Cell Communication and Signaling BioMed Central

Meeting abstract

Open Access

Role of extracellular signal-related kinase (Erk) 1 in the regulation of neuroinflammation

I Bendix*, CF Pfueller, T Leuenberger, V Siffrin, U Schulze-Topphoff, C Loddenkemper, F Zipp and S Waiczies

Address: Charité Berlin, Cecilie Vogt Clinic for Neurology in the HKBB, Berlin, Germany
* Corresponding author

from 12th Joint Meeting of the Signal Transduction Society (STS). Signal Transduction: Receptors, Mediators and Genes Weimar, Germany. 29–31 October 2008

Published: 26 February 2009

Cell Communication and Signaling 2009, **7**(Suppl 1):A106 doi:10.1186/1478-811X-7-S1-A106

This abstract is available from: http://www.biosignaling.com/content/7/S1/A106

We have previously shown that the 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor (HMGCRI) atorvastatin is therapeutic in experimental autoimmune encephalomyelitis (EAE) while also inducing a sustained phosphorylation of the MAPK Erk1 that is important for inducing T cell anergy. However it is also known, that HMGCRI also influence the antigen presenting cell compartment including dendritic cells (DC). This led us to investigate the role of Erk1 in DC biology in more detail. Indeed bone-marrow derived dendritic cells from Erk1 deficient mice had an increased migratory capacity when compared with DC isolated from wildtype littermate mice. As a likely consequence to cytoskeletal regulation, $Erk1^{-/-}$ DC had an increased surface expression of costimulatory molecules and were more potent to prime T cells in vivo. To investigate the implications of these findings in an inflammatory scenario, we induced EAE (experimental autoimmune encephalomyelitis) in $Erk1^{-/-}$ and $Erk1^{+/+}$ mice with myelin oligodendrocyte glycoprotein peptide 35–55 (MOG_{35-55}) and could show that a deficiency of this MAPK results in a moderate increase in disease severity. To differentiate the role of Erk1 between peripheral immune system and the brain compartment we induced EAE in $Erk1^{+/+}$ mice harboring $Erk1^{-/-}$ immune cells by applying bone marrow chimeras ($Erk1^{-/-}$ --> $Erk1^{+/+}$). We report that Erk1 has an important regulatory function in the immune system as shown by pronounced disease severity in $Erk1^{-/-}$ --> $Erk1^{+/+}$ bone marrow chimeras. All together these results indicate the significance of Erk1 in regulating DC functions that are relevant for T cell priming and neuroinflammation, and thus signal the importance of therapeutically targeting this MAPK for the treatment of autoimmune diseases.