S53-2 Lipid network in mast cell biology

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Tissue-resident mast cells are derived from circulating committed progenitors, which are originated from pluripotential hematopoietic stem cells in bone marrow. These progenitors migrate into extravascular tissues, where they undergo differentiation and maturation into tissue-specific mature phenotypes. When activated by IgE/antigen or SCF, mature mast cells release three classes of biologically active products, including pre-formed mediators stored in secretory granules, *de novo* synthesized lipid mediators, and newly transcribed cytokines and chemokines. Therefore, these cells have been implicated as major effector cells in anaphylactic inflammation as well as in other acute and chronic inflammatory diseases. In recent years, it has become clear that lipid mediators such as arachidonic acid metabolites (prostaglandins and leukotrienes) play crucial roles in mast cell-associated pathology. Here, we show that a particular secretory phospholipase A_2 ($sPLA_2$) isoform that is homologous to the potent extrinsic anaphylaxis inducer bee venom PLA_2 is an endogenous regulator of the differentiation and activation of mast cells and thereby of mast cell-associated allergic responses. By comparing with the phenotypes displayed in mice lacking several other PLA_2 enzymes, lipid-metabolizing enzymes or receptors acting downstream of PLA_2s, and a novel mast cell maturation-related molecule, the importance of the $sPLA_2$-directed lipid pathway in mast cell biology will be discussed.