Mechanisms behind chronic infections (TB, HBV, HIV...): molecular and cellular mechanisms, evasion mechanisms, immunity,...

> Les Pensières Fondation Mérieux Conference Center Veyrier-du-Lac - France

> > 40NDATION

2-4 May 2016

Steering Committee:

- David Durantel
- Inca Kusters
- Jacques Louis
- Nicolas Manel
- Tom Ottenhoff
- Valentina Picot
- Cindy Grasso, meeting coordinator

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Background

When a pathogenic microorganism infects the human body, a dramatic activation of the innate and adaptive immune response occurs. In most cases, the interaction between the immune system and the pathogen result in clearance of the infection. However, some pathogens are capable of maintaining their presence, despite the severe attacks of the immune system, giving rise to persistent infection.

To remain and survive for a long period of time in its host, sometimes lifelong, the pathogens have evolved a range of elaborate immune-evasion strategies which may involve (1) hiding from the immune system, (2) interfering with the function of the immune system and/or (3) exploiting the immune system for their own benefit.

Many herpes viruses hide from the immune system by entering into a state known as latency in which the virus does not replicate. No viral proteins or peptides are presented on the surface of the infected cells and the cells cannot be eliminated. Other viruses, like VZV, invade neurons, which carry very little MHC I class molecules making it hard for the CD8 T cells to recognize infected cells.

Certain pathogens interfere with the cells of the immune system to block or dampen its actions. There are similarities in the immuno-modulatory mechanisms used by viruses and bacteria that have to overcome the same host immune system. Indeed, both classes of pathogens can inhibit complement, inhibit cytokines, interfere with TLRs, and block acquired immunity allowing long-term survival.

Pathogens can also exploit immune cells for their own benefit. This mechanism is demonstrated by HIV that replicates in CD4 T cells, EBV in B cells, and Dengue virus that infects Langerhans cells. Another example is M. tuberculosis which is taken up by macrophages but prevents the fusion of the phagosome with the lysosome, protecting itself from the bactericidal actions of the lysosomal contents.

This workshop will focus on immune-evasion strategies employed by three pathogens that are responsible for a very high medical burden, namely, tuberculosis, HIV and Hepatitis B infection. We will discuss the current understanding how these pathogens employ evasion mechanisms, and how to translate this knowledge to the development and rational design of new medicines and therapeutic vaccines.



Scientific programme

Monday 2 May 2016

16:30 - 17h00	Registration	
17:15 - 17:30	Welcome address	Fondation Mérieux

Session 1

Biology of infections with HBV, HIV, and TB			
Chair: Jacques Louis			
17:30 - 17:50	Biology of HBV infection	Maura Dandri	
17:50 - 18:05	Discussion		
18:05 - 18:25	The basics of HIV infection, reservoir establishment and the dynamics of immune responses	Asier Saez-Cirion	
18:25 - 18:40	Discussion		
19:15	Welcome dinner		

Tuesday 3 May 2016

Session 1 Continued

08:30 - 08:50	Biology of TB infection	Tom Ottenhoff
08:50 - 09:05	Discussion	

Session 2

Early host/pathogen interplay: impact on the outcome of infection			
Chair: Inca Kusters			
09:05 - 09:25	SERINCs: novel restriction factors counteracted by HIV Nef	Heinrich Gottlinger	
09:25 - 09:40	Discussion		
09:40 - 09:55	The regulatory HBx protein contributes to evasion from intrinsic antiviral response	Christine Neuveut	
09:55 - 10:10	Discussion		
10:10 - 10:30	Coffee break		
10:30 - 10:50	Early events in TB infection	Olivier Neyrolles	
10:50 - 11:05	Discussion		

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Scientific programme

Session 3

Determinant of persistence in chronic infections			
Chair: David Durantel			
11:05 - 11:25	How are newly integrated human retroviruses silenced?	Paul Lehner	
11:25 - 11:40	Discussion		
11:40 - 12:00	cccDNA biology and strategy to silence or degrade it	Massimo Levrero	
12:00 - 12:15	Discussion		
12:15 - 12:35	Latent TB, a spectral entity	JoAnne Flynn	
12:35 - 12:50	Discussion		
13:00 - 14:30	Lunch		

Session 4

Molecular mechanism of innate immune evasion			
Chair: Nicolas Manel			
14:30 - 14:50	Subcellular mechanisms of innate immunity evasion in HBV infection	David Durantel	
14:50 - 15:05	Discussion		
15:05 - 15:25	Restriction by SAMHD1 limits cGAS/STING- dependent innate and adaptive immune responses to HIV-1	Jan Rehwinkel	
15:25 - 15:40	Discussion		
15:40 - 16:00	Intracellular DNA sensing mechanisms during infection with Mtb	Andrea Ablasser	
16:00 - 16:15	Discussion		
16:15 - 16:40	Coffee break		

Session 5

Molecular mechanism of adaptive immune evasion			
Chair: Tom Ottenhoff			
16:40 - 17:00	Induction of protective innate immune responses: lessons learned from HIV-2	Nicolas Manel	
17:00 - 17:15	Discussion		
17:15 - 17:35	Metabolic regulation of immunity in chronic HBV infection	Laura Pallet	
17:35 - 17:50	Discussion		

Scientific programme

17:50 - 18:10	TB adaptive immune evasion	Simone Joosten
18:10 - 18:25	Discussion	
19:30	Dinner	

Wednesday 4 May 2016

Session 6

Immune cell exhaustion in chronic infections and strategies to revert it			
Chair: Tom Ottenhoff			
08:30 - 08:50	CD8-T cells and natural HIV control: emerging clues to improve function of exhausted cells	Asier Saez-Cirion	
08:50 - 09:05	Discussion		
09:05 - 09:25	HBV and T cell Exhaustion	Gabrielle Missale	
09:25 - 09:40	Discussion		
09:40 - 10:00	The manifold nature of myeloid cells in TB	Anca Dorhoi	
10:00 - 10:15	Discussion		
10:15 - 10:45	Coffee break		

Session 7

Immunopathogenesis: mechanisms and therapeutic options			
Chair: Olivier Neyrolles			
10:45 - 11:05	HBV Immunopathogenesis	Robert Thimme	
11:05 - 11:20	Discussion		
11:20 - 11:40	Metabolite clusters in acute and chronic infection	Hendrik Streeck	
11:40 - 11:55	Discussion		
11:55 - 12:15	NN cell and viral dynamics within lymph nodes during pathogenic and non pathogenic SIV infection	Michaela Muller- Trutwin	
12:15 - 12:30	Discussion		
12:30 - 14:00	Lunch		
14:00 - 14:20	Sensing of HIV-1 entry triggers a type I interferon response in primary macrophages	Philippe Benaroch	
14:20 - 14:35	Discussion		
14:35 - 14:50	Understanding and Intervening in HIV Associated Tuberculosis	Robert Wilkinson	
14:50 - 15:05	Discussion		
15:05 - 15:15	Concluding remarks and end of the meeting		