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Postdoctoral Fellowship Positions (x2)

Molecular Microbiology and Cancer Research in the

Laboratory of Infection Oncology

sponsored by

FORSCHUNG GEGEN INFEKTION UND KREBS
FOCUS BIOMED Stiftung

Research topics:

(1) Bacterial infections of the hematopoietic system and their relationship to cancer pathogenesis

(2) Mutational signatures and causality of bacterial infections in human cancer development

We are looking for highly qualified early career researchers holding a Ph.D. and/or M.D. in Cellular Microbiology and Cancer Biology. The appointed candidates will be involved in cutting-edge studies on the role of microbes and microbiota in human pathology and the origin of cancer. The fellowships are sponsored by the Focus Biomed Foundation and will be available for the duration of two years with an option of prolongation. The fellowships are intended to promote young researchers and encourage them to establish their own research direction and ultimately attract their own funding resources.

The laboratory of Thomas F. Meyer (previously at the Max Planck Institute of Infection Biology, Berlin) has established a new laboratory at the University of Kiel in order to investigate the sequels of persistent microbial infections. The Laboratory of Infection Oncology laboratory is incorporated within a network of prominent institutions and consortia, emphasizing research on the role of microbiota in inflammation, immunity, inherited diseases and cancerogenesis. Furthermore, our lab offers a stimulating, ambitious and supportive research environment with strong national and international links. Its location is in the Institute of Clinical Molecular Biology (IKMB) at the University Hospital Schleswig-Holstein (UKSH) and the Carl Albrecht's University of Kiel (CAU).

If you show interest in the projects described below, please send an application and CV, including a summary of research experiences, a list of publications, and letters of reference, directly to Prof. Dr. Thomas F. Meyer at tfm(at)mpiib-berlin.mpg.de by January 9, 2022. Successful candidates are expected to contribute experimentally and intellectually to the project's performance and development.

Laboratory for Infection Oncology, Institute of Clinical Molecular Biology, Christian Albrechts University of Kiel
https://www.meyer-laboratory.de/
https://www.mpiib-berlin.mpg.de/1911472/molecular_biology

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(1) Bacterial infections of the hematopoietic system and their relationship to cancer pathogenesis

Several bacterial pathogens are capable of invasion and accommodation within host cells. We have previously investigated the underlying infection processes and the mechanisms of intracellular accommodation of various pathogens in epithelial cells. However, little is known about the intracellular accommodation of bacteria in professional phagocytes and circulating monocytes and their potential impact on their physiological behavior and fate. Intriguingly, infected circulating cells may acquire altered features, and there is a possibility that circulating infected cells could migrate to their original environment, the bone marrow. This notion

corresponds with previous observations, which indicate the presence of intracellular bacteria in the bone marrow stem cell compartment. Considering the potentially deleterious effects of certain bacteria on host cell genomes, e.g., via oxidative radicals and genotoxins, persistent intracellular bacterial infections could possibly lead to an accumulation of mutational defects, providing the basis for malignant transformation. In order to approach this hypothesis, we will investigate the prevalence and molecular and cellular features of hematopoietic cells infected with intracellular pathogens and characterize the effects on the hematopoietic stem cell compartment and the subsequent modified hematopoiesis and myelopoiesis. In the envisaged studies, emphasis will be placed on characterizing genetic and functional alterations that we have recently observed to occur during the course of infections of hematopoietic stem cells by certain pathogens.

(2) Mutational signatures of bacterial infections and the origin of human cancer development

Mounting evidence suggests a role for bacterial infections in human carcinogenesis. However, only a few cases could draw causality between infection and resulting cancer. One such example is the human papillomavirus (HPV), for which a telltale signature comprised by the deposition of viral transforming genes could be demonstrated in the genome of cervical cancer cells. In contrast to transforming viruses, bacteria do not usually deliver transforming DNA in infected cells, therefore, rendering any demonstration of causality more difficult. Knowledge of such causalities is, however, important as it opens an avenue of approaches to generate preventive means, such as vaccines.

For the first successful time, we have recently identified a highly specific signature of DNA damage caused by the bacterial genotoxin Colibactin; this signature is detected in the cancer genomes of a subset of human colon cancer patients. Moreover, we have identified a route of DNA damage resolution after colibactin action distinct from the signature-prone pathway, leading to signs of transformation in colon organoid cells. These data provide the basis for a comprehensive understanding of the impact of Colibactin-producing bacteria in driving human carcinogenesis.

Yet, several other infection-dependent pathways are known to lead to DNA damage and, thus, possibly, to specific mutational signatures connected with distinct human cancers. Such pathways could be driven not only by typical gentoxins but also by extrinsinc and intrinsic factors. This particular project aims to unravel the molecular and cellular features of such highly specific genotoxic pathways that drive human cancer development.