MelEVIR – Melanoma, Extracellular Vesicles, and Immune Response

Speaker
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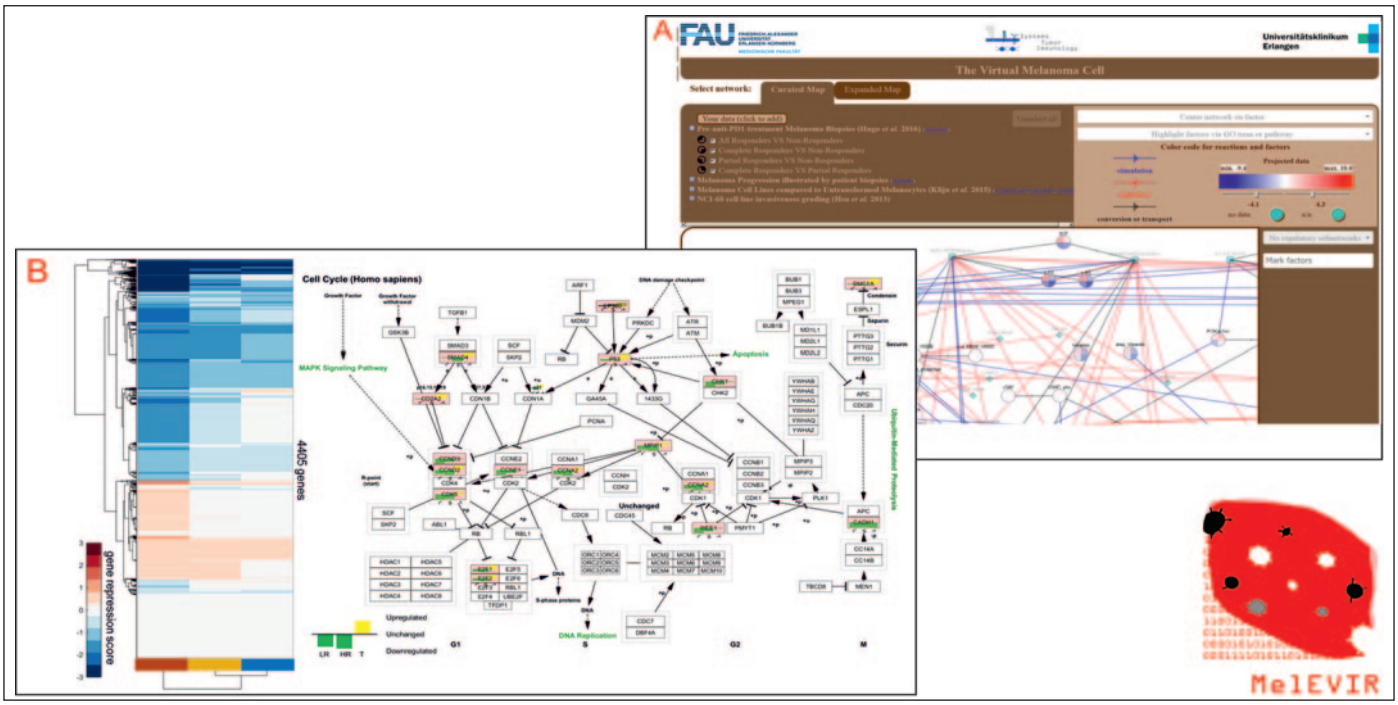
Aims and structure

The aim of the project is the development, testing, and translation into clinical practice of a systems biology-based diagnostic tool. The tool uses the profiling of miRNA and proteins contained in plasma extracellular vesicles (pEV) to assess the probability of tumor relapse in melanoma patients.
The project is conducted by an interdisciplinary team, including biomedical and translational researchers (Prof. Dr. L. Heinzerling and Prof. Dr. A. Baur, Department of Dermatology), medical informaticians (Prof. Dr. H.U. Prokosch, Chair of Medical Informatics), bioinformaticians (Prof. Dr. O. Wolkenhauer, Department of Systems Biology and Bioinformatics, Universität Rostock) and mathematical modelers (Prof. Dr. J. Vera-González, Department of Dermatology).
The project is funded from April 1, 2016 until September 30, 2019 with 1.6 million euro by the BMBF under the e:Bio initiative for Systems Biology.

Research

Experimental results indicate that macroscopic tumors can produce and load into the blood large amounts of extracellular vesicles (pEV). It is also known that the immune system can produce and secrete pEVs in response to stimulus. In the project we are exploring the hypothesis that the minimal residual disease (MRD), the small amount of disperse tumor cells, and micrometastases left after the tumor resection cannot be the unique origin of the high levels of pEV that are found in high risk patients. Rather, large amounts of pEV are also produced by the immune system upon detection of circulating tumor cells. We hypothesize that these pEV are part of the systemic immune response against the micrometastases and participate in the immune control of the MRD. In MelEVIR we are developing, testing, and translating into clinical practice a computer modeling based diagnostic tool which uses the profiling of pEV and tumor samples.

Precisely:
1. We have collected and quantified samples for primary tumors and pEV from melanoma patients.
2. We have performed experiments to elucidate the role of pEV in the tumor-immunity interaction.
3. We are using these data to develop and characterize mathematical and computational models describing the tumor-immunity interaction and assessing the risk of tumor relapse in the patients.
The final aim is to integrate the predictive model into the clinical routine and in the electronic records of the patient.
In MelEVIR we have profiled the content of melanoma patient's pEV in miRNAs, chemokines, cytokines, and other soluble factors. Further, we have used Nanostring technology to profile the immunogenicity of melanoma patients' tumor samples.
As part of the project we have developed the Virtual Melanoma Cell, an online tool developed to facilitate the mining of high-throughput data by biomedical researchers. The tool relies in the use of computational modelling and network biology algorithms to analyze, compare, and visualize high-throughput data from melanoma samples.



A. Screenshot of the Virtual Melanoma Cell, the online platform for network biology-based analysis of melanoma high-throughput data
B. Functional analyses of miRNA contained in melanoma patient pEVs. Left: Heat map showing repression scores of miRNA targets based on the pEV miRNA expression fold changes and the biological evidence on the miRNA-target interactions (Red: Tumor bearing; Orange: High risk; Blue: Low risk) Right: The mapping of the gene repression scores in a network accounting for cell cycle regulation in melanoma