

Genes-4U

GHR fl - d3

(Full Length / Deletion of Exon 3 – Variants of the Human Growth Hormone Receptor)

Human growth hormone is a substance secreted by the pituitary gland that promotes growth during childhood and adolescence. Growth hormone acts on the liver and other tissues to stimulate production of insulin-like growth factor I (IGF-I), which is responsible for the growth-promoting effects of growth hormone and also reflects the amount produced. The human Growth Hormone Receptor (GHR) is indispensable for the action of human Growth Hormone. While about 60 % of Caucasians carry the full-length version of GHR (GHRfl), about 40 % carry a deletion of exon 3 (GHRd3) in their genome in either heterozygous (about 30%) or homozygous form (about 10%). The d3 Allele has been associated with enhanced growth in children treated with human Growth Hormone (1). The fl-d3 polymorphism has also been associated with body composition (BMI, fat mass, waist circumference) and metabolic risk factors (fasting insulin, uric acid, HDL, triglycerides, apolipoprotein B, leptin and diastolic blood pressure, (2,3)) and may thus be involved in the pathogenesis of obesity, diabetes and atherosclerosis.

The GHRd3 variant arose during primate evolution probably as the result of intragenic recombination between 2 highly homologous 251 bp repeats of retroviral origin in the full-length version of GHR. In the full-length version of GHR the region flanked by these repeats is about 2.7 kb and contains repeat 1 and exon 3 followed by repeat 2, whereas in the d3-Version it retains only repeat 2 but lacks repeat 1 and exon 3. Repeat 1 and 2 are identical except for 3 SNP's in positions 14, 245 and 246 (4). By choosing one primer in the conserved region 5' of the repeats and one primer in a conserved region within the repeats, PCR generates products of identical lengths from both the full-length version and the d3 version of the GHR gene. These products however differ by the 3 above mentioned SNP's which can be distinguished by appropriate hybridisation probes. This approach to genotyping the Full Length/Deletion of Exon 3 – Variants of the Human Growth Hormone Receptor is embodied in the Genes-4U GHR fl - d3 ToolSet™ for LightCycler™ and yields the same results as conventional procedures (1,4) but is technically much easier.

References :

- (1) Dos Santos C. Nat Genet. 2004; 36(7) : 720-4 (PubMed ID 15208626)
- (2) Kratzsch J. Clin Endocrinol 2001; 54(1) : 61-8 (PubMed ID 11167927)
- (3) Seidel B. Eur J Endocrinol. 2003; 148(3) : 317-24 (PubMed ID 12611612)
- (4) Pantel J. JBC 2000; 275(25):18664-9 (PubMed ID 10764769)