Hosting group information for applicants

Name of DKFZ research division/group:
T cell metabolism group, D140

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RESEARCH PROFILE AND PROJECT TOPICS:

Short title: Identification of new immune-metabolism checkpoints

Immune checkpoint molecules, such as PD-1, play an essential role in regulating T cell response. Dysregulation of the checkpoints may result in chronic infections, cancers and autoimmune disorders. Checkpoint blockade-based immunotherapies have been tested for treatment of chronic infections and cancers. The clinical trial results are very promising and have created unprecedented enthusiasm in immune checkpoint study. However, up till now, the currently available immunotherapies are only effective for some but not the majority of patients. There are several reasons, such as lack of T cell infiltration into tumors and metabolic suppression in the tumor microenvironment. Thus, identification of new checkpoint molecules, both immune checkpoints and metabolic checkpoints, is of great importance to design new immunotherapies for the treatment of infectious diseases and cancers. Our lab uses tumor models (implantation models and GEMMs), infection models and autoimmune models combined with chemical analysis such as mass spectrometry analysis to identify new checkpoint molecules (Wu et al Immunity 2019). Our lab has a panel of genetically engineered mouse strains deficient of these candidate checkpoint genes. We recruit postdoc fellows to identify new immune-metabolic checkpoints using these mice for the disease treatment.

First, the postdoc fellow will do the basic immune characterization of the checkpoint candidate gene (for ease of reference, let's name this gene ABC) knockout mice and wild-type control mice by flow cytometry. The T cell metabolism will be measured by a set of metabolic assays, which are already established in the lab. Second, the postdoc fellow will induce disease development (tumor, infection or autoimmunity models) in the ABC KO or wildtype mice and evaluate the disease development. The T cell phenotypes will be measured by flow cytometry, western blot, qPCR and other assays with the help of core

facilities, such as RNA-sequencing and mass spectrometry. Third, using the information gained from the first and second steps, the postdoc fellow will perform rescue experiments to dig out mechanisms behind the phenotypes. Finally, if patient samples with gene ABC mutation are available (it differs case by case), a proof-of-concept mini-study will be performed to test the conclusion drawn from the mouse study.