yes
		<i>Ifnagr1</i> ^{-/-}	0.002	Yes	0.022	Yes
	<i>Ifnar1</i> ^{-/-}	unimm	<0.001	Yes	0.004	Yes
		<i>Ifngr1</i> ^{-/-}	0.026	Yes	0.015	Yes
		<i>Ifnagr1</i> ^{-/-}	0.006	Yes	0.028	Yes
	<i>Ifngr1</i> ^{-/-}	unimm	0.001	Yes	0.002	Yes
		<i>Ifnagr1</i> ^{-/-}	0.153		0.317	
		unimm	<0.001	Yes	0.007	Yes
IL-13	WT	unimm	0.004	Yes	0.003	Yes
		<i>Ifnar1</i> ^{-/-}	0.189		0.007	Yes
		<i>Ifngr1</i> ^{-/-}	0.027	Yes	0.002	Yes
		<i>Ifnagr1</i> ^{-/-}	0.042	Yes	0.002	Yes
	<i>Ifnar1</i> ^{-/-}	unimm	0.024	Yes	0.365	
		<i>Ifngr1</i> ^{-/-}	0.084		0.079	
		<i>Ifnagr1</i> ^{-/-}	0.140		0.101	
	<i>Ifngr1</i> ^{-/-}	unimm	0.096		0.240	
		<i>Ifnagr1</i> ^{-/-}	0.128		0.178	
		unimm	0.023	Yes	0.274	
G-CSF	WT	unimm	<0.001	Yes	<0.001	Yes
		<i>Ifnar1</i> ^{-/-}	0.038	Yes	0.474	
		<i>Ifngr1</i> ^{-/-}	0.002	Yes	0.045	Yes
		<i>Ifnagr1</i> ^{-/-}	0.015	Yes	0.008	Yes
	<i>Ifnar1</i> ^{-/-}	unimm	0.002	Yes	0.026	Yes
		<i>Ifngr1</i> ^{-/-}	0.024	Yes	0.049	Yes
		<i>Ifnagr1</i> ^{-/-}	0.035	Yes	0.018	Yes
	<i>Ifngr1</i> ^{-/-}	unimm	<0.001	Yes	0.007	Yes
		<i>Ifnagr1</i> ^{-/-}	0.187		0.211	
		unimm	<0.001	Yes	<0.001	Yes

^a Students unpaired t-test was performed for all comparisons.

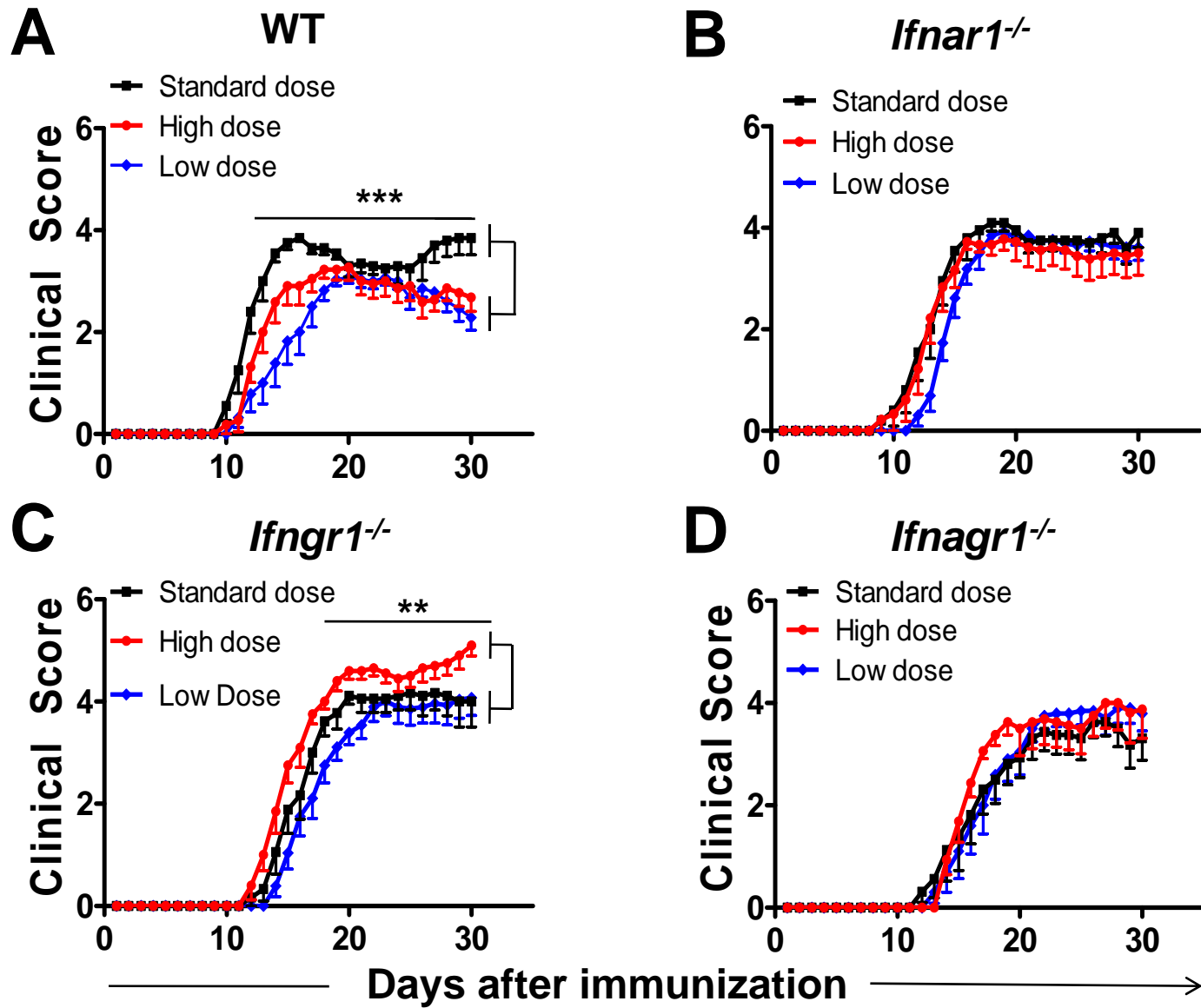
^b p<0.05

Supplemental table I (continued) Statistical analysis of cytokine and chemokine levels in spinal cord (SC) and brain (cerebellum and brain stem)^a

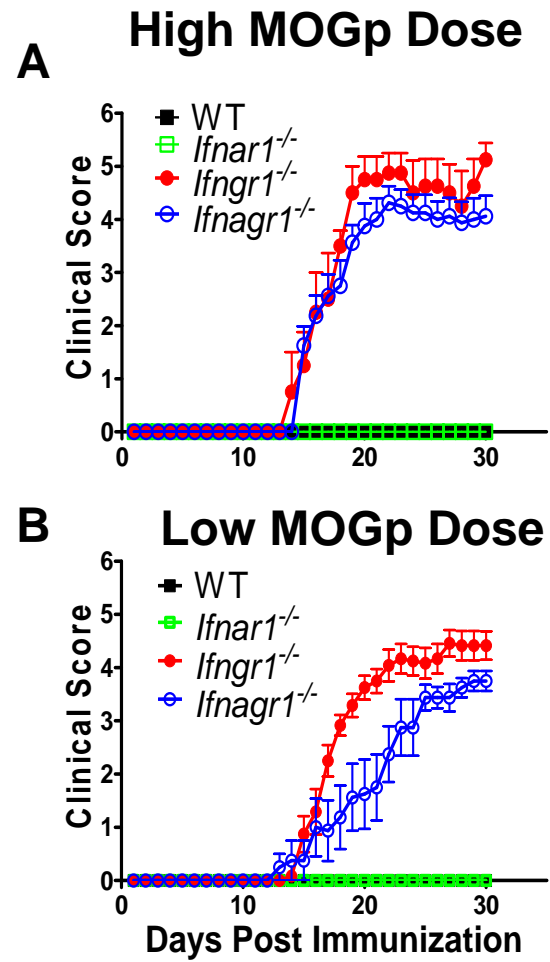
			SC		Brain	
Chemokine			p	Significant ^b	p	Significant ^b
CXCL10	WT	unimm	0.023	Yes	0.004	Yes
		<i>Ifnar1</i> ^{-/-}	0.100	No	0.044	Yes
		<i>Ifngr1</i> ^{-/-}	0.039	Yes	0.026	Yes
		<i>Ifnagr1</i> ^{-/-}	0.035	Yes	0.020	Yes
	<i>Ifnar1</i> ^{-/-}	unimm	0.021	Yes	0.003	Yes
		<i>Ifngr1</i> ^{-/-}	0.046	Yes	0.050	Yes
		<i>Ifnagr1</i> ^{-/-}	0.033	Yes	0.017	Yes
	<i>Ifngr1</i> ^{-/-}	unimm	<0.001	Yes	<0.001	Yes
		<i>Ifnagr1</i> ^{-/-}	0.001	Yes	0.003	Yes
		unimm	0.013	Yes	0.289	No
CXCL9	WT	unimm	<0.001	Yes	<0.001	Yes
		<i>Ifnar1</i> ^{-/-}	0.291	No	0.085	No
		<i>Ifngr1</i> ^{-/-}	<0.001	Yes	0.003	Yes
		<i>Ifnagr1</i> ^{-/-}	<0.001	Yes	0.003	Yes
	<i>Ifnar1</i> ^{-/-}	unimm	<0.001	Yes	0.001	Yes
		<i>Ifngr1</i> ^{-/-}	0.001	Yes	0.008	Yes
		<i>Ifnagr1</i> ^{-/-}	0.001	Yes	0.008	Yes
	<i>Ifngr1</i> ^{-/-}	unimm	0.104	No	0.171	No
		<i>Ifnagr1</i> ^{-/-}	0.107	No	0.248	No
		unimm	0.350	No	0.461	No
CCL5	WT	unimm	0.002	Yes	<0.001	Yes
		<i>Ifnar1</i> ^{-/-}	0.197	No	0.471	No
		<i>Ifngr1</i> ^{-/-}	0.018	Yes	0.015	Yes
		<i>Ifnagr1</i> ^{-/-}	0.016	Yes	0.003	Yes
	<i>Ifnar1</i> ^{-/-}	unimm	<0.001	Yes	0.003	Yes
		<i>Ifngr1</i> ^{-/-}	0.008	Yes	0.048	Yes
		<i>Ifnagr1</i> ^{-/-}	0.007	Yes	0.016	Yes
	<i>Ifngr1</i> ^{-/-}	unimm	<0.001	Yes	0.065	Yes
		<i>Ifnagr1</i> ^{-/-}	0.139	No	0.083	No
		unimm	0.002	Yes	0.376	No

^a Students unpaired t-test was performed for all comparisons.

^bp<0.05



Supplemental Fig. 2



Supplemental Fig. 3