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From NSD1 to Sotos syndrome : a genetic and functional analysis

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Stellingen

behorende bij het proefschrift

From *NSD1* to Sotos syndrome

A genetic and functional analysis

1. Non-allelic homologous recombination between directly orientated low-copy repeats is the cause of the common 1.9-Mb microdeletion in Sotos syndrome. (*this thesis*)
2. Epimutations or genetic abnormalities of the *NSD1* promoter region are unlikely to be the main culprit for patients with characteristic manifestations of Sotos syndrome but without detected *NSD1* alterations. (*this thesis*)
3. High-resolution genome-wide SNP array is, in comparison to a candidate gene approach, a powerful method to attain a molecular diagnosis in patients with features of Sotos syndrome in whom no *NSD1* abnormalities were found. (*this thesis*)
4. The MAPK/ERK signaling pathway is deregulated in Sotos syndrome and altered activity of this pathway provides a possible explanation for the increased statural growth. (*this thesis*)
5. Patients with *NSD1* intragenic mutations are significantly taller than patients with 5q35 microdeletions, whereas patients with 5q35 microdeletions have more-severe learning disability. (*adapted from Tatton-Brown et al., Am J Hum Genet, 2005, 77:193-204*)
6. An intricate issue for data integration in the future will be categorizing structural variants of the human genome in terms of whether they are 'normal', 'disease-causing' or 'phenotype-associated', as these designations can be part of a continuous range. (*adapted from Scherer et al., Nat Genet 2007; 39: 57-15*)
7. For the detection of human gene mutations to have practical application, clear clinical descriptions of the affected individuals (as well as those clinically affected in whom mutations are not found) should be part of the publication. (*Hall JG, Nat Genet. 2003; 33: 440-2*)

8. The lack of specific health policies for rare diseases and the scarcity of the expertise, translate into delayed diagnosis and difficult access to care. This results in additional physical, psychological and intellectual impairments, inadequate or even harmful treatments and loss of confidence in the health care system, despite the fact that some rare diseases are compatible with a normal life if diagnosed on time and properly managed. (*Communication on rare diseases from the commission of the European communities, Brussels, 2008*)
9. The detection of a mutation in the PHD-domain of the *NSD1* gene has prognostic value for the outcome of one's PhD project.
10. Success is 99 percent failure. (*Soichiro Honda, 1906-1991*)
11. Doctors are men who prescribe medicines of which they know little, to cure diseases of which they know less, in human beings of whom they know nothing. (*Voltaire, 1694-1778*)
12. Even a monkey falls from a tree. (猿も木から落ちる; Japanese proverb: 'Nobody is perfect')

Leiden, 26 mei 2011

Remco Visser