Translational Cancer Metabolism Laboratory

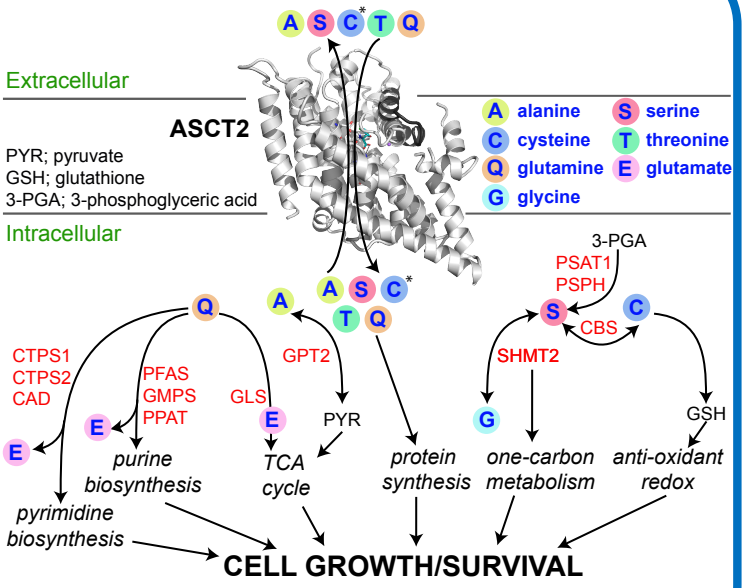
Prof Jeff Holst j.holst@unsw.edu.au
School of Medical Sciences, Lowy Cancer Research Centre
Opportunities for PhD, Honours, ILP, Med Honours

Key Publications

Wang *et al., Cancer Res*, 71(24):7525-36, 2011
Wang *et al., JNCI*, 105(19):1463-73, 2013
Wang *et al., Int J Cancer*, 135(5):1060-71, 2014
Wang *et al., J Pathology*, 236(3):278-89, 2015
Van Geldermalsen *et al., Oncogene*, 35(24):3201-8, 2016
Van Geldermalsen *et al., BMC Cancer*, 18(1):689, 2018
Wang, Guan *et al., J Pathology*, 254(2):135-146, 2021

Techniques

Cell culture	Gene expression
shRNA and CRISPR/Cas9	Amino acid uptake
Cell based assays	Western blotting
Explant culture	Immunohistochemistry
Metabolomics	Immunofluorescence
Drug screening	In vivo mouse xenografts
Seahorse bioanalyser	Analysis of clinical samples



Project 1: Breast cancer

Triple-negative breast cancer (TNBC) accounts for ~15% of cases and has a low 5-year survival rate compared to estrogen receptor or HER-2 positive breast cancers.

We have discovered an adaptive stress mechanism that occurs in TNBC where they alter the way they take up and use nutrients from their environment. This project will dissect out the mechanism behind this adaptation and try and target it to block resistance mechanisms such as macropinocytosis.

Project 2: Prostate cancer

We have discovered that ~25% of prostate cancer patients have an increased expression of glutamine metabolic enzymes and may therefore rely critically on glutamine to fuel their growth.

In this study, we will determine which enzymes in purine and pyrimidine biosynthesis are responsible for driving glutamine metabolism using a range of cancer cell lines and preclinical models. We will use both genetic knockdown/ knockout, as well as drug targeting approaches.

Project 3: Melanoma

Understanding adaptation of melanoma cells that results in resistance to therapies such as BRAF/MEK inhibitors and immunotherapies is critical.

This project will use clinical samples in collaboration with researchers at the Melanoma Institute of Australia to determine how metabolic adaptations occur, using a range of techniques such as Seahorse and metabolomics. We will also test whether these adaptations can be targeted to block or treat therapy resistance.

Project 4: Glioblastoma multiforme

Cancer cell metabolic alterations allow cancer cells to survive low nutrient levels within the cancer microenvironment. We have developed a method that enables us to grow glioblastoma patient samples in the laboratory in these low nutrient levels.

This study will use ^{13}C-metabolomics to profile metabolic changes that occur in glioblastoma patient samples. These data will be used to determine and develop new therapies that target their metabolism and starve cancer cells.