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SIgN Immunology Seminar



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TREM2 regulates microglia activation in response to CNS demyelination

Host
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Date
Wednesday 10 June 2015

Time
11am – 12pm

Venue
SIgN Seminar Room
Immunos Building
Level 4
Biopolis

Microglia are phagocytic cells that survey the brain and perform neuroprotective functions in response to tissue damage. Triggering receptor expressed on myeloid cells 2 (TREM2) is a microglial immunoreceptor whose loss-of-function mutations in humans cause presenile dementia, while genetic variants are associated to increased risk of neurodegenerative diseases. In myeloid cells, TREM2 has been involved in the regulation of phagocytosis, cell proliferation and inflammatory responses *in vitro*. However, it is unknown how TREM2 contributes to microglia function *in vivo*. We identify a critical role for TREM2 in the activation and function of microglia during cuprizone (CPZ)-induced demyelination. TREM2-deficient ($TREM2^{-/-}$) mice had defective clearance of myelin debris and more axonal pathology, resulting in impaired clinical performances compared to wild-type (WT) mice. $TREM2^{-/-}$ microglia proliferated less in areas of demyelination and were less activated, displaying a more resting morphology and decreased expression of the activation markers MHC II and inducible nitric oxide synthase as compared to WT. Mechanistically gene expression and ultrastructural analysis of microglia suggested a defect in myelin degradation and phagosome processing during CPZ intoxication in $TREM2^{-/-}$ microglia. These findings place TREM2 as a key regulator of microglia activation *in vivo* in response to tissue damage.