

The genetic research that has changed the life of Mandy Sellars

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Aim of the poster

With this case presentation we wish to illustrate the positive effect of genetic research in a participant attending the NIHR/Wellcome Trust Clinical Research Facility in Cambridge.

Background

Mandy Sellars was born with abnormally large legs and feet and throughout her life continued to have severe and progressive overgrowth of her body from the waist down with lack of upper-body adipose tissue.

In 2010, at the age of 35, an above-knee amputation of the left leg was undertaken. However, her leg stump continued to grow exponentially, and left her with extremely impaired mobility. Her legs alone were considered to weigh 17 stone.

Her condition was progressive, undiagnosed and untreated.

Method

Mandy has visited the NIHR/Wellcome Trust Clinical Research Facility in Cambridge since 2010 to take part in an endocrine/metabolic/genetic research study overseen by Dr Robert Semple.

Extensive testing of Mandy's condition was carried out including dual energy X-Ray absorptiometry (DEXA) scans and taking biopsies from Mandy's affected leg and unaffected arm.

Whole exome (genetic) sequencing at the Sanger Institute was used to investigate the biopsy samples for possible causes of Mandy's segmental overgrowth.

Contacts

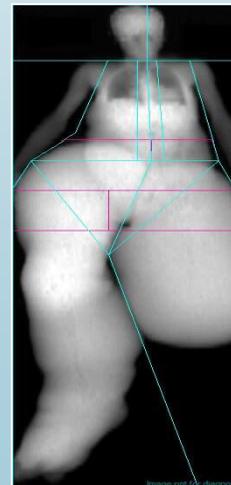
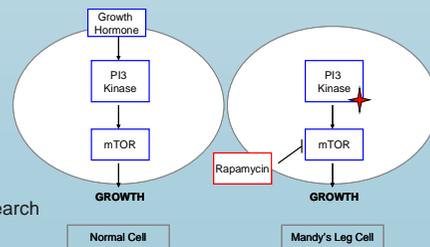
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Mandy Sellars at the Cambridge CRF in 2012



DEXA scan of Mandy Sellars

Result

The exome sequencing revealed there to be a mosaic mutation in PIK3CA exclusively in leg cells but not in arm cells. PIK3CA encodes P13 kinase which is an important protein in cells. This diagnosis was tested out further and subsequently has led to the commencement of the treatment of Mandy with Rapamycin in September 2012.

Mandy lost 10kg from her legs within the first 3 months of treatment and a further 3kg in the next 3 months. Now she is able to wear her prosthesis and continue with physiotherapy and mobilisation.

This diagnosis and life changing positive outcome of the ensuing treatment has been featured in the Channel 5 TV documentary 'Shrinking my 17 stone legs' (18 Feb 2013).

'This research & treatment has saved my life & changed my life, without it I would have become bedridden & lost any chance at an independent life.' (Mandy Sellars 2013)

Future application

The research area is now being expanded with recruitment of new patients from around the country.

Role of the Cambridge Clinical Research Facility

Dr Semple's study team is being assisted by the CRF nursing team in performing a wide variety of clinical tests – tissue and blood sampling, fat/skin biopsies, oral glucose tolerance testing. The metabolic research area team perform and assist in the analysis of DEXA scanning, body composition measurements, magnetic resonance imaging and magnetic resonance spectroscopy as well as calorimetry.

It is the existence of a CRF like the one in Cambridge that enables such research to continue and to improve the lives of individuals such as Mandy Sellars.

References: Lindhurst MJ, Parker et al (2012) Mosaic overgrowth with fibroadipose hyperplasia is caused by somatic activating mutations in PIK3CA. *Nature Genetics* Vol. 44 (8): p.928-933

Channel 5 (18 Feb 2013) Shrinking my 17 stone legs (video)
<http://www.channel5.com/shows/extraordinary-people/episodes/shrinking-my-17-stone-legs-an-extraordinary-people-special> available to be viewed until 18 Feb 2014

We are grateful to Mandy Sellars for her permission to feature her story and photos in this poster.