Characterization of candidate genes in unexplained polyposis and colorectal cancer

Abayzeed Elsayed Osman, F.

Stellingen behorende bij het proefschrift

Characterization of candidate genes in unexplained polyposis and colorectal cancer

1. Pathogenic germline variants in *POLE* can result in secondary somatic MMR variants and MMR deficiency and give rise to a Lynch syndrome-like phenotype. (This thesis)

2. Pathogenic variants in the exonuclease domain of *POLE* and *POLD1* are a rare cause of multiple colorectal polyps. (This thesis)

3. Mutational signature analysis can be used as a novel approach to characterize rare hereditary polyposis and CRC syndromes. (This thesis)

4. Biallelic loss of function variants in *NTHL1* predispose to a multitumor syndrome and is not restricted to colorectal adenomatous polyposis and colorectal cancer only. (This thesis)

5. Individuals carrying monoallelic loss of function variants in *NTHL1* do not have increased risk for polyposis and colorectal cancer. (This thesis)

6. Mutational signature analysis is a powerful tool could help to identify germline DNA repair defects. (*Alexandrov et al, Nature, 2020*).

7. Most cancer mutations are due to random DNA copying mistakes (most cancers arise from bad luck). (*Tomasetti and Vogelstein, Science, 2015*).

8. Classification of the variants represents a crucial step in clinical decision-making. Therefore accurate assessment of the predictions of the clinical significance of the variants is essential.

9. Only publishing positive results tend to only give a limited and skewed view of research. All scientific data should be published, positive and negative, so long as it advances the state of knowledge.

10. Scientific research in developing countries face significant challenges due to limited resources and inadequate infrastructure. Efforts for research collaboration should enhance scientific research and drive socioeconomic development in these regions.

11. Where there is a will, there's a way.