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Analysis of Tie2 function in mast cells

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Background

Mast cells are most widely acknowledged as a central mediator of allergic reactions. Recent literature has also implicated mast cells in a variety of biological and pathological conditions, spurring an interest in the genetic regulation of mast cell function and development. In a survey of global gene expression, we identified higher Tie2 mRNA expression in bone marrow derived mast cells (BMMC) in relation to a $Lin^{-}Sca1^{+}cKit^{+}$ (LSK) bone marrow population. Tie2 (gene name *Tek*) is a receptor tyrosine kinase more commonly known for its expression on endothelial cells and a receptor for angiopoietins including Ang1 and 2. Our objective is to explore the function of Tie2 in mast cell development and biology.

Materials and methods

The mRNA level of Tie2 in of BMMC were established via a microarray and confirmed at the protein level through FACS and Western Blot. Mature BMMC were stimulated with Ang1 (200 ng/ml) and probed for phospho-Akt and phospho-Erk. Tie-2 deficient mast cells were derived from $Tie2^{-/-}$ and $Tie2^{+/-}$ embryonic stem (ES) cells, as reported previously [1]. Briefly, embryoid bodies were generated from ES cells and incubated for 14 days, after which the embryoid bodies were dissociated into single cell suspensions and grown in media containing SCF and IL-3.

Results

BMMC express Tie2 mRNA and Tie2 protein at the membrane surface; to our knowledge, this is the first report of Tie2 protein expression in mast cells. Functional analysis and intracellular signaling response following stimulation with Tie2 ligands has revealed that Tie2 is a functionally active Ang1 receptor, as evidenced by activation of Akt and Erk. ES cell derived mast cells (ESMC) can be derived from $Tie2^{-/-}$ and $Tie2^{+/-}$ ES cell lines, and these ESMC do not possess any observable morphological abnormalities.

Conclusions

Given the importance of mast cells in the pathology of human disease, analysis of novel genetic factors regulating mast cell function and development may provide insight into suitable therapeutic targets. To further explore the role of Tie2 in mast cells, future aims include evaluating the ability of $Tie2^{-/-}$ ESMC to reconstitute mast cell-deficient mouse models *(eg, $Kit^{W/Wv}$)* and *in vitro* assays of $Tie2^{-/-}$ ESMC function such as degranulation and migration.

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Reference

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