University of Glasgow | College of Medical, Veterinary & Life Sciences

Head of College Scholars List Scheme

Summer Studentship 2019

Report Form

This report should be completed by the student with his/her project supervisor. It should summarise the work undertaken during the project and, once completed, should be sent by email to: mvls-scholarsscheme@glasgow.ac.uk **within four weeks of the end of the studentship**.

1. Student

Surname: Kong Forename: Yong Fai

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2. Supervisor

Surname: Park Forename: James

E-mail address: james.park@glasgow.ac.uk

3. Research Project Report

3.1 Project Title (maximum 20 words):

The relationship between the tumour microenvironment and metabolism in patients with colorectal cancer

3.2 Project Lay Summary (copied from application):

Colorectal cancer comprises cancer cells surrounded by a supporting environment which supports growth. This tumour microenvironment may support sustained growth by reciprocating in the metabolism of tumour cells, by mopping up waste products of metabolism and recycling them into substances which can be used again by the tumour cell. This project intends to investigate the relationship between markers of metabolism in the tumour cell and the surrounding microenvironment, and ultimately how this may impact upon other characteristics of the tumour and patient survival.

3.3 Start Date: 3rd June 2019 **Finish Date:** 20th September 2019

(5 weeks in total, with a break between these two dates)

3.4 Original project aims and objectives (100 words max):

We hypothesise that markers of lactate shuttling between the tumour cell and its environment are associated with poor prognosis in patients with colorectal cancer and may promote a tumour growth-promoting, immunosuppressive microenvironment.

The aims of this present study are:

- To validate the prognostic significance of tumour cell expression of LDH5 and MCT2, particularly in the context of high tumour stromal infiltration.
- To investigate the relationship between LDH2 and MCT2 and other components of the tumour microenvironment including immune cell infiltration, tumour budding and necrosis.

3.5 Methodology: Summarise and include reference to training received in research methods etc. (250 words max):

Methods: We constructed a tissue microarray of 680 patients who underwent surgery for stage I-IV colorectal cancer in Glasgow 1997-2007. Using the tissue microarray, we examined tumour cell expression of LDH5 and MCT2 in addition to two other markers of metabolism (LDH1 and MCT1) using previously published methodology (Roseweir T, et al. 2019). Tumour cell expression of these markers was assessed using the weighted histoscore. The relationship between high and low expression of each marker and survival (cancer-specific and overall) was then examined using Kaplan Meier and log-rank analysis to compare survival curves.

The initial plan also included the investigation of the relationship between markers of tumour cell metabolism and tumour microenvironment characteristics (immune cell infiltrate, tumour stroma percentage and tumour budding). However, this could not be completed within 5 weeks, and therefore is not included in this report.

Training: Laboratory work was performed in Professor Edwards' laboratory (Wolfson Wohl Translational Research Centre). I underwent training in basic laboratory etiquette and tissue handling and learnt to perform immunohistochemistry and subsequent histoscoring. I also

learnt to assess basic colorectal cancer pathology. All laboratory work was performed under supervision.

Despite the time constraint, I took initiative to learn how to perform statistical analyses using the SPSS software from Sara, a Masters student. My supervisor, Dr. Park, also helped me with data interpretation.

3.6 Results: Summarise key findings (300 words max). Please include any relevant tables or images as an appendix to this report:

Due to time constraint and technical issues, the histoscoring and statistical analyses for the full cohort could not be completed within the 5 weeks allocated for this summer project. I decided to stay with the team until they complete the work.

For the preliminary analysis for this report, approximately 10% of the histoscores obtained from the MCT1 marker were used for survival analysis. After excluding patients who died within 30 days of surgery, patients with stage IV colorectal cancer and patients who received neoadjuvant therapy, the remaining cohort consisted of 69 patients.

<u>Distribution of levels of MCT1 expression:</u>

Examples of low and high expression of MCT1 in colorectal cancer are shown in Figures 1 and 2 respectively.

Figure 3 shows that the expression of MCT1 was mostly below a score of 150/300.

<u>Association of MCT1 expression with cancer specific survival:</u>

Patients with high MCT1 expression had improved survival compared to those with low MCT1 expression, however this did not reach statistical significance (Figure 4).

<u>Association of MCT1 expression with cancer specific survival in relation to tumour site:</u>

In patients with right-sided colon cancer, we found no significant relationship between levels of MCT1 expression and cancer specific survival, as shown in Figure 5.

In patients with left-sided colon cancer, we found no significant relationship between levels of MCT1 expression and cancer specific survival, as shown in Figure 6.

In patients with rectal cancer, we found no significant relationship between levels of MCT1 expression and cancer specific survival, as shown in Figure 7.

3.7 Discussion (500 words max):

Staining and analysis of the tissue sections took longer than anticipated due to unforeseen circumstances. As such, it was not possible to analyse the full cohort at the time of writing this report. However, preliminary analysis of 10% of the cohort for MCT1 was performed. There was no obvious relationship with survival on analysis. This may, however, be a type 2 error due to an underpowered cohort.

Future work will concentrate on scoring the rest of this cohort for analysis of the full patient cohort with respect to MCT1 expression and its relationship with survival and characteristics of the tumour microenvironment.

4. Reflection by the student on the experience and value of the studentship (300 words max):

I am grateful to be offered the studentship. I am particularly thankful to my supervisor, Dr. James Park, who planned and supervised the studentship. I am also thankful to Professor Edwards and the members of her research team, especially Dr. Quinn, Sara and Megan. They not only taught me many new laboratory skills, but also patiently answered all my questions. They passed their scientific knowledge on to me and made my experience in the laboratory invaluable.

Working with Professor Edwards' team has equipped me with a range of laboratory skills which I would not have learnt as part of medical school. These range from performing immunohistochemistry and histoscoring, to statistical analyses using the SPSS software, all of which were completely new to me. After being taught how to perform immunohistochemistry and histoscoring correctly, I was encouraged to carry out the procedures independently. This built my confidence in my practical skills and gave me a real sense of responsibility.

I learnt the importance of being flexible and adaptable in the field of scientific research as projects do not always go as planned and run on time. Due to time constraint and technical difficulties which were out of our control, I was not able to complete the statistical analyses within the 5 weeks. Therefore, I learnt to use my initiative to achieve the learning objective by

analysing part of the cohort. I decided to stay with the team and contribute as much as I can as they complete the research project.

This is my first research experience and I am grateful it has been very productive and rewarding. I am very grateful to the university for the opportunity afforded by the grant. This research experience, and successfully achieving the grant funding as an undergraduate will help with my future career.

5. **Dissemination: (note any presentations/publications submitted/planned from the work):**
   This work will contribute to an ongoing research project in Prof. Edwards' laboratory looking at tumour metabolism in colorectal cancer. This will result in presentations and publications. I will be included as a contributing author for these publications.

6. **Signatures:**

Supervisor	Date	Student	Date
	11/10/19		28/09/2019

Appendix:

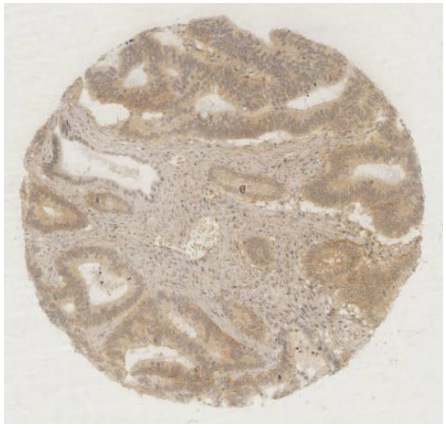

Figure 1: Low expression of MCT1

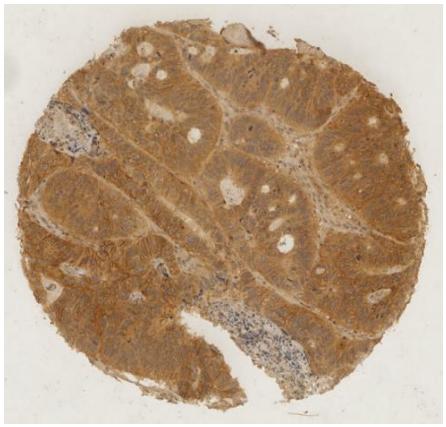

Figure 2: High expression of MCT1

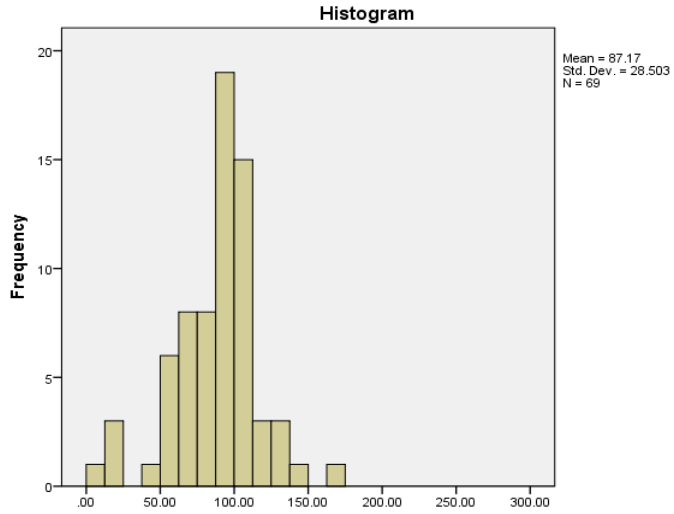

Figure 3: Histogram showing the distribution of levels of MCT1 expression in 69 patients

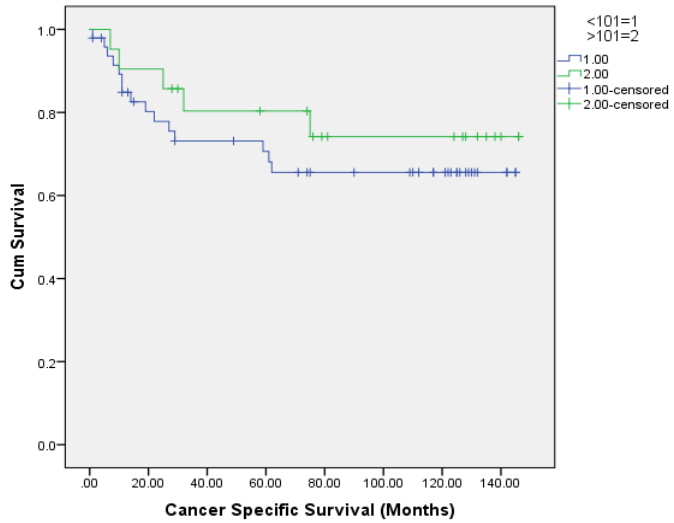

Figure 4: Relationship between MCT1 expression and cancer specific survival

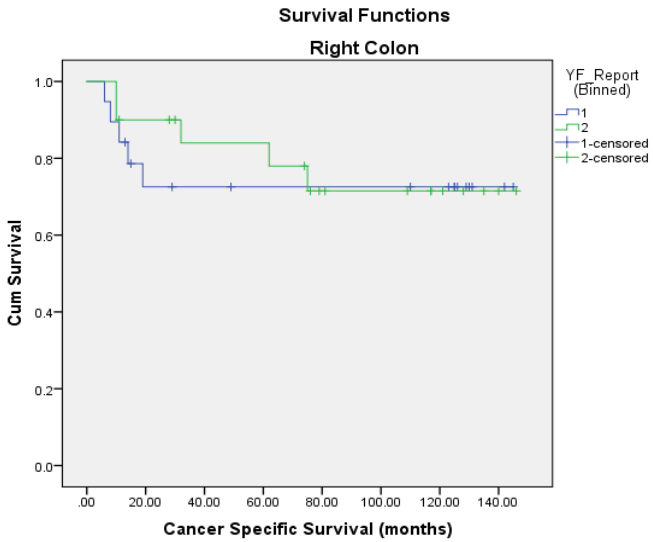

Figure 5: Relationship between MCT1 expression and cancer specific survival in patients with right-sided colon cancer

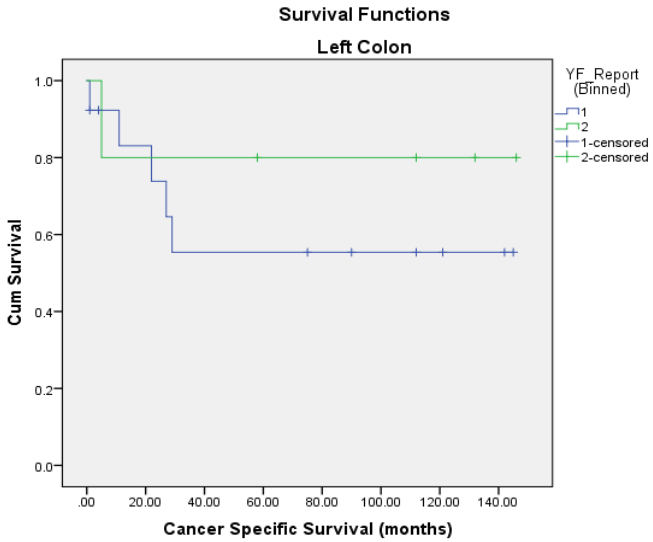

Figure 6: Relationship between MCT1 expression and cancer specific survival in patients with left-sided colon cancer

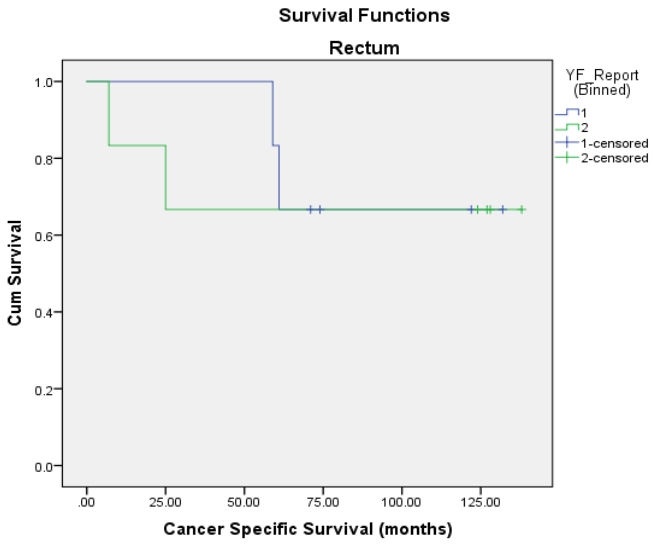

Figure 7: Relationship between MCT1 expression and cancer specific survival in patients with rectal cancer