

Name : Emma Cohen

Year : 2024

Medical School : University of Cambridge

Topic of Elective: Investigating DNA fork replication dynamics in human melanoma cells treated with DNA replication inhibitors

Department: Boemo Group Department of Pathology, University of Cambridge

The aim of my summer project was to investigate how DNA inhibitors affect DNA breaks at replication forks. DNAscent, a software developed by the Boemo group, was used to detect base analogue pulses in Oxford Nanopore sequencing to perform such analysis. By measuring the movement of replication forks across the genome of human melanoma cells treated with hydroxyurea, ATR inhibitors and WEE1 inhibitors, the effect of these inhibitors on DNA breaks was elucidated by comparison with untreated data.

Significant differences between treated and untreated DNA samples were not initially found and so more complex analysis of fork break characteristics was performed. Investigation into the proportion of 5' compared to 3' fork breaks revealed unexpected biases towards replicating DNA fork 'tips' compared to 'backs'. While an aim of the project was to build a probability model of DNA break dynamics, these unexpectedly complex findings mean that the project will now be continued by another student in the next academic year. These finalised results will hopefully be presented on a departmental level and in conference in the future.

This research has allowed me to build on a set of computational skills that are becoming increasingly relevant to histopathological image analysis as such technology evolves. As a medical student with a passion for oncology, I am particularly interested in how such analysis could be applied to tumour histopathological imaging. I am sure the experience gained this summer will benefit me when pursuing this interest.

I would like to thank the British Division of the International Academy of Pathology for providing financial support to the project. In addition to being widely academically stimulating, it has also been very enjoyable! I would also like to thank the Boemo Group for having me this summer and supporting me throughout the project.

