

TRANSCRIPTIONAL DEREGULATION OF METABOLISM AS A HACKER OF METASTASIS: DECODING THE COMMUNICATION NETWORKS BETWEEN TUMOURS AND MICROENVIRONMENT

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The advances towards curative treatments for cancer are nowadays based on three pillars of research: (i) early detection, (ii) stratification of high-risk of recurrence patients, based on the molecular characterization of each individual cancer and (iii) the selection of the most appropriate therapeutic strategy based on these molecular characteristics. The advances in the molecular understanding of cancer has led to a paradigmatic change in the way we combat the disease, introducing the concept of **precision medicine: patient's stratification and personalized therapy**. We are interested in the cross-interaction between transcriptional regulation of metabolism and prostate cancer, which has led us to identify the tumour and metastasis suppressive potential of the transcriptional co-activator PGC1 α (Torrano et al., Nature Cell Bio 2016; Valcarcel et al., Cell Cycle 2016; Valcarcel et al TEM 2017). The study of this transcriptional co-activator and its biological activity can potentially lead to the development of a therapeutic strategy based on precision medicine. But, three critical questions need to be address in order to develop a precision medicine approach: **WHAT** are the key regulators of the metastatic process induced by the reduction of mitochondrial metabolism? **HOW** can we effectively treat prostate cancers with high risk of recurrence? **WHO** among PCa patients is better fitted to benefit from this therapeutic approach?

To answer these questions we aim first to define the mechanisms underlying the anti-metastatic activity of mitochondrial metabolism in PCa. Based on a multidisciplinary approach, from bioinformatics to cell biology, we are studying the contribution of mitochondrial metabolism to the acquisition of invasive properties and the preparation of the metastatic niche. I propose that the anti-metastatic activity of PGC1 α -mediated mitochondrial metabolism goes beyond the activation of catabolic processes presenting the transcriptional co-regulator as a key metabolic player that modulates cell signalling pathways and transcriptional programs involved in cell motility and invasion.