Interdisciplinary FIAS Colloquium

Thursday, November 20, 2008, 14:30
FIAS, Ruth-Moufang-Str. 1, 60438 Frankfurt am Main
Lecture Hall 0.100

Speaker: Prof. Dr. Dorothee von Laer, Georg Speyer Haus, Universität Frankfurt
Title: T cell homeostasis: keeping the norm

Abstract: T lymphocytes are the central cellular component of the immune system. On the one hand, they produce essential factors that stimulate and orchestrate the immune response to invading pathogens (CD4 T helper lymphocytes). In addition, a subpopulation of T lymphocytes kills abnormal host cells such as cancer or virus-infected cells (CD8 killer cells = cytotoxic T lymphocytes, CTL). During childhood and adolescence a repertoire of T lymphocytes is established that is capable of dealing with the majority of relevant potential pathogens. During this period, T lymphocytes originate from stem cells in the bone marrow, from where they migrate as immature thymic precursor lymphocytes to the thymus for further proliferation and differentiation. In the thymus, functional T lymphocytes are 'positively selected', while non-reactive as well as self-reactive T lymphocytes, i.e. T lymphocytes that falsely attack normal host cells, are eliminated ('negative selection'). Mature lymphocytes of the CD4 or CD8 type then immigrate from the thymus through the blood stream to the lymphatic tissues in lymph nodes, spleen, bone marrow and gut mucosa. In adulthood, thymic output seizes and mature T lymphocytes compensate their natural cell death by cell division. In both settings, during active thymopoiesis early in life as well as after thymic degeneration in the adult, the T lymphocyte pool is highly stable and subject to effective homeostatic control mechanisms. These bring the T cell pool rapidly back to the normal size after massive cell expansion during an immune response, as well as after T cell depletion following e.g. irradiation, cytotoxic drug treatment or certain viral infection. In addition to this quantitative homeostasis, the composition of T lymphocytes is carefully controlled. The T cell population consists of over $10^8$ different T cell clones, each specialized for recognition of a distinct molecular pattern derived from an intruding pathogen or a malignant host cell. This large set of T cell clones, the T cell repertoire, is largely preserved during life, despite regular perturbation of the clonal composition, e.g. by expansion of pathogen-specific clones during an infection. The homeostatic mechanisms that control numbers as well as the polyclonality of the T cell pool are highly relevant for understanding the pathogenesis of HIV-induced acquired immune deficiency (AIDS) and T lymphocyte malignancies.