**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., BMC Cancer, 18(1):689, 2018
- Wang, Guan et al., J Pathology, 254(2):135-146, 2021

**Techniques**

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

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**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.

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**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.

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**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.

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**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 13C-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.