MicroRNAs change and target genes involved in longitudinal growth in patients with IGHD on GH treatment

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Background
The growth response in patients on GH treatment is extremely variable depending both on the patient’s basal conditions and on personal innate sensitivity to therapy. MiRNAs are non-coding RNAs that function as epigenetic regulators of biological and metabolic processes by binding mature mRNA determining the inhibition of protein synthesis or mRNA degradation. MiRNAs could be potential biomarkers of response to GH treatment and could disclose new information on the effects and regulation of GH.

Aim
Identify all the miRNAs varying on GH treatment (Global Profiling approach) and identify the principal pathways/biological processes, within growth, impacted by these miRNAs.

Patients and Methods
Ten prepubertal normal weight patients with Isolated Idiopathic Growth Hormone Deficiency (IGHD) were enrolled (5 males, 5 females; CA: 8.12 ± 0.73 yr). Global miRNA profiles (TaqMan Advanced Human Card A) were evaluated as follows: miRNA expression levels at -3 and 0 months were compared and the miRNAs showing a p-values<0.05 were excluded allowing to identify those miRNAs changing only in response to treatment (+3 months) by either a factor log₂DDCt>1.5 or log₂DDCt<-1.5 (up- or down-regulated, respectively). Single miRNA target genes were evaluated and DIANA-miRPath v3.0 software was used for KEGG pathway and Gene Ontology analyses.

Results
Overall 30 miRNAs were regulated by GH, 27 were up-regulated, and 3 down-regulated.

Conclusions
GH treatment regulates miRNAs that in turn regulate genes, pathways and biological processes involved with growth. MiRNAs could be explored as biomarkers of response to treatment, as accurate prediction of growth still represents a considerable challenge for physicians in their daily clinical practice. Further, some novel genes implicated in the regulation of growth could be identified using this approach.