Utilisation of the Cabrini Monash University Department of Surgery Tissue Microarray platform in collaborative research projects

Christine Georges^{1,3}, Shehara Mendis^{2,3}, Simon Wilkins^{1,4}, Rebekah Engel^{1,5,6}, David Cheng⁷, Vana Madelli¹, Mohammad Asghari-Jafarabadi^{1,4}, Wing Hei Chan^{5,6}, Thierry Jarde⁸, Raymond Yap¹, Anne Fletcher⁸, Helen Abud^{5,6}, Paul J. McMurrick¹

1. Cabrini Monash University Dept. of Surgery, Cabrini Hospital, Melbourne 2. Oncology Research Department, Cabrini Health, Malvern 3. Faculty of Medicine, Nursing and Health Sciences, Monash University, Clayton 4. School of Public Health and Preventative Medicine, Faculty of Medicine, Nursing and Health Sciences, Monash University, Clayton 5. Department of Anatomy and Developmental Biology, Monash University, Clayton 6. Stem Cells and Development Program, Monash Biomedicine Discovery Institute, Monash University, Clayton 7. Cabrini Health, Malvern 8. Biomedicine Discovery Institute, Monash University, Clayton

Background

Tissue microarrays (TMAs) serve as a powerful tool in colorectal cancer (CRC) research, allowing for high-throughput analysis of multiple tissue samples on a single histological slide. Here we highlight how TMAs can advance CRC research and address clinically relevant questions through our collaborative research programs.

The integration of TMAs, TMA-related analyses, with laboratory techniques and clinical data from the Cabrini Monash Colorectal Neoplasia Database (CMCND) offers a unique opportunity to address pressing clinical questions. Currently, we are engaged with five TMA-related collaborative research programs that are currently underway:

- 1. The role of biomarkers for personalising chemotherapy treatments in Stage III colon cancer patients.
- 2. A comparison of surgery alone versus surgery plus adjuvant chemotherapy in stage III colon cancer.
- 3. The Role of neuregulin-1 in colon cancer.
- 4. Regulation of the immune response in the CRC tumour microenvironment and its role in patient outcomes.
- 5. Defining the role of regenerative stem cells in chemoresistance and tumour recurrence in CRC.

Method

TMAs will be assessed for specific predictive and prognostic biomarkers through various techniques, including multiplex immunohistochemistry, spatial biology and next generation proteomics. Results will be combined with laboratory data from in vivo and in vitro experiments, including organoids and tissue slice assays, and results correlated with clinical outcomes. All projects have CRGO approval: 04-15-05-17, 05-02-09-21, 03-21-01-19, 04-19-01-15.







TMA-ANALYSIS

Multiplex immunohistochemistry (i.e. Opal) Spatial biology (i.e. Akoya) Next generation proteomics (i.e. Olink)

LABORATORY EXPERIMENTS -FRESH TISSUE Organoids

Tissue Slice assays



Figure 1. Illustration of workflow. Post CRC resection, surgical specimens are utilised in the form of formalin fixed paraffin embedded (FFPE) tissue or fresh tissue. TMAs are created from FFPE blocks and analysed by various techniques. Fresh tissue is utilised to create organoids and for tissue slice assays. Results from these experiments is coupled with clinical outcome data to determine predictive and prognostic biomarkers.

Results

Conclusion

TMAs, when coupled with laboratory data and matched clinical data provides a powerful research tool. Allowing researchers to link the molecular features of the tumour (such as gene expression or protein levels) to laboratory data and clinical data, like patient survival or response to therapy, allows for improved identification of prognostic and predictive biomarkers.

Overall, TMAs significantly enhance the ability of researchers to understand predictive and prognostic biomarkers and are a powerful research tool when combined with laboratory data and clinical outcomes.

