

Meeting abstract

Open Access

Tfg (Trk fused gene) is a Carma-1/IKK γ interacting protein involved in CD40-induced canonical NF- κ B signaling

M Grohmann^{*1}, I Hermann¹, M Hampel², M Karas², H Kalbacher³, HM Jäck¹ and D Mielenz¹

Address: ¹University of Erlangen-Nürnberg, Division of Molecular Immunology, Nikolaus-Fiebiger-Centre, Erlangen, Germany, ²Instrumental Analytical Biochemistry, University of Frankfurt, Frankfurt/Main, Germany and ³Medizinisch-Naturwissenschaftliches Forschungszentrum, University of Tübingen, Tübingen, 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):A4 doi:10.1186/1478-811X-7-S1-A4

This abstract is available from: <http://www.biosignaling.com/content/7/S1/A4>

© 2009 Grohmann et al; licensee BioMed Central Ltd.

Carma-1 is required for B cell receptor-/CD40- and T cell receptor-/CD28-induced B- and T-cell activation via JNK and NF- β B. In B cells, Carma-1 becomes phosphorylated by PKC β , leading to its oligomerization. Subsequent Bcl10 binding induces IKK β -activation and, thereby, canonical NF- κ B signalling. Despite these findings it is still unknown how exactly Carma-1 is connected to the plasma membrane and to the IKK-complex. Therefore, we purified Carma-1 complexes from mouse CH12 B cells using anti-Carma-1 affinity columns. Mass spectrometric analyses of the column eluates demonstrated the presence of Carma-1 as well as three previously uncharacterized adaptor proteins in B cells, one of which was the Trk-fused gene (Tfg), an adaptor protein containing PB1 and coiled-coil domains. Whereas Tfg was originally identified as fusion partner of oncogenic Trk tyrosine kinase mutants, the normal cellular homologue of Tfg has so far not been described in B cells. However, Tfg has been shown in other systems to interact with IKK γ and to enhance TNF-induced NF- κ B activation.

Tfg and Carma-1 co-localized at the plasma membrane and perinuclear structures in B cells. We further corroborated the interactions of Tfg, IKK γ and Carma-1 by Blue Native gel electrophoresis, where Carma-1 and Tfg formed a 0.7–1 MDa complex. Ectopic expression of Tfg increased the molecular mass of IKK γ complexes, fused IKK γ , Bcl10 and Carma-1 complexes to a \sim 2 MDa complex, and increased basal and CD40-induced canonical activity of

NF- κ B and IKK β . In contrast, shRNA-mediated silencing of Tfg decreased CD40-induced IKK β activity.

Very interestingly, in primary B cells, highest expression of Tfg was detected in marginal zone and B1 B cells, and Carma-1 and Tfg formed complexes in these B cells. Since Carma-1 is required for marginal zone B cell and B1 B cell development, we suggest that a functional interaction between Carma-1 and Tfg contributes to development and maintenance of these cells by means of canonical NF- κ B signals.