Integrated whole genome and transcriptome sequencing to identify the etiology of ROHHAD syndrome.

Rapid-onset obesity, hypoventilation, hypothalamic dysfunction and autonomic disturbance (ROHHAD) syndrome was characterized by Ize-Ludlow et al in 2007 from the study of a group of children with similar clinical features. For the past decade, the etiology of the syndrome has eluded us. The lack of a unifying genetic finding has been recognized by many groups working around the world. As a next step, we are looking to identify the functional changes in the hypothalamus that may be responsible for the characteristic clinical features.

In our labs at Columbia University Medical Center, we aim to do this by obtaining the peripheral blood cells from children with ROHHAD syndrome and their unaffected parents, turn them into stem cells that will be reprogrammed to pluripotent cell derived hypothalamic neurons, specifically of the region that is known to control breathing, weight regulation and other autonomic controls. We will perform RNA-seq study of these patient-specific cells and compare this profile to that of their parents to look for changes in the protein expression. When we identify the differences, we can go back and look at the DNA structure of the individuals to understand if there are changes in the DNA that can be responsible for the disease. Our hope is that better characterization of such changes will help towards solving the mystery of ROHHAD syndrome.

We need samples from many families to work on this project. For the families who are willing to participate, we will need clinical information (through our forms, or the medical records of the child), medical history of the family, and biological samples. We can send kits for blood collection to the families with shipping labels to be sent to us by overnight shipping. For any families who have not had exome sequencing, we will arrange for this prior to undertaking the experiments elaborated here. This study has been approved by Columbia University Institutional Review Board, and we need the samples in the calendar year 2019 for some of these studies.

More information can be found here: https://clinicaltrials.gov/ct2/show/NCT02602769

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