Oncoviral infection and the innate immune responses

Prénom : Uzma
Nom : Hasan
Contact information Phone : 0033426235978
E-mail : uzma.hasan@inserm.fr

Area of Expertise

Key words : Innate immunity, pattern-recognition receptors, oncoviral infection, transformation

Viral infections are sensed by the innate immune system via several pattern-recognition receptors (PRR), including RIG-I like helicases, cytosolic DNA sensors, DNA-dependent activation of interferon (DAI), Absent in Melanoma 2 (AIM2) and the Toll like receptors family (TLRs). Recognition of viral infection by PRR leads to a pro-inflammatory and IFN antiviral immune response. How oncoviruses activate the PRR is poorly investigated as these viruses have development escape strategies to avoid recognition by the host immune system. Our area of expertise is to understand the mechanisms of onco-viral induced innate inflammation or deregulation of inflammation. We strongly believe this is important for both cell transformation and the response of the organism to the transformed cells; key events that lead to development of cancer.

Research interests

Epidemiological studies have determined that amongst all current human cancers known > 20% are attributed to infections. Human papillomavirus type 16 (HPV16), Epstein Barr (EBV) and Hepatitis B viruses (HBV) are DsDNA viruses associated to the development of cervical, non hodgkin's lymphoma and liver cancers, respectively. In most cases the host can control the infection by inducing an efficient immune response. However in certain cases these viruses persist and progress because they have developed several strategies to induce cellular transformation and to evade the immune system, two esssential factors in cancer development.

The first line of immune defense comes from a panel of innate immune sensors that can recognise pathogen associate molecular patterns (PAMPs) expressed by all infectious agents. The innate immune system senses pathogen components via Pathogen Regonition Receptors (PRR) family members called Toll Like Receptors (TLRs) and by cytosolic receptors. PRRs range from recognizing proteins and nucleic acid intermediates during viral replication. Our line of research focuses on PRR sensors that would recognize dsDNA oncoviral genomes i.e. TLR9 and AIM2. TLR9 recognises unmethlylated dsDNA sequences viruses in the form of CpG motifs and activates a strong type IFN I response, and AIM2 acts as part of the multidisicplinnary inflammasome cascade which leads to the production of IL-1B in response to viral infection. Furthermore a new line of investigation suggest they also control homeostatic events related to cellular proliferation in response to PAMPs and to endogenous danger signals released by infectious or non infectiousdisease that induces host tissue damage.

The main goal of our group is understand how oncoviruses that cause human cancer regulates the innate immune response, with particular focus on TLR9 and inflammasome responses.

Selected publications

-Zannetti, C., F. Bonnay, F. Takeshita, P. Parroche, C. Menetrier-Caux, M. Tommasino, U. A. Hasan. C/EBP delta and STAT-1 are required for TLR8 transcriptional activity. J Biol Chem. Epub, Sep 1, 2010

-Ikbal Fathallah, P. P., Henri Gruffat, Hanna Johansson, Jiping Yue, Evelyn Manet, Massimo Tommasino, Bakary S. Sylla, Uzma A Hasan. Epstein Barr Virus latent membrane protein 1 is a negative regulator of TLR9. J Immunol,. J Immunol Oct 27. 2010.

-Hasan, U. A., C. Caux, I. Perrot, A. C. Doffin, C. Menetrier-Caux, G. Trinchieri, M. Tommasino, and J. Vlach. 2007. Cell proliferation and survival induced by Toll-like receptors is antagonized by type I IFNs. Proc Natl Acad Sci U S A 104:8047-8052.

-Hasan, U. A., E. Bates, F. Takeshita, A. Biliato, R. Accardi, V. Bouvard, M. Mansour, I. Vincent, L. Gissmann, T. Iftner, M. Sideri, F. Stubenrauch, M. Tommasino. 2007. TLR9 expression and function is abolished by the cervical cancer-associated human papillomavirus type 16. J Immunol 178:3186-3197.