LEGGENDS AND FACTS: POPULATION SCREENING FOR AIP MUTATIONS IN NORTHERN IRELAND

WRITTEN BY SERBAN RADIAN & MARIA HERINCS

THE SCIENCE BEHIND THE LEGEND
Ireland’s folklore has long been preoccupied with giants. Recent discoveries suggest that its stories, including that of Finn McCool and the Giant’s Causeway, and Ulster’s numerous landmarks mentioning giants, may actually represent something with real roots in fact.

Giants are within the realms of the endocrinologist because they have a growth hormone secreting pituitary tumour that has developed before puberty. It has always been felt that gigantism has a genetic flavour, although until recently there has been little science to substantiate this myth.

Our group from Barts and the London School of Medicine, Queen Mary University of London led by Márta Korbonits, have collaborated with the Departments of Clinical Genetics and the Regional Endocrinology Centre in Belfast, to put some science behind the legend of the Irish giant.

THE AIP GENE AND ITS IRISH ROOTS
The discovery of a predisposition to young-onset acromegaly and gigantism in several Northern Irish families and their connection with the famous Irish giant Charles Byrne has been shown by Márta’s group to be due to a founder mutation in the AIP gene.1 Many current and historical patients with gigantism have been traced back to a small region at the border of South Derry and East Tyrone, and all studied DNA samples share precisely the same AIP mutation. This, in combination with the fact that the penetrance of the gene is low (10-30%), lends support to the hypothesis that this mutation may be relatively frequent in this geographical area, and may be the explanation for the many legends of Irish Giants.

IRISH HOSPITALITY, MEDIA COVERAGE AND COLLECTING SAMPLES
Realising that this part of the world is very special in terms of the genetics of pituitary tumours, we decided to go on a genetic epidemiology ‘expedition’ to two small Northern Irish towns over two weekends in February and March 2013. We travelled with the following research questions in our minds: how prevalent is this rare gene variant in the population of this small area? To what extent might this affect the local population? Do they need to be screened more widely?

To answer our questions, we needed to find a way of persuading the local population to give us samples of saliva for genetic testing! A local man, Brendan Holland, himself a former patient, and his family and friends, were enthusiastic supporters of the expedition and a great help in providing local knowledge and support. It was Brendan’s idea for us to set up a ‘recruiting stand’ in local Tesco stores. A TV documentary, a number of radio interviews, local advertising and the frequented location led to a large number of people presenting for screening. Will the weekend shop ever be the same again?

Giving up 10 minutes of time and providing personal details, as well as 2ml of saliva for DNA extraction, may not seem like much, but it is probably not what most of us have in mind when we rush out for our shopping at the local supermarket!

With the ideal mixture of determination, resourcefulness and skill from all those involved, but most of all, with the generosity of the volunteers taking part in the study, the team managed to collect an impressive 956 saliva samples in 48 hours (collecting samples over 12 hours each day at about 19 samples per hour).

COMMUNICATION ISSUES
Hard work and good humour went hand in hand, especially when the great mix of international researchers were coping with the local regional accents and speech nuances. Vice versa, local people had to understand our ‘international’ English! On one occasion, while our excellent Italian colleague was explaining how to provide a saliva sample,
FIND OUT MORE...

READ...

VISIT...
www.fipapatients.org, a website to increase awareness about Familial Isolated Pituitary Adenoma (FIPA).

WATCH...
BBC news report on this research: http://bbc.in/Z3dVkP.

VIEW...

he asked the volunteer to ‘spit’ into the test-tube he received the candid reply, “What do you want me to say to it?”

A LIFELONG FRIENDSHIP
We ourselves were enriched by the people we have met and have grown to love and admire them in such a short time: our new friends Brendan and all his family members, our colleagues from Belfast (Lisa Bradley, Michal Azensztejn, Patrick Morison, Brew Atkinson and Steve Hunter) as well as Ronan McClosky and many other helpers. Special thanks go to the extremely generous and kind study participants for patiently putting up with our inquisitive questions and trusting us with their personal information and DNA.

What we hope to achieve with this research, in addition to our scientific goals, is to serve the local community and increase awareness for AIP-related disease, extremely rare in the world at large but not so rare in this area. Immediate signs of success were evident: volunteers came intentionally to our cabins, after learning about the study in the local media. Some brought photographs, newspaper cuttings and stories of local ‘giants’, many of which are not known to the medical community. We were also visited by parents of (very) tall children, and were able to point them in the right direction, possibly leading to early discovery and treatment, something which our previous studies have already achieved in our known AIP families and which will be an important outcome of our community screening initiative.

Members of Márta Korbonits’ laboratory are supported by the Wellcome Trust, William Harvey Research Foundation, an unrestricted education grant from Pfizer, an EU Marie Curie Fellowship, NIHR and Barts and the London Charitable Trust.

SERBAN RADIAN MD, PHD, MARIE CURIÉ FELLOW, AND MARIA HERINCS MD, PHD STUDENT

Members of Márta Korbonits’ laboratory are supported by the Wellcome Trust, William Harvey Research Foundation, an unrestricted education grant from Pfizer, an EU Marie Curie Fellowship, NIHR and Barts and the London Charitable Trust.

A local lady brought a newspaper cutting from May 1913 showing her 21-year-old uncle arriving to Canada from Ireland. The uncle, no doubt suffering from gigantism, unfortunately died within a month of having this picture taken, possibly of a hypertensive crisis.