

Towards in vivo imaging of immune cell dynamics using X-ray fluorescence

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Despite of ongoing advances in diagnosis and therapy, diseases related to cellular malfunction such as immune system dysregulation and cancer are among the leading causes of death worldwide. Current medical imaging methods based on ionizing radiation are either able to generate morphological information with high spatial resolution (e.g. CT) or functional information with low resolution (e.g. PET) [1]. In contrast, light microscopy-based approaches are limited to preclinical models due to the need for genetically encoded fluorescent labels [2].

X-ray fluorescence imaging of functionalized nanoparticles combines the visualization of biochemical and pathological processes in vivo with a potentially high spatial resolution. However, despite the long measurement times and comparatively high doses, the sensitivities are currently still too low due to the low signal-to-noise ratio due to Compton scattering. The use of gold as a nanoparticle-based contrast agent in X-ray fluorescence imaging has proven to be advantageous both from a technical perspective due to its photoelectric properties and from a molecular point of view through specific functionalization options [3].

The immediate, pre-clinical goal is to improve the X-ray fluorescence imaging with gold nanoparticles in small animals (e.g. mice) with further diagnostic and therapeutic development for humans in the long-term perspective.

This talk highlights various research tasks related to spatial and temporal cell dynamics of the immune systems at the Otto von Guericke University, especially associated with the Health Campus Immunology, Infectiology and Inflammation (GC-I3) and the Research Center Dynamic Systems: Systems Engineering (CDS). In particular, we aim at employing mathematical modelling and correlative intravital imaging approaches in order to establish the use of gold nanoparticles for non-invasive analysis of the dynamics of nanoparticle-loaded immune cells within the living tissue.

This research should critically contribute to the understanding of the dynamics of immune cellular processes during tumour formation, infection or autoimmunity, as well as innovative diagnostic and therapeutic options.

[1] Larsson J, Vogt C, Twengström W, Toprak M, Dzieran J, Henriksson M, Hertz, H (2018). High-spatial-resolution X-ray fluorescence tomography with spectrally matched nanoparticles. *Physics in Medicine and Biology*. 63. 10.1088/1361-6560/aad51e.

[2] Handschuh J, Amore J, Müller AJ (2020) From the Cradle to the Grave of an Infection: Host-Pathogen Interaction Visualized by Intravital Microscopy. *Cytometry A*. 2020 97 10.1002/cyto.a.23938.

[3] Grüner F, Blumendorf F, Schmutzler O, Staufer T, Bradbury M, Wiesner U, Rosentreter T, Loers G, Lutz D, Richter B, Fischer M, Schulz F, Steiner S, Warmer M, Burkhardt A, Meents A, Kupinski M, Hoeschen C (2018). Localising functionalised gold-nanoparticles in murine spinal cords by X-ray fluorescence imaging and background-reduction through spatial filtering for human-sized objects. *Scientific Reports*. 8. 10.1038/s41598-018-34925-3.

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