SCIENCES & BIOENGINEERING SCIENCES

The Research Group

Cellular and Molecular Immunology (CMIM)

has the honor to invite you to the public defense of the PhD thesis of

Chloé ABELS

to obtain the degree of Doctor of Bio-Engineering Sciences

Title of the PhD thesis:

Unraveling the role of liver-associated myeloid cells in sterile inflammation and infection

Promotors:
Prof. Dr. ir. Jo Van Ginderachter
Prof. Dr. Em. Patrick De Baetselier
Dr. Alain Beschin

The defence will take place on
Tuesday September 26 2017 at 17.00h

in Congrescentrum U-Residence, green hall at the Campus Humanities, Sciences and Engineering of the Vrije Universiteit Brussel, Pleinlaan 2 - 1050 Elsene, and will be followed by a reception.

Members of the jury:

Prof. Dr. Daniel Charlier (chairman)
Prof. Dr. Carl de Trez (secretary)
Prof. Dr. Eline Menu (fac. GF)
Prof. Dr. Eric Muraille (ULB)
Prof. Dr. Frank Tacke
(University Hospital Aachen, D.)

Curriculum vitae

Chloé Abels acquired here master in the Bio-engineering sciences – medical biotechnology at the VUB in June 2012. Subsequently she started a PhD in immunology, where she researched the role of liver associated myeloid cells in liver inflammation and repair. This research led to 1 co-first author publication and 7 co-author publications in peer-reviewed international journals. She also presented her work at numerous occasions at international congresses. She guided and trained 3 master thesis students.
Her research was financed by the VUB and het Fonds voor Wetenschappelijk onderzoek.

Abstract of the PhD research

The liver is a central organ in the metabolism of nutrients, immune surveillance and toxin clearance. As such, liver dysfunction caused by toxic substances and infections can disturb important physiological processes and ultimately result in death if left untreated. Myeloid cells are vital in the immune response against threats and are key players to maintain and restore tissue integrity. Therefore, efforts to unravel the respective functions of myeloid cell subsets in liver inflammation could provide original concepts to restore homeostasis in this vital organ in a therapeutic setting. In this context, this PhD investigated the role of 2 myeloid cell populations during sterile and pathogen induced liver inflammation: Patrolling monocytes (PM) and liver resident macrophages, the Kupffer cells (KCs).

First, we demonstrated that PMs perform a crucial protective role during APAP induced liver inflammation (AILI), the leading cause of acute liver injury in the western hemisphere. PMs stimulated the differentiation of hepato-destructive inflammatory monocytes (IM) into macrophages (Mf) with hepato-regenerative functions, which are essential to repair the damaged liver. This differentiation was mediated through the M-CSF receptor. Promoting this Mf differentiation through PMs might therefore be a promising new therapeutic target for the treatment of AILI.

Secondly, using a KC-depleter transgenic mouse generated by our lab (MCI, CMIM, Vrije Universiteit Brussel), Clec4f-DTR mice, we unveiled a protective role of KCs during *Listeria monocytogenes* infection. This food borne intracellular bacterium affects primarily immuno-compromised persons and pregnant women and can result in death and abortion. Mice lacking KCs had a decreased protective innate monocyte-derived dendritic cell response due to a blockage in differentiation from IM. Moreover, the absence of KCs resulted in inadequate adaptive CD8 T cell immune response, coinciding with reduced DC-poietin production, a drop of the pre-cDC population and a reduction in conventional DC expansion. Consequently, these altered immune responses lead to an uncontrolled bacterial expansion pointing out the KCs as key initiators of immune responses during experimental listeriosis.
Finally, by addressing the fate of KCs in infected mice, we evidenced that IM engraft the liver and become KCs upon resolution of the infection.