

STELLINGEN

Behorende bij het proefschrift

CHEK2 1100delC and polygenic susceptibility to breast cancer and colorectal cancer

1. *CHEK2* 1100delC is a susceptibility allele for HNPCC-related colorectal cancer (*this thesis*).
2. The *CHEK2* 1100delC mutation partakes in a polygenic cancer model that additionally involves at least one breast cancer susceptibility allele and at least one colorectal cancer susceptibility allele (*this thesis*).
3. The observation that *p53* and *CHEK2* mutations occur mutual exclusive in human cancer cell lines suggests that the abolished function of the encoded proteins results in similar effects on carcinogenesis (*this thesis*).
4. *MDM2* SNP309 and *MUTYH* Y179C, G396D and P405L do not play a major role in the polygenic *CHEK2* cancer model (*this thesis*).
5. Comprehension of the genotypic and phenotypic characteristics associated with *CHEK2* 1100delC cancer families and *CHEK2* 1100delC tumors will aid the identification of other risk alleles involved in the polygenic *CHEK2* cancer model (*this thesis*).
6. A 1% population frequency as cutoff for pathogenicity of a gene variant has become outdated since the discovery of *CHEK2* 1100delC as a breast cancer susceptibility allele.
7. The difficulty in most scientific research lies not in the experiments themselves but in formulating the hypothesis and designing the study.
8. Recent progress has been made in mapping the DNA sequence associated with disease but, like early world maps, many crucial details remain unclear (*P. Donnelly, Nature 2008; 456:728-731*).
9. Given the extensive genotypic and phenotypic heterogeneity of breast cancer, it is insufficient to state that a patient is diagnosed with breast cancer (*H.T. Lynch et al., The Breast Journal 2008; 14:3-13*).
10. A human being is more than the sum of its genes.
11. Een verre vriend is beter dan een goede buur.