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GRANULOCYTE MACROPHAGE - COLONY STIMULATING FACTOR INHIBITS C-KIT EXPRESSION AND STEM CELL FACTOR EXPRESSION BY DENDRITIC CELLS

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Purpose: Stem Cell Factor (SCF), the ligand of c-kit, is a key cytokine for hematopoiesis. c-kit is expressed by hematopoietic precursors but not by their differentiated descendants, with few exceptions including Natural killer (NK) cells and mast cells. Despite it has long been reported that dendritic cells (DCs) can express c-kit, several questions regarding SCF/c-kit axis in DCs remain unanswered. This is particularly relevant for DCs found in those organs where SCF is highly expressed, for instance the Bone Marrow (BM). Our aim is to characterize c-kit expression by DC subsets in mouse and human BM, and to investigate the effects of GM-CSF on SCF/c-kit axis in DCs generated in vitro from mouse BM (Bone Marrow-derived Dendritic Cells, BMdDC).
Methods: DCs from either C57BL6/J mice or human samples (femur heads) were analyzed by flow cytometry. BMdDCs were obtained from mouse BM with GM-CSF. c-kit expression and SCF production were analyzed by flow cytometry, RT-qPCR and ELISA. SCF gene silencing in BMdDCs was performed by lipid-based transfection with SCF siRNA. DC survival was evaluated either by flow cytometric analysis or Cy-QUANT Assay.
Results and Discussion: We observed that a higher proportion of c-kit^{+} cells was found among cDC1s than cDC2s from BM. Results were similar in mouse and human BM. In contrast, similar c-kit expression by cDC1s and cDC2s was observed in mouse spleen. We set the conditions to obtain a pretty homogeneous population of c-kit^{+} CD40^{hi} MHCII^{hi} CD11c^{+} BMdDCs in vitro. Notably, c-kit and SCF were both expressed by BMdDCs, increased when cells were kept at high density, with striking up-regulation when culture medium was not supplemented with GM-CSF for 2 days. A small but significant reduction of BMdDC survival was observed upon SCF silencing.
Conclusions: We described a pro-survival circuit mediated by SCF/c-kit in DCs, and inhibited by GM-CSF. Our study has implications for GVHD, GVL and anti-tumor immunity.