Cultured human mast cells

Christine Dahl

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Official Opponents: Peter Ebbesen, Anders Milner and Else Tønnesen.

Tutors: Peter Oluf Schiøtz, Henrik Vendelbo Nielsen and Thomas Ledet.

Correspondence: Christine Dahl, Ormslevvej 293, 8260 Viby J, Denmark.

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ABSTRACT

The PhD study was carried out at a research laboratory, Department of Pediatrics at Skejby University Hospital.

The human mast cell is a highly granulated Fc∈RI receptor bone marrow tissue resident cell. Mast cells are widely distributed throughout the body, in connective tissue and on mucosal surfaces where they are frequently located in close proximity to blood vessels and peripheral nerves. Although diverse effector functions of mast cells are implicated in the pathophysiology of allergic diseases, mast cells are also known to be key elements of innate immunity to bacteria, adaptive immunity to parasites, and may even be involved in angiogenesis, wound healing and collagen turnover. Mast cells are implicated in the pathophysiology of a range of diseases characterized by tissue remodelling and fibrosis. Additionally, mast cells and their progenitors can be infected by human immunodeficiency virus, suggesting they could serve as a reservoir for viral replication and spread.

Mature mast cells are not observed in the circulation, and the number of mast cells that can be obtained from peripheral blood is limited. We were not able to generate a considerable number of mast cells from cord blood progenitors if we supplemented the media with serum from the beginning of the culture period. In these cultures many adherent macrophage-like cells were seen and the total cell number rapidly declined after 6 weeks. On the other hand, a substantial number of mast cells developed under serum free conditions but these lacked essential features of mature mast cells. They did not release histamine upon anti-IgE stimulation and the expression of Fc∈RI was not detected.

In order to be able to study this central cell we set up a method combining serum free and serum containing conditions for culturing a large number of functionally mature human mast cells from progenitor cells in cord blood. These cells expressed Fc∈RI (35%), released 35% of their histamine upon anti-IgE stimulation, expressed tryptase (96.7%) and chymase (35.7%) and had one nucleus.

Further characterization during development was carried out showing that human mast cells can be cultured from $CD34^+$/ $CD117^+$/ $CD13^+$/ $CD33^+$ progenitor cells and that they are tryptase, chymase and Fc∈RI negative. Previously, CD38 has been suggested as a marker of progenitors but our results cannot support this conclusion. The study shows that developing and mature mast cells express a wide range of chemokine and cytokine receptors. We thus found high levels of expression of the receptors for IL-3, IL-5 and GM-CSF.

This method provides a unique tool for performing studies regarding the human mast cell in the further advancement of the knowledge of mast cell biology.