Autophagy is a highly conserved catabolic pathway aimed at recycling cellular components and damaged organelles. This involves the sequestration of cytoplasmic material in autophagic vesicles that are subsequently delivered to the lysosome for degradation. Autophagy functions at a basal level to maintain cellular homeostasis and can be further induced in response to various stresses to mediate cytoprotection. It is well-established that autophagy is tightly linked to cancer, even though the relation is highly complex and context-dependent, as autophagy can display both tumor-suppressive and tumor-promoting properties. The mechanisms facilitating these effects are multifactorial and remain poorly understood.

In the present thesis, we report a novel connection between autophagy and centrosomes. The centrosome is a small tubular organelle that functions as the major microtubule-organizing center of the cell and thereby regulates microtubule-dependent processes such as vesicle trafficking, cell orientation and mitosis. Depletion of central components of the autophagy pathway leads to structural alterations in interphase centrosomes, characterized by accumulation of centrosome factors at the centrosome, as well as re-organization of centriolar satellites. These phenotypes are accompanied by mitotic centrosome fragmentation and resulting formation of poorly structured spindle poles and multipolar mitoses. Accordingly, centrosome fragmentation results in a high level of chromosome missegregation and mitotic cell death. Reversely, overexpression of upstream autophagy proteins leads to loss of centrosome components and structural and functional centrosome defects. We therefore propose a novel role for autophagy factors in regulating centrosome structure and function and uncover a putative mechanism by which autophagy manipulation may promote chromosomal instability.

In addition, we have established an *in vivo* system for studying the role of the upstream pro-autophagic protein Ambra1 in a model of lung adenocarcinoma. While this project is still in its early phases, our preliminary evidence supports a tumor suppressive role for Ambra1.