It REALLY is in your genes: a review of obesity-related genetic testing results.

Obesity is a widespread, complex, progressive, and relapsing chronic disease characterized by abnormal or excessive body fat (adiposity) that impairs health (Obesity Canada, 2020). Clinically, adults with a body mass index (BMI) greater than 30 kg/m^2 are considered obese. BMI is a multifactorial trait typically influenced by multiple genes (Gusev et al., 2014, PubMed ID: 25439723), as well as by environmental and lifestyle factors. However, in some cases, obesity is inherited through a monogenic or single-gene mutation or alteration. Monogenic obesity can be either non-syndromic, presenting as a single, isolated feature, or syndromic, occurring with multiple comorbid phenotypes (Rhythm Pharmaceuticals, 2024). Although rare, conditions such as Bardet-Biedl syndrome and missing receptors in the MC4R pathways are increasingly being observed in non-syndromic obesity.

The prevalence of non-syndromic obesity is not well understood due to a lack of testing and reporting. Although it is suggested to patients that weight is 70% genetically determined (Macklin, 2020), there is limited data on actual genetic variations. Rhythm Pharmaceuticals, in partnership with Prevention Genetics, provides sponsored genetic testing for 87 genes and 1 chromosome sequence associated with obesity.

This presentation will review the genetic testing results of approximately 40 patients from Southern Ontario to near Northern Ontario, all of whom have a history of childhood obesity and a current BMI over 40. Interestingly, 95% of these patients, meeting the specified criteria, exhibit between 1 and 4 genetic variations associated with obesity. One-third of these patients have one variation, while two-thirds have two to four variations. In this study, all subjects were found to be heterozygous with uncertain to pathogenic significance. We will also discuss demographic data, family history, associated comorbidities, and hyperphagia scoring.

While the primary focus of this presentation will be on reviewing the genetic testing data and associated findings, we will also explore the potential treatment option of Setmelanotide. Current treatments with GLP-1 agonists and other medications used to address hyperphagia will also be covered.