Joint Symposium 12
Translational Molecular Imaging & Therapy + Inflammation & Infection + Oncology & Theranostics Committee / European Society of Molecular Imaging (ESMI) / World Molecular Imaging Society (WMIS)
Wednesday, June 29, 2022 / 08:00-09:30 / Channel 4

Session Title
Translating Inflammation Imaging into Immunooncology - Focus on Macrophages

Chairperson
Anne Roivainen (Turku, Finland)

Programme

08:00 - 08:22	**Eric Aarntzen** (Nijmegen, Netherlands): Same Target, Different Story - Inflammation and Cancer
08:22 - 08:44	**Johanna Joyce** (Lausanne, Switzerland): Yin and Yang - Macrophages in the TME
08:44 - 09:06	**Suzanne Lapi** (Birmingham, United States of America / WMIS): Tracers for Imaging Macrophages
09:06 - 09:27	**Nick Devoogdt** (Brussels, Belgium / ESMI): Moving Macrophage Imaging Towards the Clinic
09:27 - 09:30	Session Summary by Chairperson

Educational Objectives
1. Understand the close links between inflammation and the role of infiltrating immune cells in tumours
2. Get a comprehensive overview over the multiple roles of macrophages and their polarization in the tumour microenvironment (TME)
3. Comprehend the molecular basis and predictive value of the currently investigated preclinical and clinical approaches to image macrophages and/or their polarization in the TME

Summary
The tumor microenvironment (TME) can best be described as a dynamically interacting assembly of tumor cells and normal cell types such as stromal cells, endothelial cells and numerous innate and adaptive immune cell types, supported by the non-cellular components of the extracellular matrix as well as blood and lymphatic vessel networks [1, 2]. By nature of the presence and dynamic interaction of various immune cell populations in the TME, it bears close resemblance to inflammation – and these similarities, involving the complex signaling networks, by which tumor cells and distinct immune cell populations interact to ultimately support tumor progression and actively promote malignancy, will be summarized in the first talk of this session.

Among the components of the TME, myeloid cells such as monocytes, granulocytes and macrophages represent the largest population of leucocytes found in tumors, constituting up to 50% of the tumor mass [3]. Upon their homing, macrophages are "educated" by a number of factors released by the TME, differentiating to tumor associated macrophages (TAMs), with potent multifaceted roles in regulating cancer progression and modulating the response to therapeutic intervention [4, 5]. Based on their biological functions, they are classified into two polarization phenotypes: classically activated, proinflammatory M1 macrophages and alternatively activated, anti-inflammatory M2 macrophages.

Clinically, high densities of total TAMs (M1 *and* M2) have often been found to be associated with more advanced tumor stages and a negative impact on patients' overall survival in a broad spectrum of solid cancers. However, the M1/M2 ratio has been recently established as the biologically more relevant indicator for prognosticating cancer [5], with a higher M1/M2 ratio being a reliable positive prognostic factor for a more favorable outcome in various cancer types [6-8]. While the second talk of this session focuses on the multifaceted biology of macrophages in the TME and the current intensely investigated experimental therapies for macrophage "reeducation" (from M2 to M1 macrophages), the third presentation will give an overview over the currently available imaging probes for the visualization and quantification of macrophages and their polarization in the TME.

Since there is ample evidence that TAMs are preferentially M2-polarized (roughly 70% non-small cell lung cancer [9]), M2-targeted imaging approaches have advanced furthest into clinical application. Thus, the fourth presentation will provide a synopsis of the different steps leading from the preclinical development to the clinical translation of a CD206 (macrophage mannose receptor) targeted scFv-based tracer for the quantification of M2-like macrophages.

References

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2. *Kowal J, et al., Immunotherapy.* ***2019****; 11: 677-89.*
3. *Larionova I, et al., Front Oncol.* ***2020****; 10: 566511.*
4. *Roszer T, Mediators Inflamm.* ***2015****; 2015: 816460.*
5. *Jayasingam SD, et al., Front Oncol.* ***2019****; 9: 1512.*
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7. *Hwang I, et al., J Transl Med.* ***2020****; 18: 443.*
8. *Vankerckhoven A, et al., Cells.* ***2020****; 9.*
9. *Ma J, et al., BMC Cancer.* ***2010****; 10: 112.*

Key Words
Tumour microenvironment, TME, macrophages, M1, M2, CD206, imaging, PET