

Structured Reports for the Pathological Society Grant Awards: Career Development Fellowships (CDF), Path-Soc / J Shanks Fellowship, PhD Studentships, International Collaborator Awards, Small Grant Scheme (several types) Awards, CRUK/Path-Soc Pre-Doctoral Research Bursary & Early Career Pathology Researcher (Hodgkin & Leishman) Grants.

Recipients of grant awards from the Pathological Society of Great Britain and Ireland should submit a scientific report detailing the work undertaken with support from this award and any outputs arising from this. The reports should be set out using the following subheadings and should consist of:

Annual Reports: Final report on ICA

Title: H pylori negative gastric MALT lymphoma: genetic profiling for biomarker in treatment stratification

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Background and aims:

Gastric mucosa-associated lymphoid tissue (MALT) lymphoma is commonly derived from a background of chronic H pylori gastritis, and its development is driven by H pylori mediated immune stimulation, particularly T helper cells. Clinically, ~70% H pylori positive gastric MALT lymphoma show durable complete remission following H pylori eradication, while the majority of those not responding to H pylori eradication harbour t(11;18)/API2-MALT1 or t(1;14)/BCL10-IGH. The prevalence of H pylori infection in Western populations has declined over the last decade, and the number of gastric MALT lymphoma has also significantly dropped. However, there is a significant increase in the proportion of H pylori negative gastric MALT lymphoma (defined by negative histology, breath test and serology) from 18-32% in the 1995-2004 period to 32-61% in the 2005-2013 period. Only a small proportion (15-38%) of H pylori negative gastric MALT lymphomas responded to antibiotic treatment. Currently, there is no established biomarker that can predict the response of H pylori negative gastric MALT lymphomas to antibiotic therapy. We propose to comprehensively investigate the genetic changes of these cases by targeted sequencing and interphase FISH analyses.

Results:

We have collated a series of 72 cases of H pylori negative gastric MALT lymphoma, and have successfully performed interphase FISH for MALT1 and IGH involved translocation in 57 cases, and targeted sequencing of 90 marginal zone lymphoma associated genes in 35 cases. We found highly frequent translocation (57%) involving MALT1 and IGH, and mutations in TNFAIP3 (23%), NOTCH1 (20%), ATM (17%), KMT2D (17%), CREBBP (14%), ARID1A (11%) and CARD11 (11%). Among these genetic changes, MALT1 and IGH translocation appeared to be mutually exclusive from TNFAIP3 mutation. These genetic changes appear more frequent than those of unselected H pylori positive gastric MALT lymphoma. Based on the analysis to date, there was no association between the above genetic changes and clinical outcome in this cohort.

The ICA award enabled Dr Barbara Kiesewetter to come to Cambridge during February-July 2019 for a 6 months visiting research. She thoroughly enjoyed her research in Cambridge and obtained the above laboratory data with the help of my research team.

Since returning back to Medical University Vienna, Barbara has been trying hard to get the data prepared for a manuscript. Unfortunately, she has been overwhelmed by clinical duties, then working at the front line

during the COVID-19 pandemic. We have been frequently in contact, and aim to get the manuscript written in the coming few months when the COVID-19 situation is under control. We very much appreciate the PathSoc ICA support, allowing us to extend our research collaboration on H pylori negative gastric MALT lymphoma and beyond.