Title: Mechanistic understanding the crosstalk between mast cell and dendritic cell

Abstract: Currently, 4-5 persons per 100,000 experience anaphylactic shock each year and these life-threatening incidences keep growing in the population, most especially food associated reactions. IgE-bound mast cells (MCs) are the primary effectors of these reactions because immediately upon contacting allergens, MCs degranulate releasing a myriad of inflammatory mediators into the circulation triggering systemic shock. Since MCs have an extravascular location, a critical but overlooked question is how these cells perceive circulating allergens. Here, we describe the existence of a distinct subset of abluminal CD301b$^+$ perivascular dendritic cells (DCs) that continuously sample the blood with protoplasmic protrusions. Upon acquisition of allergens, these DCs promptly relay them to neighboring perivascular MCs which vigorously degranulate, triggering anaphylaxis. Specific depletion of this DC subset in mice significantly abrogated their capacity to experience anaphylactic shock. Interestingly, DC mediated antigen-transfer involved active discharge of surface-bound allergens on 0.5-1.0 μm sized microvesicles (MVs). This DC capacity to convey antigen-bearing MVs derived from the circulation to MCs in the perivascular space appears to be a powerful innate mechanism to initiate inflammatory responses to blood borne extrinsic agents. However, antigen sharing was not limited to MCs, as other CD301b$^+$ cells proximal to the probing DC also acquired antigen-bearing MVs. In addition to their well-known capacity to internalize, process and present antigens to immune cells, DCs appear to actively distribute antigens they have acquired to surrounding immune cells even before they are internalized. This property of DCs to “share” recently acquired extrinsic antigens could be a powerful strategy to potentiate downstream immune responses.