

Investigating AMPK signalling regulation of autophagy in a model of ovarian tumour dormancy

Background:

Ovarian cancer is the most deadly gynecologic malignancy in women. A particular subset of this disease, epithelial ovarian cancer (EOC), is responsible for over 70% of all diagnosed ovarian cancer cases, yet the mechanisms governing disease progression are poorly understood. One of the unique hallmarks of EOC metastasis lies in the process of spheroid formation, whereby tumour cells aggregate into larger 3D structures. These EOC spheroids have been shown to be metabolically dormant, while concurrently up-regulating autophagy (cellular waste recycling) processes. This particular change in cellular activity seems to promote increased EOC chemotherapy resistance. My project examines the role of AMP-activated protein kinase (AMPK), a cellular metabolic sensor, and its role in regulating autophagy induction in EOC spheroids.

Methods:

Following AMPK knockdown using siRNA, protein markers for both AMPK and autophagy signalling will be assessed through immunoblotting, immunocytochemistry and fluorescence microscopy. Additional experiments will examine cellular viability of AMPK deficient EOC spheroids compared to their wild type counterparts following chemotherapy treatment.

Expected Results:

I expect that reducing the levels of cellular AMPK will disrupt autophagy induction, thereby sensitizing EOC spheroids to chemotherapy treatment.

Discussion & Conclusion:

Uncovering the mechanisms that govern autophagy induction in EOC spheroids will allow researchers to target a vulnerability in EOC to further develop therapeutics against this type of malignancy.

Interdisciplinary Reflection:

My research bridges molecular biology with clinical oncology, allowing for a more detailed understanding of the pathology of this deadly disease.