The pivotal effector cells of allergic inflammation are the mast cells and the eosinophils. Mast cells, as activated by IgE mechanisms via allergens, are the recognized primum movens while eosinophils infiltration and persistence in the inflamed tissue with the mast cells are the accepted features of the late stage and of the chronic outcome of allergy.

During the years we have defined a pro-inflammatory cross-talk between these two cells that we have named the Allergic Effector Unit (AEU). We found that mast cell/eosinophil interactions result in increased eosinophils chemotaxis, survival, degranulation, cytokine production and in mast cell survival, IgE-dependent and independent degranulation and cytokine production. These effects are mediated by both released mediators (soluble interactions) and by receptor/ligands binding (physical interactions). Prominent players of the activating "physical" AEU are the two activating receptors (ARs)/ligands CD48 and 2B4. Nevertheless we have also described the presence and functional activity of two inhibitory receptors (IRs), i.e. CD300a and Siglec-7, on mast cells and on eosinophils that can indicate a possible anti-inflammatory or even pro-resolution activity within the AEU and globally as mediated by mast cells and by eosinophils.

The goal of our research is to define potential new targets for immunopharmacological intervention in allergic diseases by blocking ARs, i.e. CD48, or by activating IRs, i.e. CD300a and Siglec-7. We indeed found that CD48 is significantly upregulated on human and murine asthma on mast cells and eosinophils and in the presence of S. aureus, the prominent bacteria infecting atopic tissues. We have therefore studied CD48 modulation in vitro and in vivo and the outcome of its blockade and found that CD48 is a key player in allergic diseases. Similarly we have found that CD300a and Siglec-7 are expressed by eosinophils and mast cells of allergic patients and described their role in downregulating these cell functions.

Thus, our strategy is to treat allergy by inhibiting activation and/or by activating inhibition of mast cells, eosinophils and the AEU. Translationally this strategy will have to take into account the allergic patient endotype.