

JAMES RENNIE BEQUEST

REPORT ON EXPEDITION / PROJECT / CONFERENCE

Expedition/Project/

Conference Title: Genetic Engineering using CRISPR/Cas – 3-week course

Travel Dates: 02/08/26-23/08/26

Location: Aarhus, Denmark

Group member(s): Emma Kelsey

Aims: Learn and understand key principles and uses of CRISPR/Cas gene editing. To use this knowledge to evaluate experimental parameters and results of CRISPR experiments and independently design and use CRISPR/Cas editing in a group project.

Photography consent form attached: ☐ Yes
(please refer to your award letter) ☒ No

OUTCOME (a minimum of 500 words):-

Using the funds generously donated by the James Rennie Bequest, in August I travelled to Aarhus University in Denmark to partake in a 3-week CRISPR/Cas genetic engineering course. This course provided me with the opportunity to gain an in-depth understanding of an extremely topical technique and learn from one of the leading experts in this field.

This course was theory based and covered the key underlying principles of the CRISPR/Cas system as both a bacterial defence system and in its adapted use for gene editing. To highlight the revolutionary impact of this technique on the scientific community, we looked at the history of gene editing through primary papers; researching zinc finger nucleases and TALENs. This provided me with a true appreciation for the low-cost, speed and accuracy of CRISPR.

One of the most important lectures aiding my understanding broke CRISPR down into its individual components, discussing them according to its role and responsibility within the system. These components included gRNA scaffold and targeting sequences, the Cas enzyme, PAM and seed sequence, spacer and protospacer. As I progressed through the course the thorough understanding I gained from this lecture provided a framework to build upon when learning more advanced CRISPR-based editing techniques and the ability to read and analyse CRISPR related articles during the course and in the future. I found these alternate CRISPR based techniques such as base/prime editing incredibly interesting to learn about, and I am excited to see the future research and advancements that occur with these.

An aspect of the course that I particularly enjoyed was the dry lab simulations. The dry lab sessions helped to bridge the gap between reading about experimental techniques and understanding how they are designed. Using online tools such as Snapgene and CRISPOR, we followed experimental protocols to create the most efficient guideRNA's and HDR templates with the lowest number of off-target effects in important regions. While designing gRNA's, Dr Rasmus O. Bak explained his own breakthrough research where he co-

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developed chemically modified gRNAs to prevent them from degrading too quickly in the body. These chemical modifications also limited the immune response to gRNAs. I learnt how to use simple online tools to analyse the efficiency of gene editing and measure off targets. We also discussed simple practical things, such as how to order gRNA's online, which I know will benefit me greatly in future experiments I may undertake. This gave me a clearer understanding of the process involved in planning a genetic engineering experiment and will be valuable in future laboratory work.

Importantly, we also had a debate session, where we discussed and argued the ethical dilemma of genetic engineering in different situations. It reinforced the idea science is political and cannot be separated from the cultural climate of the world. Not only was it illuminating to hear different perspectives and viewpoints that I had not considered before, but the international aspect of this course also meant we could analyse genetic engineering from different legal systems and cultures.

In the final week, we discussed further applications of CRISPR, such as in screens, cancer and immunotherapy. We followed clinical trials and studies that are currently being undertaken to understand the real-world implications that are possible through CRISPR/Cas gene editing. The course culminated in a group project, where we picked a particular genetic disease and presented a complete theoretical cure using CRISPR/Cas editing, considering the type of edit, the CRISPR system and gRNA's/templates used, the mode of delivery and how to measure the results. Our group chose Duchenne Muscular Dystrophy (DMD), specifically when it is caused by the deletion of exon 52. We comprehensively presented our chosen prime editing strategy to the rest of the class and other staff. Not only did a full walkthrough of the CRISPR/Cas protocol in terms of DMD validate my understanding, but another opportunity also to speak in front of a crowd increased my confidence.

Overall, this course was a transformative experience. It was my first small glimpse into the international scientific community, and I particularly enjoyed interacting with other students from different academic and cultural backgrounds. As I move into my third year of my degree here in Edinburgh, I will specialise in molecular genetics, and I know that this course will aid in my further education and allow me to more confidently engage with my classes and literature. In addition to my studies, I made lots of friends, explored the city of Aarhus and had lots of fun. I want to reiterate my thanks to the committee as I could not have had this experience and gained the skills, knowledge and confidence that I will carry forward without them.