CENTER FOR CANCER IMMUNTERAPI
HÆMATOLOGISK AFDELING
PAVILLON 9 · 65Q9
KØBENHAVNS UNIVERSITETSHOSPITAL · HERLEV
HERLEV RINGVEJ 75
2730 HERLEV

T +45 3868 9339
F +45 3868 4153

HEH-CCIT@REGIONH.DK
WWW.HERLEVHOSPITAL.DK/CCIT-DENMARK

INVITATION TO CCIT SEMINAR

Monday December 10th, at 14.00, 2018

SPEAKER

Alexander J. Muller, Ph.D.
Associate Professor
Lankenau Institute for Medical Research
Wynnewood, Pennsylvania, US

Title

"IDO Enzymes in Cancer and Therapy"

Place

Meeting room 53K2D
Herlev University Hospital
Herlev Ringvej 75
2730 Herlev

We welcome you all to this exciting seminar!

Kindly
Mads Hald Andersen

How to get there; you can enter the hospital at entrance 57 via the covered parking lot, you are then at level 3 and the Auditorium is in room K2 D.

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Abstract

Alexander J. Muller, Ph.D.
Lankenau Institute for Medical Research

"IDO Enzymes in Cancer and Therapy"

The presentation will cover three related projects focused on the IDO1 and IDO2 enzymes in cancer. IDO1 and IDO2 together with TDO2 initiate catabolism along the kynurenine pathway accounting for ~95% of tryptophan catabolism. Unlike the predominantly hepatic enzyme TDO2, IDO1 is not responsive to circulating levels of tryptophan. Rather, IDO1 is expressed at sites of inflammation and much of IDO1 activity can be accounted for by its responsiveness to the inflammatory cytokine IFNγ. Preclinical studies have demonstrated that elevated IDO1 activity can foster a tumor promoting inflammatory milieu. Interest in the therapeutic potential of targeting IDO1 activity has led to the clinical testing of a small molecule inhibitor in combination with the anti-PD1 antibody pembrolizumab in a Phase 3 trial. Unfortunately, the anticipated benefit of including the IDO1 inhibitor was not observed. This failed trial has necessitated a reconsideration of how to effectively target IDO1. One novel approach is the emergent idea of an IDO1-directed vaccine, currently being developed by IO Biotech. Part 1 of the talk will cover our own preclinical work showing that specific IDO1-derived peptides can indeed elicit effective anti-tumor immune responses. Delving further into biological role of IDO1, it is now apparent that tolerization of T cell mediated responses may be just one aspect of a multifaceted involvement of IDO1 in tumor promotion. Part 2 will cover our recent findings showing IDO1 to also be an important driver of inflammatory neovascularization, a vital process in the development of tumors well as other diseases. IDO2 is a recently identified paralog of IDO1, and while much less is known about IDO2, recent work has revealed genetic interactions between the two enzymes as well as distinct biological roles. Part 3 will present results from retrospective clinical studies of pancreatic cancer patients that include the intriguing possibility that IDO2 genetic status may serve as a predictor of responsiveness to neoadjuvant radiotherapy. The new information accruing from these ongoing laboratory investigations into the biological functions of both IDO enzymes has revealed important new considerations for future therapeutic development.