Alterations in cancer metabolism are a hallmark of metastasis. Cancer cells necessarily adapt to the tumour microenvironment (TME) to survive. The TME presents multiple cues that shape the transcriptomic and metabolic cancer phenotypes, which in turn impact the colonising potential of cancer cells. Furthermore, TME signals contribute to heterogeneity in the response to immunotherapy.

Our lab studies how nutrients and metabolites in the TME at different sites impact the course of melanoma progression and therapy response. We have found the TME context is shaped by site specific cues, by the age of the patient, and by the diet and lifestyle of the individual. We are looking at how these signals contribute to melanoma spread, patient survival and therapy response, and how we can use TME vulnerabilities to improve therapy response.

A key feature of cancer and melanoma cells is that they scavenge TME nutrients for membrane and energy synthesis, for invasion and cell proliferation. In addition, nutrients can generate metabolites that will affect cell signalling, shaping cancer behaviour and metastasis. Specifically, our lab has preliminary data investigating the impact of TME lipids (which vary by age, diet, lifestyle) on melanoma metastasis, tropism, T cell biology and immunotherapy response.

In this project, we plan to systematically disrupt cancer metabolism in metastatic melanoma cells and animals to identify the key tumour and host factors that allow melanoma progression and limit immunotherapy response by anatomic site. We will combine computational approaches, in vivo and in vitro assays. We will have access to human tissue to use as discovery and validation of our findings.

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