FBS seminar

Date: May 30 (Thu), 2019
Time: 11:00-12:00
Place: 2F Seminar room, Biosystems Building

Speaker: Dr. Ruth Newbury-Ecob
Department of Clinical Genetics
University Hospitals Bristol NHS Foundation Trust

Title: Genetic and genomic studies of Rare Disease in the UK

Abstract:

Patients from clinical genetic clinics have participated in research projects utilising exome and whole genome sequencing to identify novel disease genes. Identifying specific mutations allows greater accuracy of diagnosis, counselling of reproductive risks and reproductive options. Genes identified for congenital malformations have also contributed to the understanding of normal developmental pathways. My research group has specialised in identifying genes important in cardiac and limb development. (TBX5 MYH6 ,SALL4 and RBM8A) and for other rare diseases as part of multi centre collaborative studies (DDD, 100K)

Single patients with mutations in novel genes present a challenge to the geneticist Collaboration with clinicians world-wide, laboratory scientists and developmental biologists is required to determine if the mutation is causative.

Our case presented as a newborn with severe microcephaly and epilepsy. Cranial MRI showed calcification and a neuronal migration defect described as band heterotopia - the phenotype often associated with mutations in the Occludin gene. However DNA analysis of the Occludin gene was negative.

Exome sequencing identified a de novo variant in CLDN5., a member of the Claudin gene family. Extensive literature searches did not find any published patients. The online tool Genematcher successfully matched to a patient in Canada and subsequently two other similar cases have been ascertained . Zebrafish models have been used to explore the phenotype further.

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