

P017 Phosphatidylinositol-3-kinase γ (PI3K γ) in mast cell adhesion

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Mast cells (MCs) are primary effector cells in allergy and inflammation. We have recently documented that class IB PI3K (PI3K γ) plays a major role in MC hyper-activation: antigen/IgE stimulation triggers autocrine/paracrine stimulation of bone marrow-derived MCs (BMMCs) through G protein-coupled receptors (GPCRs), e.g. the adenosine the A3 adenosine receptor (A3AR). Moreover, adhesion of MCs is important for the recruitment of progenitors to tissues, and modulation of differentiation, survival and the activation of mature MCs. Activated BMMC adhere to extracellular matrix proteins like fibronectin (FN) and express various integrins such as $\alpha 5\beta 1$, $\alpha V\beta 3$ and $\alpha IIb\beta 3$.

Challenged subcutaneously with IgE injections, wild type mice increased local numbers of MCs, while PI3K γ null mice did not respond. Activation of cell surface receptors like c-kit and Fc ϵ RI enhance BMMC adhesion. Wild type and PI3K γ -deficient BMMC adhere to FN upon PMA and SCF stimulation, whereas adenosine and IB-MECA (a specific A3AR agonist) induce adhesion to FN in a PI3K γ -dependent fashion. Here, adhesion to FN is $\alpha 5\beta 1$ integrin-mediated.

Due to these results, we think that PI3K γ might take an important role in recruitment of BMMC progenitors into tissues. As expression levels of integrins are equal in both wild type and PI3K γ -deficient cells, we are investigating how PI3K γ regulates integrins avidity and migration.