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Editorial

Introduction to the Special Issue on Next Generation Sequencing: Short General Overview of NGS

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The publication of the double helix DNA structure in 1953 [1] was the kick-off of numerous efforts to understand and unravel the complexity of the human genome. It took 50 years until the human genome project, based on Sanger sequencing, was completed in 2003 [2]. This was followed by what may be considered a revolution in the field of DNA analysis: the introduction of Next Generation Sequencing (NGS) in 2005 consisting of massively parallel sequencing of DNA fragments which allows the high throughput analysis of large numbers of genes or of the whole genome [3]. NGS technologies evolved quickly in parallel to a considerable drop of costs [for review see 4]. It rapidly became a standard method in research and led to the identification of thousands of disease genes. In the diagnostic field NGS technology has allowed a few years ago to move from Sanger sequencing of single genes to parallel sequencing of groups of genes ('multi gene panels') for genetic conditions known to be heterogeneous like cardiomyopathies, epilepsy or retinitis pigmentosa. Today, clinical exome sequencing by NGS with diagnostic results from the

analysis of flexible and customisable *in silico* panels is increasingly a routine diagnostic. Beyond the field of gene identification and analysis, NGS technologies have pharmacological applications and largely promoted precision medicine, e.g. in classification, risk prediction and targeted therapy in oncology.

There is no doubt that NGS technologies have radically changed the way of working of DNA diagnostic laboratories, and a bunch of critical points had to be addressed. Meanwhile, clinical laboratory standards for NGS have been published by the American College of Medical Genetics and Genomics (ACMG) in 2013 [5], followed two years later by ACMG guidelines for the interpretation of sequence variants [6], and also the European Society of Human Genetics (ESHG) agreed on guidelines for diagnostic NGS [7]. Recommendations for the integration of genomic technology into clinical practice from patient selection to the return of findings have been given by Bowdin et al. [8]. The number of NGS applications is increasing and includes the diversity of material analysed. Since the interpretation of NGS data remains challenging both in a research and diagnostic setting, reference standards have recently been published [9]. At this time, whole-genome analysis (WGA) by NGS is being introduced, and critical points resulting from the size and complexity of the whole genome are under discussion [10].

This special NGS issue aims at illustrating a couple of the many prevailing facets of NGS. Geis and co-workers illustrate the benefit of a combined phenotype- and NGS-based approach to unravel the underlying diseases in critically ill hypotonic neonates, whereas Schaaf and colleagues report on NGS as a means to understand the etiology of autism spectrum disorders. The paper by Dikow and co-authors addresses the need of interdisciplinary work-up in the identification of hereditary cancer predisposition syndromes in children with brain tumors. Bauer and colleagues developed national guidelines for the diagnostic use of NGS building on existing Eurogentest guidelines, and the group around Paramasivam and Schlesner presents their bioinformatics pipeline to identify causal sequence variants. These papers are good examples that 'bioinformaticians, clinical scientists and specialist clinicians all have important roles to play in the safe and effective practice of genetic medicine', as Wright, FitzPatrick and Firth stated in their recent extensive and most readable review on paediatric genomics [11].

References

1. Watson JD, Crick FH. The structure of DNA. Cold Spring Harb Symp Quant Biol. 1953; 18: 123–131.
2. Collins FS, Morgan M, Patrinos A. The Human Genome Project: lessons from large-scale biology. Science. 2003; 300: 286-290.
3. Shendure J, Balasubramanian S, Church GM, Gilbert W, Rogers J, Schloss JA, et al. DNA sequencing at 40: past, present and future. Nature. 2017; 550: 345-353.
4. Goodwin S, McPherson JD, McCombie WR. Coming of age: ten years of next-generation sequencing technologies. Nat Rev Genet. 2016; 17: 333-351.
5. Rehm HL, Bale SJ, Bayrak-Toydemir P, Berg JS, Brown KK, Deignan JL, et al. Working Group of the American College of Medical Genetics and Genomics Laboratory Quality Assurance Commitee. ACMG clinical laboratory standards for next-generation sequencing. Genet Med. 2013; 15: 733-747.

6. Richards S, Aziz N, Bale S, Bick D, Das S, Gastier-Foster J, et al. ACMG Laboratory Quality Assurance Committee. Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. Genet Med. 2015; 17: 405-424.
7. Matthijs G, Souche E, Alders M, Corveleyn A, Eck S, Feenstra I, et al. EuroGentest; European Society of Human Genetics. Guidelines for diagnostic next-generation sequencing. Eur J Hum Genet. 2016; 24: 2-5.
8. Bowdin S, Gilbert A, Bedoukian E, Carew C, Adam MP, Belmont J, et al. Recommendations for the integration of genomics into clinical practice. Genet Med. 2016; 18: 1075-1084.
9. Hardwick SA, Deveson IW, Mercer TR. Reference standards for next-generation sequencing. Nat Rev Genet. 2017; 18: 473-484.
10. White SJ, Laros JFJ, Bakker E, Cambon-Thomsen A, Eden M, Leonard S, et al. Critical points for an accurate human genome analysis. Hum Mutat. 2017; 38: 912-921.
11. Wright CF, FitzPatrick DR, Firth HV. Paediatric genomics: diagnosing rare disease in children. Nat Rev Genet. 2018; 19: 253-268.

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