ANCA-associated vasculitis (AAV) are a group of autoimmune diseases characterized by inflammation of small blood vessels. The primary feature is the presence of anti-neutrophil cytoplasmic antibodies (ANCA) that target proteins in neutrophils, leading to their activation. This leads to vascular inflammation, tissue damage and organ dysfunction, most commonly affecting the kidneys, lungs and sinuses. The three main types are granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), and eosinophilic granulomatosis with polyangiitis (EGPA). Early diagnosis and treatment with immunosuppressive therapies are critical to the management of these potentially life-threatening diseases.

EVs are a diverse group of spherical membrane structures released by various cell types, including immune cells. They have been identified in several human body fluids, including urine, blood, semen, and amniotic fluid. As carriers of molecules such as proteins, nucleic acids and lipids, EVs are thought to play an important role in intercellular communication. However, their function and role in the pathophysiology of autoimmune vasculitis, particularly in the regulation of autophagy in granulocytes and endothelial cells, are not well understood. Therefore, a primary goal of this project is to investigate these phenomena.

The project will have three main parts:

1. The first part will focus on the analysis of the profiles of miRNA, mRNA, lncRNA and lipid compounds (eicosanoids, ceramides) in granulocytes and extracellular vesicles isolated from the plasma of AAV patients and healthy volunteers.

2. In the second part, the molecular mechanisms underlying granulocyte activation and the regulation of autophagy-related processes by circulating extracellular vesicles will be investigated, with emphasis on the role of active lipid compounds and non-coding RNAs (miRNAs and lncRNAs).

3. The third part will extend this investigation to endothelial cells.

We hope that this project will improve our understanding of autoimmune vasculitis. In particular, insights into the role of autophagy may open new therapeutic avenues aimed at restoring cellular balance and reducing the inflammatory responses that drive the disease.