Preface

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Genetics of Growth

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The first ‘special topic issue’ of Hormone Research in Paediatrics is completely dedicated to genetics of growth, a rapidly developing area of paediatric endocrinology. The main reason of this fast development is the stormy progress of genetic techniques. We believe that in the coming years genetic studies on growth and other areas of paediatric endocrinology will generate numerous novel insights, particularly due to the rapidly increasing availability of next generation sequencing. Since a few years whole exome sequencing is available at a reasonable price, and it is expected that whole genome sequencing will soon follow. These techniques will be primarily used for unravelling the genetic causes of congenital disorders, and recent examples illustrate that this can lead to the discovery of novel gene defects of known clinical syndromes such as mutations in SRCAp causing Floating-Harbor syndrome [1], and even to uncovering novel endocrine syndromes such as IGSF1 deficiency syndrome [2]. However, it is expected that next generation sequencing will soon also be used in genome-wide association studies, which so far have been based on multiple single nucleotide polymorphisms [3].

This special topic issue can be roughly divided into four parts. The first part consists of a paper describing the role of zinc in the process of secretory granule biogenesis in somatotrophs, illustrating that for proper growth hormone (GH) secretion more is needed than a normal GH1 gene, and that multiple genes are involved in the full trajectory from GH1 transcription to pulsatile GH secretion. The second part describes patients with mutations in various parts of the GH-IGF axis, including GH1, GHR, IGFALS and IGF1R, and ends with a paper describing a website containing clinical, biochemical and genetic information about presently known genes in this axis. The third part consists of two papers describing clinical features of large groups of patients with relatively frequent (epi)genetic defects: SHOX defects and Beckwith-Wiedemann syndrome. Finally, the fourth part contains two papers using association analysis and pharmacogenetics in relation to growth and growth response to GH.

We wish to emphasize three important messages from the papers in this issue. In the first place, the clinician should be aware of the limitations of a genetic test that was carried out at a certain time, and should consider re-testing if the genetic techniques have been changed or if novel defects have been published in parts of the gene that were not investigated in the patient’s DNA. This is even more indicated if the clinical presentation is typical for that particular gene defect. In this issue this message is illustrated for type II GH deficiency (usually caused by
splicing mutations in \textit{GHI}) and a specific intronic mutation in \textit{GHR}. It shows that close collaboration between clinicians and geneticists is becoming even more necessary than it already was. Secondly, we wish to stimulate clinicians as well as geneticists to enter clinic and genet data into web-based databases, so that more information will become available about the spectrum of the phenotype and genotype. For many genes it will become increasingly difficult to publish reports on single mutations. Thirdly, the papers on \textit{SHOX} defects and Beckwith-Wiedemann syndrome illustrate the importance of collecting data on patients with genetic syndromes for improving the criteria for genetic testing and for performing additional investigations.

We hope that this special topic issue of \textit{Hormone Research in Paediatrics} will be a pleasure to read, and will help the paediatric endocrinologist to become up to date on the genetics of growth.

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**References**

