Propositions pertaining to the thesis

Facing the Future of Craniofacial Genetics

1. Apparently synonymous substitutions in *FGFR2* can affect splicing and result in Crouzon syndrome (this thesis)
2. *TCF12*-related craniosynostosis, comprising of coronal suture synostosis, clinical features of Saethre-Chotzen syndrome and learning and behavioural problems, is caused by small heterozygous loss-of-function mutations in *TCF12* as well as large intragenic rearrangements (this thesis)
3. Heterozygous nonsense mutations in *ZIC1* cause *ZIC1*-related craniosynostosis consisting of coronal and lambdoid suture synostosis with severe brachycephaly, learning disabilities, brain malformations and progressive scoliosis. A slightly milder phenotype is caused by missense mutations (this thesis)
4. Compound heterozygous mutations in *TXNL4A* cause Burn-McKeown syndrome which is characterized by asymmetry of the face, short palpebral fissures, defects of the lower eyelids, preauricular tags, maxillary and mandibular hypoplasia and choanal atresia. Homozygous deletions of the promoter of *TXNL4A* cause choanal atresia and other (mild) clinical features of Burn-McKeown syndrome (this thesis)
5. More and more genetic causes of craniosynostosis are identified, the phenotypes of related syndromes are getting less specific and some of the genes are only rarely associated with craniosynostosis, making next generation sequencing a valuable diagnostic tool in these patients (this thesis)
6. Cranial capacity, and hence brain size, is only a crude indication of cerebral function, as illustrated by the fact that the similar cranial capacities of Neanderthals and anatomically modern humans are not matched by equivalent artistic creativity or flexibility in tool-making (Morriss-Kay, Journal of Anatomy, 2010)
7. Five generations of the Abraham Lincoln family, including the former president of the United States, showed signs of isolated unicoronal suture synostosis with an autosomal dominant inheritance pattern (Fishman, Gene, 2013)
8. DNA is an attractive medium for long-term, high-latency data storage (Erlich and Zielinski, Science, 2017)
9. RNA-guided genome surgery using CRISPR-Cas9 nucleases has shown promise for the treatment of diverse genetic diseases (Kim *et al.*, Genome Research 2017)
10. The serum of healthy new-born infants contains 1.2×10^{-5} µg/g of gold (Meurling and Plantin, Acta chirurgica Scandinavica, 1981)
11. Als het klaar is, is het goed
    Als het niet goed is, is het nog niet klaar

Jacqueline A.C. Goos
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