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POSTER PRESENTATION Open Access

CD34 function in intracellular signaling and mucosal inflammatory disease development

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Objective/purpose

CD34 is a cell surface sialomucin that has been the subject of extensive interest, largely based on its use as a marker for hematopoietic stem cells (HSCs) and vascular endothelia. Despite the almost ubiquitous use of CD34 as a HSC marker, little is known about its cellular function. Our lab was the first to show that CD34 is also highly expressed on mature murine mast cells, and we and other groups have found it to be expressed on eosinophils and dendritic cells. We found that mast cells derived from *Cd34*$^{-/-}$ mice exhibit a marked increase in cell-cell aggregation. Moreover, when *Cd34*$^{-/-}$ mice were challenged in a mouse model of asthma, immune cell accumulation in the lung was drastically reduced, while the number of immune cells in the lung at baseline was similar to that of their wild-type counterparts. We have since found that deletion of the *Cd34* gene in mice renders these animals resistant to a wide range of other mucosal inflammatory diseases, including hypersensitivity pneumonitis (HP), ulcerative colitis, salmonella infection and intestinal tumor development. Our objectives are to examine the specific role of CD34 in cellular function and to see whether or not CD34 is a viable therapeutic target to treat mucosal inflammatory diseases.

Methods

Bone marrow mast cells were derived from wild-type and *Cd34*$^{-/-}$ mice after four week culture in media containing IL-3. Changes in migration, polarization, degranulation and cytokine production were measured after c-kit and/or FceRI stimulation. For *in vivo* studies, we developed transgenic mice that lack the mouse *Cd34* gene and instead express, in all the appropriate tissues, the human *Cd34* gene. These mice were put through a standard Ovalbumin (OVA) induced asthma model. Airway inflammation severity was assessed by analysis of the broncho-alveolar lavage (BAL) content, histological scoring of H&E stained lung sections and cytokine production of isolated lung inflammatory cells in response to OVA.

Findings

Preliminary experiments have suggested that CD34 plays an important role in c-kit signaling events and FceRI induced degranulation. Initial testing of our *hCd34*^{tg} mice has shown that expression of the human *Cd34* gene in CD34-deficient mice is sufficient to regain susceptibility to both allergic asthma and HP in mouse CD34-deficient animals. These findings suggest that human CD34 serves a similar function to mouse CD34 in both animal disease models.

Deliverables and relevance

We show that in mast cells, CD34 plays an important role in regulating cellular signaling through both the c-kit and FceRI pathways. In addition, we have demonstrated that expression of human CD34 serves a similar function to mouse CD34 in both asthma and HP, providing a proof-of-concept to assess therapeutics targeting human CD34 in *hCd34*^{tg} mice as a humanized mouse model to treat these diseases. Allergic asthma affects more than 10% of all North Americans and is a major cause of hospitalization of children. Current therapeutics are largely ineffective for chronic asthma and the most potent therapies can carry a number of side effects. CD34 could represent a new therapeutic target, and since we have shown that CD34 plays a role in the

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susceptibility to a wide range of mucosal inflammatory diseases, it is likely that it could serve as a viable treatment for a number of diseases.

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