Activation of KIT modulates the function of tumor necrosis factor-related apoptosis-inducing ligand receptor (TRAIL-R) in mast cells

JournalArticle (Originalarbeit in einer wissenschaftlichen Zeitschrift)

ID 4507279
Author(s) Förster, A.; Grotha, S. P.; Seeger, J. M.; Rabenhorst, A.; Gehring, M.; Raap, U.; Létard, S.; Dubreuil, P.; Kashkar, H.; Walczak, H.; Roers, A.; Hartmann, K.
Author(s) at UniBasel Hartmann, Karin ;
Year 2015
Title Activation of KIT modulates the function of tumor necrosis factor-related apoptosis-inducing ligand receptor (TRAIL-R) in mast cells
Journal Allergy
Volume 70
Number 7
Pages / **Article-Number** 764-74
Mesh terms Animals; Apoptosis, drug effects, genetics; Bone Marrow, immunology, metabolism, pathology; Cell Count; Cell Survival, drug effects; Disease Models, Animal; Gene Expression Regulation; Humans; Mast Cells, immunology, metabolism; Mastocytosis, genetics, immunology, metabolism; Mice; Mice, Knockout; Mice, Transgenic; Mutation; Proto-Oncogene Proteins c-kit, genetics, metabolism; Receptors, TNF-Related Apoptosis-Inducing Ligand, genetics, metabolism; Stem Cell Factor, metabolism, pharmacology; TNF-Related Apoptosis-Inducing Ligand, metabolism, pharmacology
Mastocytosis is characterized by the accumulation of mast cells (MCs) associated with activating mutations of KIT. Tumor necrosis factor-related apoptosis-inducing ligand receptors (TRAIL-Rs) are preferentially expressed on neoplastic cells and induce the extrinsic apoptotic pathway. Recent studies reported on the expression of TRAIL-Rs and TRAIL-induced apoptosis in cultured human MCs, which depend on stem cell factor (SCF)-induced or constitutive KIT activation.; We sought to further define the impact of TRAIL-Rs on MCs in vivo and in vitro. Using Cre/loxP recombination, we generated mice with MC-specific and ubiquitous knockout of TRAIL-R. In these mice, anaphylaxis and numbers of MCs were investigated. We also explored the expression and function of TRAIL-Rs in cultured murine and human MCs upon activation of KIT. By conducting immunofluorescence staining, we analyzed the expression of TRAIL-Rs in MCs infiltrating the bone marrow of patients with mastocytosis.; MC-specific deletion of TRAIL-R was associated with a slight, but significant increase in anaphylaxis. Numbers of MCs in MC-specific knockouts of TRAIL-R were comparable to controls. Whereas cultured IL-3-dependent murine MCs from wild-type mice were resistant to TRAIL-induced apoptosis, SCF-stimulated MCs underwent apoptosis in response to TRAIL. Interestingly, activating KIT mutations also promoted sensitivity to TRAIL-mediated apoptosis in human MCs. In line with these findings, MCs infiltrating the bone marrow of patients with mastocytosis expressed TRAIL-R1.; Activation of KIT regulates the function of TRAIL-Rs in MCs. TRAIL-R1 may represent an attractive diagnostic and therapeutic target in diseases associated with KIT mutations, such as mastocytosis.
Publisher WILEY
ISSN/ISBN 1398-9995
edoc-URL https://edoc.unibas.ch/70759/
Full Text on edoc No;
Digital Object Identifier DOI 10.1111/all.12612
PubMed ID http://www.ncbi.nlm.nih.gov/pubmed/25833810
ISI-Number WOS:000356366600003

Document type (ISI) Journal Article