Ongoing research

Genetic causes of FH

The All Wales FH Cascade Testing Service has been a major step forward for patients with inherited high cholesterol. Genetic testing for alterations in FH genes (spelling mistakes in the genetic code) is an effective way of finding family members who also have FH. To date, we have found a genetic explanation for FH using DNA testing in about 25% of the patients that we have tested. This means that for 75% of people tested we are not able to provide a definite genetic diagnosis. This may be because there are other changes in the DNA that we don't yet know about or don't yet test for. The FH research team are working with the FH clinical team (doctors and nurses) to remedy this. Two new studies are underway which aim to improve things.

Variants of Uncertain Significance Study (VUS Study)

Sometimes we identify a variant (spelling mistake) in one of the three main FH genes but cannot be sure if this is actually causing FH or not. These are called variants of uncertain significance (VUS). A VUS is found in around 8% of index patients. An index patient is the first person in a family who is diagnosed with FH. Currently, family DNA testing for VUS is not routinely offered because we don't know if they are having an effect on cholesterol levels or not. Kate Haralambos is coordinating a project for the families of index patients with a VUS to try and find out if a specific VUS causes high cholesterol. This project is lead overall by Dr Ian McDowell with the support of all Lipid consultants and FH nurses in Wales.

Who can take part in the VUS study?

Kate will be working with the Clinical Care Team to contact patients with a VUS to offer genetic testing to their families and to assess whether the VUS tracks with cholesterol levels in the family. This may help clarify the genetic diagnosis and treatment for that patient and their family.

To read more about this study you can download the participant information sheet for Index patients or the participant information sheet for relatives of FH index patients.

Cholesteryl Ester Storage Disorder (CESD) Study

Do other genetic alterations cause high cholesterol?

About two thirds of the index patients that we test for FH do not have any alteration detectable in the three main FH genes. This does not mean that they don't have a genetic cause of high cholesterol. It just means that the genetic cause or causes of their raised cholesterol levels has not yet been found. DNA samples from all patients that participate in the FH testing service are stored so that they can be re-tested if new genetic tests become available. Recently, a condition called Cholesteryl Ester Storage Disorder (CESD), which also results from a genetic alteration, has been shown to resemble FH. CESD increases the risk of early onset heart disease, but treatments are available to reduce this risk. We are about to start a project that will use stored samples from FH index patients with 'negative genetic results' to find out how common the CESD alteration is in patients with inherited high cholesterol.

Who can take part in the CESD Study?

If you were the first person in your family to have an FH genetic test (index patient) and you had a 'negative' result then you can be tested for the CESD gene. The research team will need your consent to test your stored DNA sample. You won't need to come to clinic for this – it can be done by post.

Eligible patients will receive a study pack through the post from the clinical team.

You don't have to wait for this…..
If you want your sample to be included in the study you can download the patient information sheet and consent form, then complete and post the consent form to the research office: Room 102, Wales Heart Research Institute, University Hospital of Wales, Cardiff, CF14 4XN.

To speak to someone about either of these studies please contact Kate or Pauline on 02920 743864 or email Kate (VUS Study) haralambosk1@cardiff.ac.uk or Pauline (CESD Study) ashfield-wattp1@cardiff.ac.uk