LECTURE SERIES & WORKSHOPS 2020

CANCER RESEARCH

LUXEMBOURG INSTITUTE OF HEALTH
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UNIVERSITÉ DU LUXEMBOURG

03
Dec 2020
Thursday

WEBINAR
via Webex*
45' *(talk)* + 30' *(discussion)*

11.00 am

8 9 10 11 12 1 2 3

Epigenetic signaling circuits in the tumor microenvironment that modulate invasion and metastasis

ABSTRACT

The acquired capability for invasion and metastasis stands as the most complex and pathogenic hallmark of cancer. Studies involving a prototypical genetically engineered mouse model of human cancer, one that develops pancreatic neuroendocrine tumors (PanNET), are revealing new insights into and mechanisms of the invasive/metastatic phenotype. The multistage tumorigenesis pathway that unfolds in this model (RIP1-Tag2, RT2) culminates in multifocal invasive carcinomas and infrequent metastasis to liver. There are proving to be multiple components to the invasive and metastatic capabilities in this model, and two will be presented.

One mechanism promotes both local invasion and brain metastasis, governed by an co-opted neuronal signaling pathway, involving an NMDA receptor and its ligand, glutamate. (Li and Hanahan, Cell 2013; Li, Zeng, et al, Cancer Cell 2018; Zeng et al Nature 2019).

A second paracrine signaling mechanism opposes tumorigenesis and liver metastasis in the RT2 PanNET model, and others, unless abrogated by upregulation of microRNAs that downregulate the ALK7 receptor (Michael et al, PNAS 2019), which otherwise acts as a tumor suppressor (Michael et al, Developmental Cell 2019).

Both pathways are evidently modulated epigenetically, and not directly by mutational alteration of the cancer cell genome.

SPEAKER

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Supported by:

Fonds National de la Recherche Luxembourg

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