

Project title: "Dissecting the control of dietary nutrients on cancer progression through RNA maturation"

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Research group: RNA Dynamics in Cancer

Diet is a well-established modulator of cancer risk, with specific dietary patterns strongly associated with the development of certain malignancies. For instance, high consumption of red and processed meats is linked to a 15–30% increased risk of colorectal cancer. While the role of diet in cancer initiation has been extensively studied, its impact on disease progression remains poorly understood.

RNA species involved in protein synthesis undergo over 170 distinct chemical modifications, which collectively regulate this fundamental biological process. The dynamic rewiring of these RNA modifications (epitranscriptome) is particularly critical when tumour cells encounter external cues that demand rapid synthesis of a new proteome to facilitate cancer proliferation, metastasis, and/or therapeutic resistance. Notably, some of these RNA modifications directly depend on dietary nutrients as essential substrates (such as threonine or taurine). However, the precise mechanisms by which diet provides the necessary building blocks to the epitranscriptome, enabling proteomic adaptation and cancer progression, remain largely unexplored.

Our lab focuses on how diet impacts the course of cancer progression, through the lens of mRNA translation. We have discovered that cells initiating metastasis rewire their RNA modifications landscape to synthesize proteins necessary for energy production and dissemination from primary tumours. We are looking at how these RNA modifications can be reprogrammed by certain nutrients in diet to affect tumour growth, metastasis and patient survival, and how we can use these vulnerabilities to improve cancer treatments.

In this project, we plan to modulate the tumour availability to specific nutrients through diet to identify the key RNA modifications that support cancer progression. We will map the changes in the epitranscriptome of cancer cells induced by dietary modulation and identify the mechanisms by which RNA modifications controls the cancer cell proteome to sustain cancer progression. To this end, xenotransplantation models and multimodal molecular profiling techniques will be used, combined with diverse bioinformatics approaches, centred around RNA biology (i.e., Ribo-seq, RNA-seq, Nanopore-seq). We will also have access to patients' samples to use as discovery and validation of our findings.

We are seeking an ambitious, motivated, and focused researcher to join our RNA Dynamics in Cancer Group. Our research leverages cutting-edge techniques such as unbiased high throughput screenings, xenotransplantation assays with dietary modulations, *ex vivo* tumouroids systems, and large-scale molecular biology approaches. Our ultimate ambition is to discover new vulnerabilities in malignant cancers as basis of novel therapeutic strategies and predictive biomarkers to advance precision medicine. Candidates with a strong academic track record and experience in RNA biology or cancer research are highly encouraged to apply. Applications from candidates with exceptional bioinformatics skills who are eager to gain hands-on wet lab experience are also welcome.

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