

LECTURE SERIES & WORKSHOPS 2020

CANCER RESEARCH

06

FEB 2020
Thursday

LECTURE
CHL Luxembourg
Amphitheatre

MEET, GREET & EAT
light lunch provided
CHL Luxembourg
Foyer

11.00 - 12.00 pm **12.00 - 1.00 pm**



SPEAKER

Dr Santiago ZELENAY

Group Leader Cancer Inflammation and
Immunity Group
Cancer Research UK Manchester Institute

HOST:
LIH

RESPONSIBLE LIH SCIENTISTS:

Jérôme Paggetti
(jerome.paggetti@lih.lu)
Etienne Moussay
(etienne.moussay@lih.lu)

www.lih.lu
www.uni.lu

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MANIPULATING INFLAMMATION TO RAISE CANCER IMMUNOGENICITY

ABSTRACT

Immunotherapy constitutes the most promising pan-cancer treatment approach since the development of the first chemotherapies. Unprecedented outcomes continue to be observed in multiple cancer types including malignancies once thought treatment refractory. Responses, especially complete and durable, are nevertheless only observed in a limited fraction of patients underscoring the need for basic research to elucidate the basis for these remarkable but rare outcomes. Our group at the Cancer Research UK Manchester Institute investigates the signals and pathways that regulate the establishment of tumour microenvironments that support or restrain cancer progression spontaneously or following treatment. Combining the use of genetically engineered pre-clinical cancer models with the analysis of samples from cancer patients we have identified NK cells as key drivers of cancer-inhibitory inflammation. In cancer models

rendered immunogenic by genetic ablation of the cyclooxygenase (COX)-2 pathway, NK cells were essential for initiating an inflammatory response that preceded and stimulated cytotoxic T cell-dependent tumor growth control. In agreement, pan-cancer analysis of patient datasets suggested the COX-2 pathway equally regulates the cellular and molecular inflammatory profile across multiple human malignancies. Furthermore, this analysis revealed NK cells, and crucially, a gene signature that combines both COX-2-induced tumor-promoting factors and NK cell-driven anti-tumour mediators as powerful indicators of overall patient survival and outcome from immune checkpoint inhibitor therapy. Collectively, our findings establish the COX-2 pathway and NK cells as key orchestrators of T cell-mediated cancer immunity and demonstrate the value of integrating pro- and anti-tumorigenic inflammation to predict patient outcome and response to therapy.