Project Title: Do common genetic variants explain incomplete penetrance in families with endocrine disorders?

Code: NCS8

Host School/ Institute: Northern Clinical School

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Project Type: Data Analysis, Laboratory based

Project Category: Genetics, Molecular biology, Endocrinology/Metabolism, Cancer

Project Keywords:
1. cancer research
2. molecular biology
3. endocrine disorders
4. hereditary disorders
5. sequencing

Project Description:

Phaeochromocytomas (PCs, tumours of the adrenal medulla) and paragangliomas (PGLs, tumours of sympathetic or parasympathetic ganglia) are highly heritable, with 40% associated with germline pathogenic mutations in at least 14 genes. They are associated with high burden of disease, due to extreme hypertension from excess catecholamine secretion (with clinical consequences including sudden death), local tumour pressure effects and metastatic disease. Incomplete penetrance is observed in families, with some individuals developing tumours during childhood, while others remain tumour-free (despite carrying the same pathogenic mutation). This generates a great deal of anxiety for individuals and makes their clinical management very difficult (there is currently no way of predicting when, or even if, a tumour is likely to occur), with mutation carriers undergoing annual biochemical testing (catecholamines) and semi-annual imaging (tumours). Common genetic variants have been shown to modify the penetrance of numerous diseases, including some forms of cancer.

This project will assess a set of genetic variants in families with PC/PGL to determine if any correlation exists between the presence of these variants and penetrance of disease. We hope this project will assist in the identification of those individuals at “high risk” and those at “low risk” and ultimately lead to improved clinical management of individuals and families affected by PC/PGL.

This project involves the use of a number of molecular biological techniques, with a focus on PCR and sequencing [Sanger and Next Generation]). The student will also gain experience in the interpretation of mutations and variants (using in silico tools and databases). This project will require a minimum of four days per week to be spent in our lab, requires a background in science (although prior laboratory experience is not essential), and will best suit those interested in cancer research or medicine.