SCIENCES & BIOENGINEERING SCIENCES

The Research Group

Cellular and Molecular Immunology

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

Ir. Jiri KEIRSSE

to obtain the degree of Doctor of Bioengineering Sciences

Title of the PhD thesis:

Functional role of tumour-associated dendritic cells and liver Kupffer cells during solid tumour progression and liver metastasis, respectively.

Promotors:

Prof. Dr. ir. Jo Van Ginderachter
Prof. Dr. em. Patrick De Baetselier

The defence will take place on

Wednesday 30 August 2017 at 17:00h

in the U-Residence (Green Room) 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. ir. Eveline Peeters (chairman)
Prof. Dr. Han Remaut (secretary)
Prof. Dr. Karine Breckpot
Prof. Dr. Bart Lambrecht (VIB)
Prof. Dr. Jolanda de Vries (Univ. Nijmegen, Nl.)

Curriculum vitae

Jiri Keirsse (27/05/1989, Jette, Belgium) obtained his Master in Bio-engineering Sciences – Medical Biotechnology at VUB in 2012. He went on to pursue a PhD in Immunology, investigating the role of myeloid immune cells in multiple cancer models.
His PhD research has led to 3 first-author and an additional 10 co-author publications in international peer-reviewed journals and has been presented at international conferences. During his PhD, Jiri was responsible for the organization and teaching of immunology practical courses. His research was funded by both VUB and the Flemish League against Cancer (VLK).

Abstract of the PhD research

Various steady state and inflamed tissues have been shown to contain heterogeneous populations of both resident and infiltrating dendritic cells (DC) and macrophages. Importantly, these types of immune cells play important functional roles during solid tumour progression and subsequent metastatic spread.

In this respect, we identified functionally and developmentally distinct tumour-associated DC (TADC) subsets, consisting of pre-cDC-derived conventional DC1 (cDC1), cDC2 and monocyte-derived DC (Mo-DC). We demonstrate that multiple mouse tumours, as well as human tumours, harbour ontogenically discrete TADC subsets. Monocyte-derived TADCs are prominent in tumour antigen uptake, but lack strong T-cell stimulatory capacity and perform immunosuppressive functions. Conversely, tumour-derived cDC1 and cDC2 show lymph node migratory potential and T-cell stimulatory capacity, thus inducing strong anti-tumoural immune responses. Intriguingly, prophylactic vaccination with either of the cDC subsets induces different types of anti-tumor immunity. Consequently, the distinct vaccination strategies have therapeutic potential in distinct cancer types.

Importantly, the majority of cancer-associated death can be attributed to the metastatic spread of disseminated cancer cells to vital organs, such as the liver. Due to their exposed position inside the liver sinusoids, liver-resident macrophages, Kupffer cells (KC), are hypothesized to form the first line of defence against circulating cancer cells. Using KC-specific tools, such as the newly generated KC-depleter transgenic mouse strain (Clec4f-YFP-DTR), we demonstrated that KC play an anti-metastatic role in early liver metastasis of both gastrointestinal and extra-gastrointestinal cancers. Interestingly, KC displayed the most adept cancer cell phagocytic capacity among liver phagocytes. Additionally, natural killer (NK) cells also proved crucial for the control of liver metastasis.
The importance of KC in reducing liver metastatic spread may have significant implications for the use of novel cancer therapeutics targeting pro-tumoural tumour-associated macrophages.