

PhD Thesis Defense KYRA BORGMAN 'A Journey from the Membrane into the Nucleus of Human Dendritic Cells'

KYRA BORGMAN

October 26, 2018

Friday October 26, 11:00. ICFO Auditorium

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Single Molecule Biophotonics

ICFO-The Institute of Photonic Sciences

Discrimination between foreign and potentially harmful antigens, and the body?s own tissue is one of the most crucial first steps that lays at the basis of a proper immune response. Immunoreceptors are cell membrane embedded molecules that aid immune cells in identifying and interacting with its environment. Because of their key importance, they are therefore a frequent subject of research in immunology. Over the past two decades, novel microscopy techniques and biophysical tools have been developed and exploited to directly

visualize molecular events in immune cells with unprecedented spatial and temporal resolution. In **Part I** of the presentation, I will discuss several of these advanced imaging techniques with a specific focus on their advantages in the newly emerging field of nano-immunology. In **Part II**, I will address the subcellular organization of the immunoreceptor MerTK in human dendritic cells (DCs). By exploiting super-resolution STED nanoscopy, we discovered that MerTK organizes in small nanoclusters on the plasma membrane of tolerogenic DCs, where MerTK is highly expressed. Moreover, I will show that even though MerTK is a membrane receptor, it is also found at very high levels in the nucleus of DCs. To place this finding in the context of immunity, we established a direct correlation between DC differentiation and the amount of MerTK found in the nucleus. We enquired the route by which MerTK translocate to the nucleus, and dissected some of the main molecular factors involved in promoting this translocation. In a first attempt to identify its nuclear function, we additionally mapped the spatial relationship between MerTK and chromatin with nanometre accuracy using super-resolution STORM nanoscopy, in single intact DCs nuclei at different stages of their differentiation. Taken together, our work suggests that MerTK plays a physiological role related to differentiation in the nucleus of human DCs, possibly by acting as a transcription factor. This work paves the way for a more thorough understanding of the molecular mechanism of action of MerTK in particular, and the functional role of membrane receptors in the nucleus in general.

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