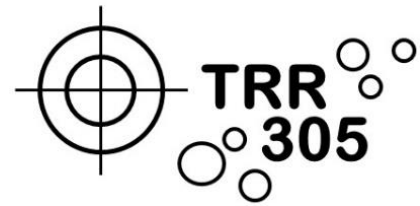


Seminar series TRR 305 – Striking a moving target: From mechanisms of metastatic organ colonisation to novel systemic therapies



Wednesday, 17 April 2024

14.00 h

hybrid (on site in Regensburg)

Seminarroom of the Chair of Experimental Medicine

(H5, 1.OG, 2.13)

University Hospital Regensburg

Colin R Goding,

Ludwig Institute for Cancer Research, University of Oxford, UK



Phenotype-switching in cancer

The intra-tumor microenvironment generates phenotypically distinct but inter-convertible malignant cell subpopulations that either fuel proliferation or metastatic spread, drug-tolerance and relapse. Understanding how specific phenotypic states are generated and maintained represents a major challenge in cancer biology. Here we use melanoma as a model to show how bi-directional interactions with the microenvironment lead cancer cells to adopt evolutionarily conserved survival strategies that underpin disease progression. These include using invasion to escape microenvironmental stresses, a process driven by reprogramming of protein translation that lies downstream from multiple triggers of cell migration. We also show that translation reprogramming tailors the fatty acid profile of melanoma cells to specific phenotypic states, and that when exposed to the same fatty acid present within the tumor microenvironment, different phenotypes exhibit distinct responses. The results presented provide an integrated and evolutionarily conserved conceptual framework to understand cancer progression.

Falletta P, Sanchez-Del-Campo L, Chauhan J, Efferm M, Kenyon A, Kershaw CJ, Siddaway R, Lisle R, Freter R, Daniels MJ, Lu X, Tüting T, Middleton M, Buffa FM, Willis AE, Pavitt G, Ronai ZA, Sauka-Spengler T, Hölzel M, Goding CR. Translation reprogramming is an evolutionarily conserved driver of phenotypic plasticity and therapeutic resistance in melanoma. *Genes Dev.* 2017 Jan 1;31(1):18-33. doi: 10.1101/gad.290940.116. Epub 2017 Jan 17. PMID: 28096186; PMCID: PMC5287109.

Yurena Vivas-García, Paola Falletta, Jana Liebing, Pakavarin Louphrasitthiphol, Yongmei Feng, Jagat Chauhan, David A. Scott, Nicole Glodde, Ana Chocarro-Calvo, Sarah Bonham, Andrei L. Osterman, Roman Fischer, Ze'ev Ronai, Custodia García-Jiménez, Michael Hölzel, Colin R. Goding, Lineage-Restricted Regulation of SCD and Fatty Acid Saturation by MITF Controls Melanoma Phenotypic Plasticity, *Molecular Cell*, Volume 77, Issue 1, 2020, Pages 120-137.e9, ISSN 1097-2765, <https://doi.org/10.1016/j.molcel.2019.10.014>.

Zoom-Meeting-Link

<https://uni-regensburg.zoom-join.com/j/61737956674?pwd=UzhmekpmSFBTZGFRcndoMWZVMCttdz09>

Meeting-ID: 617 3795 6674

Kenncode: 219353