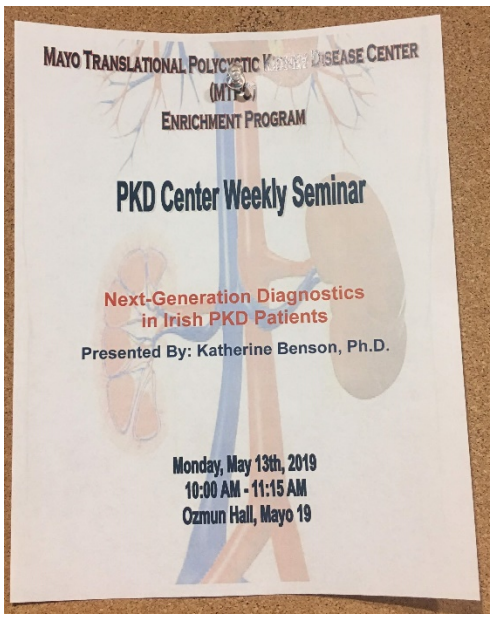
Acadamh Ríoga na hÉireann
Royal Irish Academy

Charlemont Grant Report

Recipient Name:	Dr Katherine Benson
Discipline:	Sciences
Amount and year awarded:	€2,477 in 2019
Title of Project:	Project planning and training for the study of the genomics of Polycystic Kidney Disease in the Irish and US population



Summary of findings:	**Outcome 1**: Project plan for large, collaborative research funding application on PKD Two applications for large scale project grants (PI at RCSI, Dublin, with Mayo colleagues as collaborators) are now underway with deadlines in December and January, for funding of around 200,000EUR each. These applications are a direct result of the research trip funding by the Charlemont Travel Grant and proof that this trip has fostered a lasting research collaboration. **Outcome 2:** Training Variant Classification I have learned and implemented the Mayo Clinic variant classification guidelines in our own PKD cohort of genotyped patients which has increased our diagnostic yield from 69% to 85%. I have brought the knowledge of these classification guidelines back to Ireland for implementation in future studies. Long-Range PCR and Sanger Sequencing I have now been trained in long-range PCR and Sanger sequencing for the difficult to sequence PKD genes. As part of my training at Mayo, I implemented this technique on X Irish samples in order to fill sequencing gaps missed during next-generation sequencing. As a result 25 additional candidate PKD variants (within PKD1 and PKD2) were identified and 11 diagnoses were made from our Irish cohort. This has had a considerable impact on the Irish renal clinic, providing potential diagnoses for patients who were previously without a molecular diagnosis. I have brought this knowledge back to RCSI where the protocols will be available to my Irish colleagues. This ensures that the knowledge I have gained as part of my trip will be of benefit to other Irish researchers. **Outcome 3:** Publication of Results I am now preparing a first-author publication which includes the diagnostic results obtained as a result of the implementation of the Mayo Clinic pathogenicity guidelines as well as the results of long-range PCR sequencing.

Charlemont Grant Report

	This publication compares variant classification methods used by the team at Mayo Clinic and the internationally recognized guidelines from the American College of Medical Genetics and Genomics (ACMG).
Plans for continuing collaboration:	As mentioned above, one of the key aims of this research trip was to foster collaboration between our research groups and project plan for larger scale project funding. We are now in the process of applying for this PKD project funding with the Mayo Clinic PKD centre as a named collaborator. We are applying to the HRCI/HRB Joint Funding Scheme 2020 as well as the PKD Foundation Project Grant Scheme in order to secure this funding. The grant outline for these applications have been developed as a direct result of this research trip, where I was able to identify areas of shared interest, complimentary areas of expertise and foster a lasting collaboration between our research groups.
Publication plans:	I am currently preparing a first author manuscript for submission to a peer reviewed journal which includes the results from my Charlemont Grant. This manuscript contains the result of the long-range PCR and Sanger sequencing used for gap-filling sequencing as well as the interpretation of identified PKD variants using the Mayo Clinic pathogenicity criteria learned from this trip. During this trip, I attended laboratory meetings help by Prof. Harris' team at Mayo, where I identified a potential collaboration opportunity. Prof. Harris' team has identified a number of families with variation in a novel candidate PKD locus. By using our existing data from our Irish cohort, I was able to identify additional Irish families with similar variants. As a result, we have agreed to contribute to Prof. Harris' work and my supervisors and I will be named as coauthors on the resulting manuscript.
International dissemination:	During my trip, I participated in the Mayo Clinic PKD Weekly Seminar Series where I presented my research completed in Ireland as well as the work completed at Mayo during my research trip. I attended the Mayo Clinic Bi-annual PKD Symposium where I was able to attend talks from US based PKD researchers attending the event. This was an important networking and learning experience where although I didn't not formally present my work, I informally shared my research with international colleagues.
National dissemination:	I presented my work, including that completed as part of this research trip, as a poster at the Irish Society of Human Genetics conference in Belfast, September 2019. I won a prize for 'best postdoctoral poster' for this presentation.
Additional collaborations:	The ongoing collaboration with the team at the Mayo Clinic has been developed and will now allow the application for larger scale funding. No additional collaborations have been established as a result of this funding.
Outreach:	Since my return to Ireland, I attended the Irish Society of Human Genetics meeting in Dublin, where I won a prize for the presentation of work emanating from this research trip in the format of a poster presentation. I hope to take part in school outreach events as part of my links to the RCSI FutureNeuro SFI Centre over the coming weeks where I will have the opportunity to share my work.