Welcome to the 9th FICAN seminar

Wednesday 31.1.2024 at 15-16

Topic: Cell state transitions and emergence of drug resistance in cancer

This time the seminar is organized by FICAN East. The seminar will be held online (Microsoft Teams) and is open to everyone interested in cancer research.

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Speaker

Merja Heinäniemi

Professor
Instutute of Biomedicine, School of Medicine, Faculty of Health Sciences

Get to know the Speaker: Systems Genomics - Heinäniemi lab

Abstract

Drug therapy is designed for targeting a specific molecular state in cells. In our ongoing research, we explore drug therapy in context of the new paradigm that considers transitions into alternative cell states as a central part in treatment design for cancer therapy. We have carried out characterization of cell states in context of the most common childhood cancer, acute lymphoblastic leukemia (ALL).

ALL represents a paradigmatic example of how alterations in transcription factors (TFs) initially block the normal developmental paths. Moreover, a number of recent studies have shown that cell state plasticity presently poses a challenge for treatment success. As TFs represent the master regulators defining cell states and via their regulatory interactions constrain the space of accessible alternative states, our focus has been on abstracting genomics profiles into models of TF activity. More recently, we have also established analysis methodology to examine microRNA gene regulation that impacts cellular homeostasis through post-transcriptional regulation and can thereby play a key role during disease development.

In my talk, I will present recent results from our single cell genomics projects that show how transitions to alternative cell states with aberrant TF activity, re-wired signaling activity, stem cell-like properties, even a lineage switch, can underly a poor treatment response in leukemia. Our goal is to chart such transitions to develop new drug treatment strategies that block this route to treatment resistance to avoid disease recurrence (10-15% of patients) that leads to a dramatic increase in cytotoxic burden, which endangers the life-long health, development and well-being of children. In broader context of cancer therapy our work contributes to the conceptual framework of capturing cell state evolution into predictive models to improve design of preventive measures that address the prevalent emergence of drug resistance in cancer.

Relevant references for this talk:

- Mehtonen, J., Teppo, S., Lahnalampi, M. et al. Single cell characterization of B-lymphoid differentiation and leukemic cell states during chemotherapy in ETV6-RUNX1-positive pediatric leukemia identifies drug-targetable transcription factor activities. Genome Med 12, 99 (2020). https://doi.org/10.1186/s13073-020-00799-2
- Olli Dufva, Petri Pölönen, Oscar Brück, Mikko A.I. Keränen, Jay Klievink, Juha Mehtonen, Jani Huuhtanen, Ashwini Kumar, Disha Malani, Sanna Siitonen, Matti Kankainen, Bishwa Ghimire, Jenni Lahtela, Pirkko Mattila, Markus Vähä-Koskela, Krister Wennerberg, Kirsi Granberg, Suvi-Katri Leivonen, Leo Meriranta, Caroline Heckman, Sirpa Leppä, Matti Nykter, Olli Lohi, Merja Heinäniemi, Satu Mustjoki. Immunogenomic Landscape of Hematological Malignancies.Cancer Cell. 2020. https://doi.org/10.1016/j.ccell.2020.06.002