LUXEMBOURG INSTITUTE OF HEALTH

BIO SKETCH FORM & Abstract

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Curent position:

Current	Professor of Medicine – Head of the Laboratory of Molecular Digestive Oncology, KU Leuven
Since 10/2021	Fundamental Clinical Researchers KU Leuven (BOF-FKO) grant awarded, 5 year and renewable.
Since 09/2003	Clinical Head - Dept of Gastroenterology, Digestive Oncology Unit UZ Leuven

Past positions:

-2001-2003	Supervisor Dept of Gastroenterology, Digestive Oncology Unit -UZ Leuven
-1995 -2001	Resident - Department Internal Medicine, Division of Gastroenterology, UZ Leuven

Abstract

Title of your presentation:

Epithelial states in colorectal cancer are co-determined by YAP associated fetal programming and WNT signaling

Summary of your presentation:

We present a new paradigm for the cellular heterogeneity of CRC associated with fetal programming and provides a comprehensive description of cell states that are found in human CRC samples, their biological associations and identifies the mouse model equivalents for further drug target discovery studies

We comprehensively examined further the cell states on two of the epithelial subtypes and linked it with specific biological pathways, particularly for fetal programmed tumor cells. The use of a human scRNA-seq dataset enabled the identification of diverse cellular states and the novel two types of fetal programmed cell with high YAP signaling in WNT and non-WNT tumor tissue. These two distinct types of fetal programmed cells, that have active tumor microenvironment crosstalk, were associated with genetic mutation such as *KRAS* or *BRAF*. These fetal programmed cells are correlated with poor relapse survival as well.

By conducting parallel single-cell analysis of distinct mouse models with identified genetic alterations, we have been able to examine the impact of oncogenes on driving or restraining the acquisition of certain fetal states. Specifically, *Kras* mutant models such as AKPT and KPN exhibited heterogeneous patterns in fetal programmed cell population, indicating *Kras* mutation is a significant factor in promoting plasticity. It is of particular significance that this may have considerable implications of the impact of *KRAS* inhibitors and suggest that inhibition could reduce the inherent plasticity of CRC that is often associated with resistance.