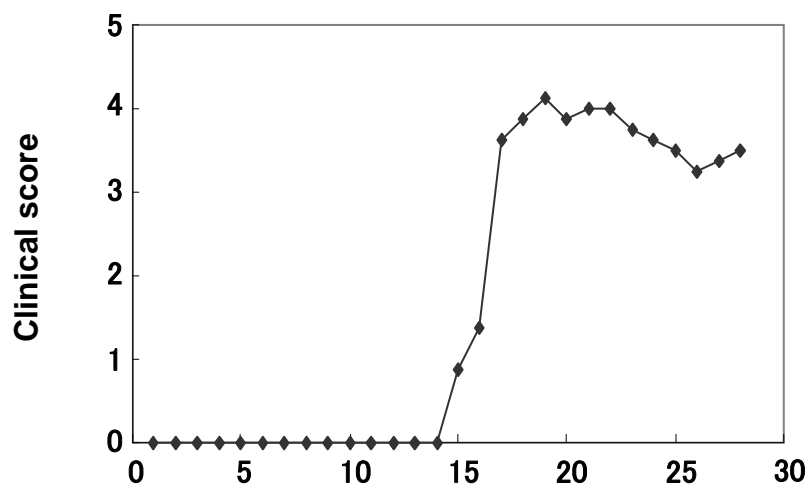


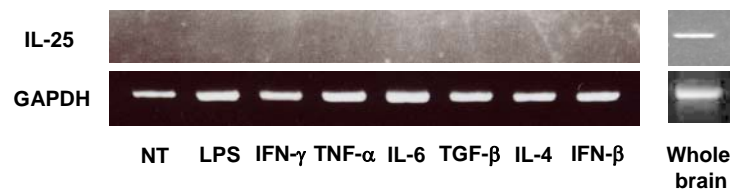
Supplementary Table 1. Summary of isozyme specificity for each of the PKC inhibitors

	PKC $\alpha$	PKC $\beta$ I	PKC $\beta$ II	PKC $\gamma$	PKC $\delta$	PKC $\epsilon$	PKC $\mu$
Gö6976	+	+	-	-	-	-	+
Bisindolylmaleimide I	+	+	-	-	+	+	-

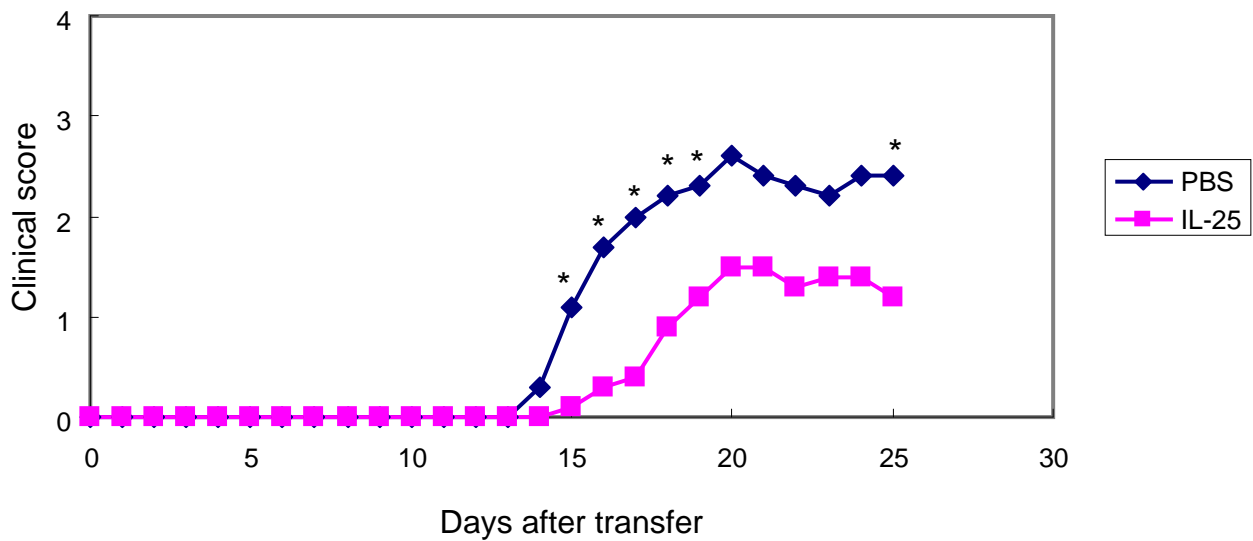
+, inhibition; -, uninhibition



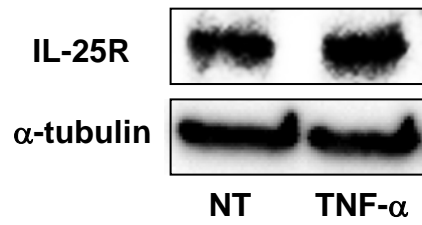
**Supplementary figure 1. The course of EAE in MOG immunized mice.** EAE was induced by immunizing C57BL/6J mice with MOG<sub>35-55</sub> and i.p. injections of PTX on days 0 and 2 after immunization. Mice were scored daily as described in Materials and Methods. A representative disease severity curve is shown (n = 4).



**Supplementary figure 2. Microglia do not express IL-25 mRNA.** Microglia were stimulated with or without LPS (1  $\mu$ g/ml), IFN- $\gamma$  (5 ng/ml), TNF- $\alpha$  (50 ng/ml), IL-6 (30 ng/ml), TGF- $\beta$  (5 ng/ml), IL-4 (20 ng/ml), and IFN- $\beta$  (1000 units/ml) for 24h. Total RNA was extracted and then the expression levels of IL-25 and GAPDH mRNA was analyzed by RT-PCR.

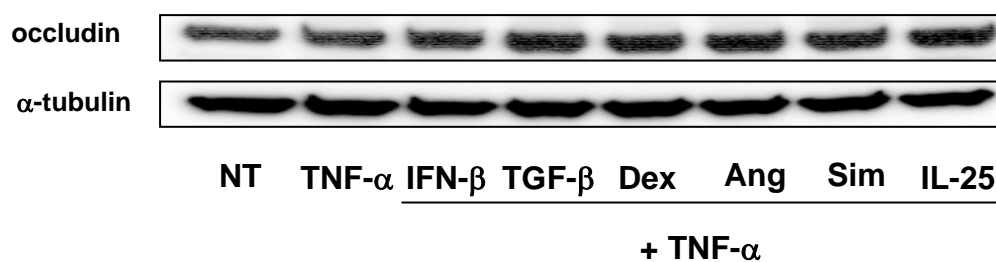


**Supplementary figure 3. IL-25 administration ameliorates passive transfer EAE.** MOG reactive CD4<sup>+</sup> T cells were generated and harvested as described in Experimental Procedures. Cells ( $5 \times 10^6$ ) were injected into wild type C57BL/6 mice. IL-25 (500ng/ mouse) or PBS was administered from day -2 to day 14 every other day. Data shown are the average of five mice per group.

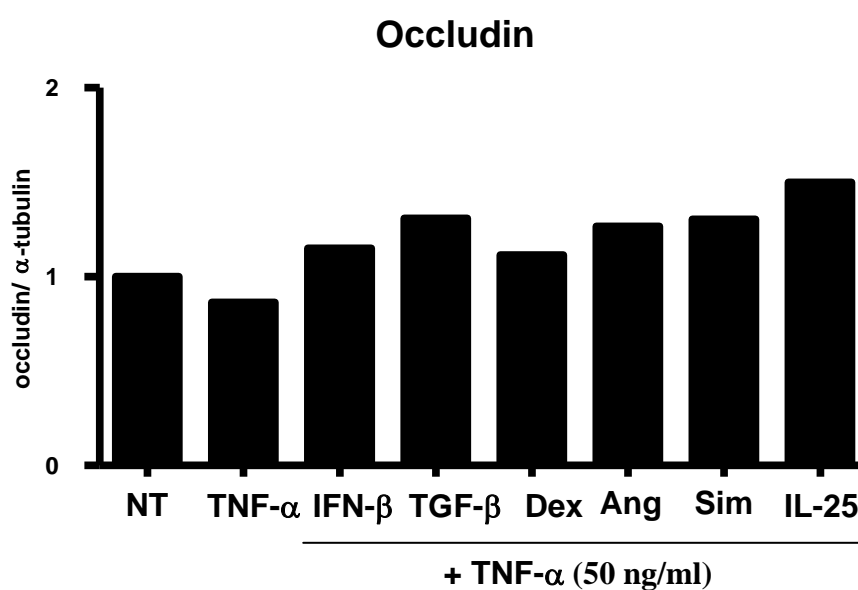


**Supplementary figure 4. BCECs express IL-25R.** Primary BCECs were treated with or without TNF- $\alpha$ . The whole cell lysates were extracted and the IL-25R expression was assessed by Western blotting.

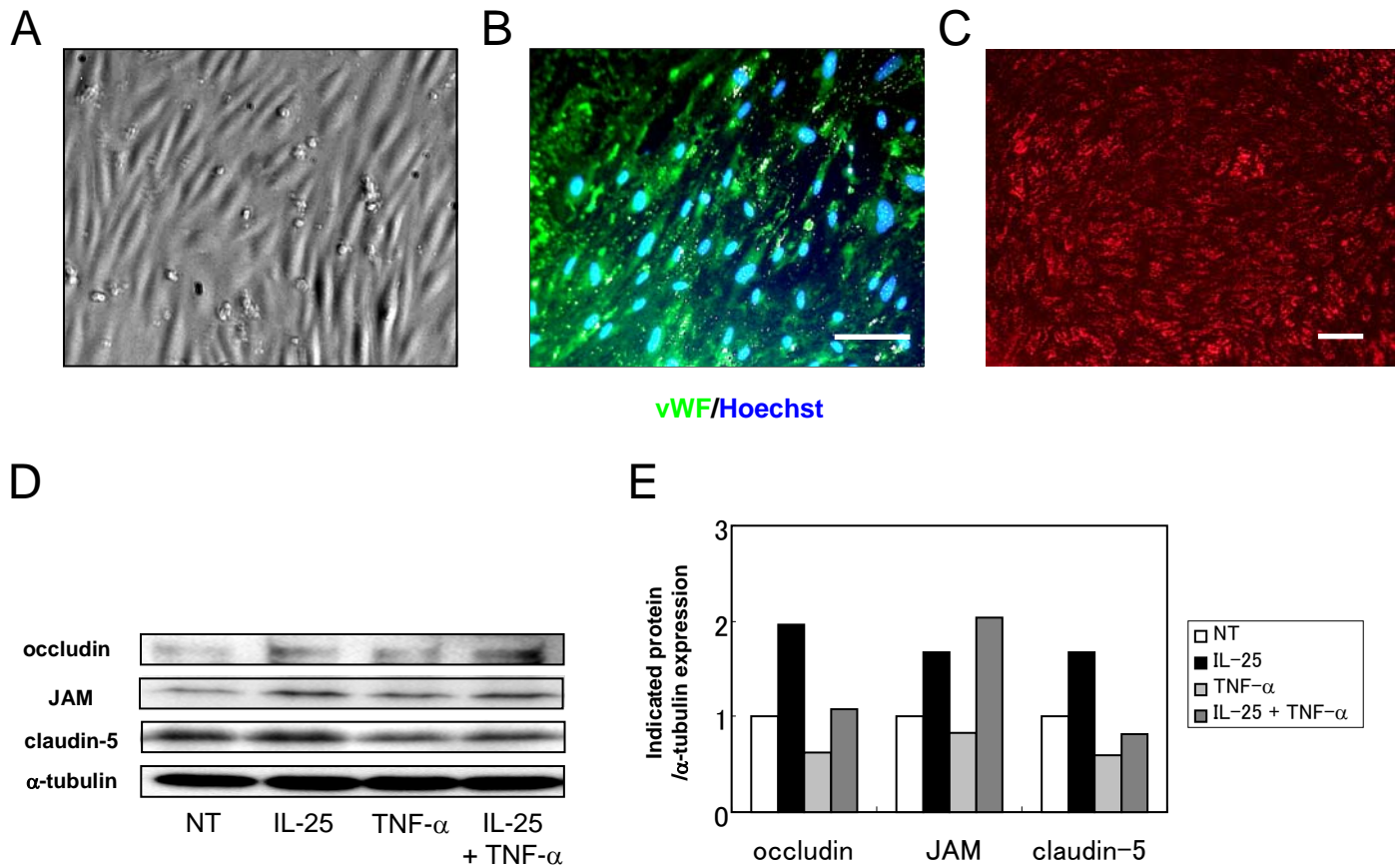
A



B



**Supplementary figure 5. IL-25 most efficiently restores the reduced expression of occludin, induced by TNF- $\alpha$ .** MBEC4 cells were incubated for 24h with 50 ng/ml TNF- $\alpha$  in the presence or absence of IFN- $\beta$  (1000 U/ml), TGF- $\beta$  (5 ng/ml), dexamethasone (Dex; 100 nM), angiotensin II (Ang; 10 nM), Simvastatin (Sim; 10  $\mu$ M) and IL-25 (50 ng/ml). The expression of occludin in whole cell lysates was analyzed by Western blotting. The results of (A) is expressed graphically in (B). The expression levels in untreated cells were set to 1.



**Supplementary figure 6. IL-25 also upregulates the expression levels of occludin, JAM, and claudin-5 in primary BCECs.** (A-C) Primary BCECs were purified using MACS system and grown with endothelial cell growth supplement. The final purity of the primary BCECs was determined by the morphology (A), vWF staining (B), and LDL uptake (C). Scale bar = 100  $\mu$ m. (D) Primary BCECs were treated with or without IL-25 and TNF- $\alpha$ . The whole cell lysates were extracted and the expression levels of TJ protein, occludin, JAM, and claudin-5 were assessed by Western blotting. (E) The results of (D) was quantified in a graphical form.