Epigenetic alterations in the predisposition to and progression of melanoma

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STELLINGEN

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Epigenetic Alterations in the Predisposition to and Progression of Melanoma

1. Clarifying the genetic basis of melanoma predisposition is of major clinical importance since new genetic testing can accurately identify individuals at increased risk of melanoma to whom early diagnosis can be offered. (this thesis)

2. Heritable promoter hypermethylation is not a common cause of familial occurrence of melanoma. (this thesis)

3. Specific CpG sites and regions with significantly lower hmC levels in melanoma than in nevus might serve as diagnostic markers. (this thesis)

4. In several *TERT*-expressing uveal melanoma cell lines there is a significantly higher chromatin accessibility state despite of the dense methylation of CpG dinucleotides in the promoter region. (this thesis)

5. Early promise in sensitising tumour cells to immunotherapy comes from the use of drugs targeting epigenetic alterations, such as inhibitors of DNA methyltransferase and histone deacetylase. (Moran B *et al.*, Semin Cancer Biol. 2018)

6. The well-controlled dynamic level of 5-hmC during transition from embryonic stem cell to melanocyte progenitor to terminally differentiated melanocyte is an epigenetic signature of melanocyte differentiation, the perturbation of which may lead to the induction of oncogenic pathways underlying melanoma progression. (Lian CG *et al.*, Cell. 2012)

7. Somatic mutations in regulatory regions of the genome may represent an important tumorigenic mechanism. (Huang FW *et al.*, Science. 2013)

8. The high recurrence and specificity of the TERT promoter mutations, together with the evidence that they have a functional effect on transcription, suggest that these mutations are driver rather than passenger events. (Horn S *et al.*, Science. 2013)

9. Most people say that it is the intellect which makes a great scientist. They are wrong: it is character. A scientist who is able to inspire and mentor those around is a successful scientist. (Adapted from Albert Einstein)

10. Science is more than a body of knowledge. It's a way of thinking, a way of sceptically interrogating the universe. It is the critical thinking acquired during scientific research that allows one to more accurately question and better judge any other situation in life. (Adapted from Carl Sagan)