Study of Rare Forms of Severe Early Monogenic Obesity by Homozygote and Heterozygote Mutation of Leptin gene and Leptin-Receptor in Children

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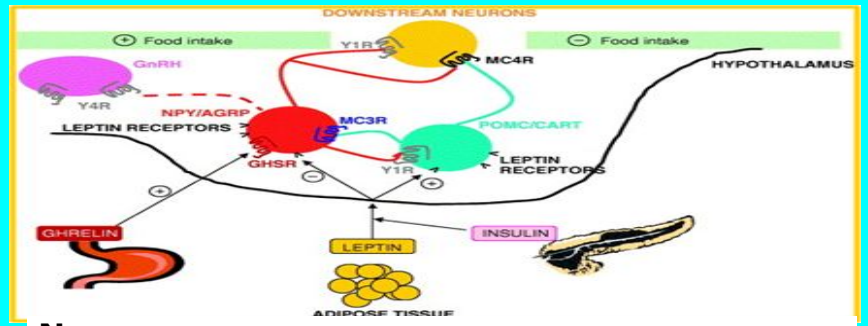
INTRODUCTION : Monogenic obesity is a rare condition with autosomal recessive transmission caused by the mutation of the leptin pathway gene or melanocortin that are involved in the central nervous regulation of hunger and satiety .Severe early obesity (SEO) begins in the first few months of life, moving towards massive obesity at puberty. Objectives: Identify the genetic mutations that cause SEO.

MATERIEL AND METHODES : 29 subjects had a high suspicion of monogenic SEO onset of obesity 6 months .9 Index cases are retained (2012-2017) and they were studied in molecular biology (NGS).

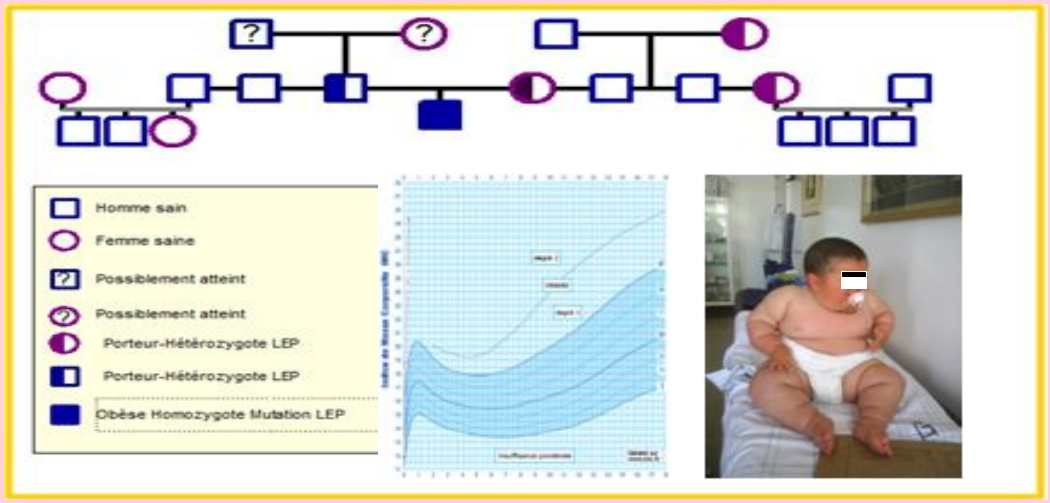


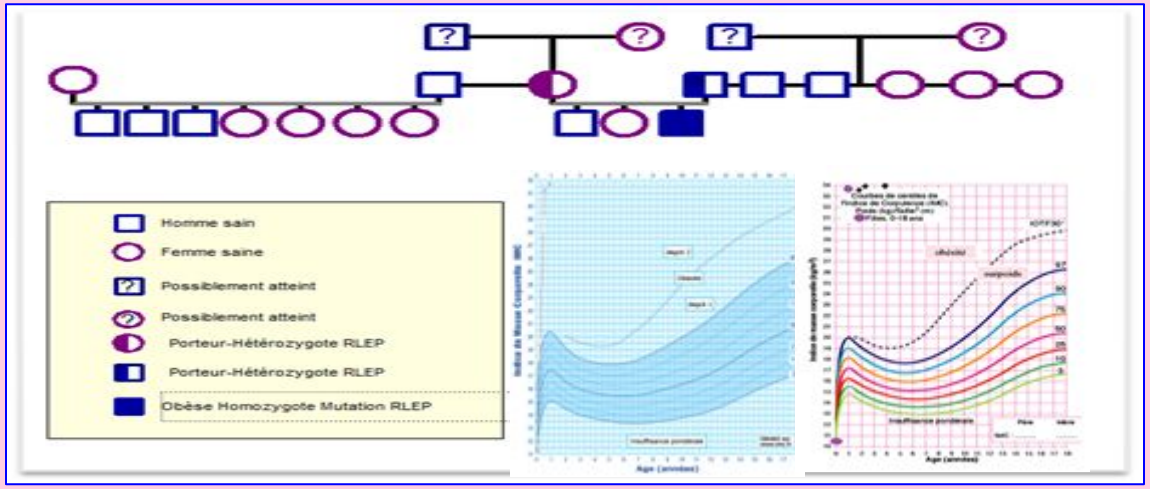
Neural network involved in energy balance Regulation

Patients have severe obesity from birth and they come from inborn parents.Biochemical and hormonal markers are analyzed by EIA

Genetic analysis byRain Dance and NGS .

RESULTS AND DISCUSSION : The obese CI-1 2 years 2 months old, BMI: 31.7 Kg/m2 with a micropenis.It presents a new homozygous mutation in the leptin gene (7q31.3) with congenital leptin deficiency (12 ng/ml 1st percentile). (rare 1/ 1,000,000 : 30 World cases) The CI-2 with massive obesity (age: 4 years 2 months ,BMI: 40.5 Kg/m2) with a new harmful homozygous mutation of the gene LEPR (1p31).(loss of function). It is associated with dyslipidemia and hypothalamic pituitary abnormalities (hypogonadism and hypothyroidism) with resistance to leptin (leptin: 69.75 ng/ml >99th Percentile). The CI-3 with PAHO (age: 2 months, BMI: 19.7 Kg/m2) presents a new deleterious heterozygous mutation of the LEPR gene (leptin: 12.9 ng/ml).





Family trees of patients with SEB with two new homozygous mutations LEP (Case Index 1) and RLEP (Case Index 2) Health care the obeses

CONCLUSION : The originality of our research work is based on the discovery of three new mutations: Homozygous mutation of the leptin gene (LEP) which generates the phenotype due to dysregulation at the hypothalamus level Homozygous mutation on the leptin receptor (LEPR) expressed by hypothalamic-pituitary endocrine impairment (tyreotrope and gonadotropic axis) resulting in severe early obesity. Heterozygous mutation on leptin receptor (LEPR) .The detection of genes that are involved in genetic forms of severe early obesity may contribute to new therapeutic implications. This can improve the quality of patient care, as well as the patient's vital prognosis.