Single-Cell and Cluster-Level Investigations of Mammalian Cells via Atomic Force Microscopy and Correlative Techniques

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Atomic force microscopy (AFM) is an extremely versatile technique enabling the study of different aspects of biological systems with ultra-high resolution. Conventionally, AFM has been used to assess the morphology of living biological systems and to monitor the evolution of their mechanical properties at the nanoscale, which provides information on the cellular structure and stiffness even in living systems. Further applications of AFM for biological matter involve the combination of ultrastructural information with conventional or fluorescence optical microscopy. Correlative analyses via combining advanced AFM with high-magnification optical and fluorescence microscopes allow for a more comprehensive understanding of the cellular status.

In this presentation we will show how an AFM coupled with a Nikon fluorescence microscope can perform studies on living biological systems such as erythrocytes and neuroblastomas. By using conventional optical and fluorescence images, we identify cells that are most interesting for our studies. We use the AFM to determine their morphology and mechanical properties at ultra-resolution level, monitoring the response of the cells to environmental conditions such as pharmacological stimuli or starvation. Also, we prove how AFM cantilevers can be used as nanomechanical sensors to provide complementary information on the cellular behavior in different environments.

The combined results on neuroblastomas represent the first steps of the COMA-SAN project (COMplexity Analysis in the Simplest Alive Neuronal network), in which we investigate the communication-mediated group behavior of these cells. Overall, our study opens a path to better understand the interactions between cells and to evidence the complexity of group dynamics in cells.

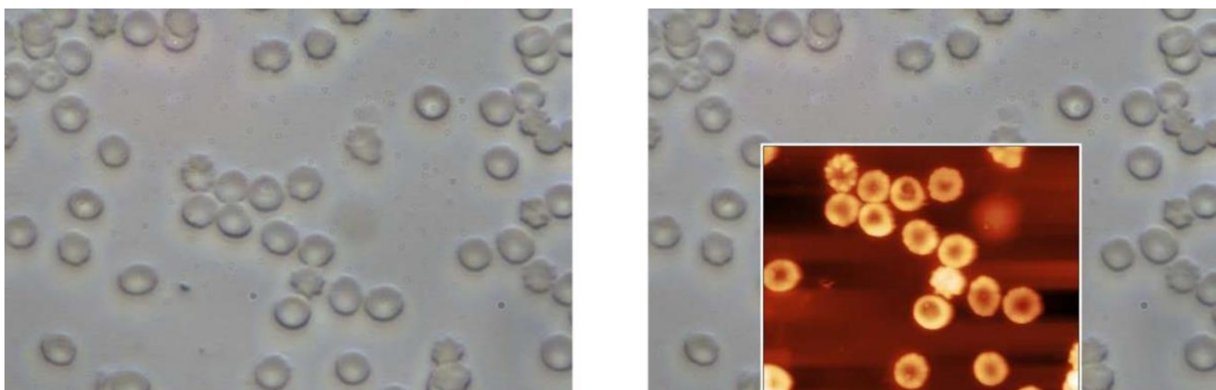

Fig. 1 Correlative Optical imaging/AFM morphology on favism red blood cells

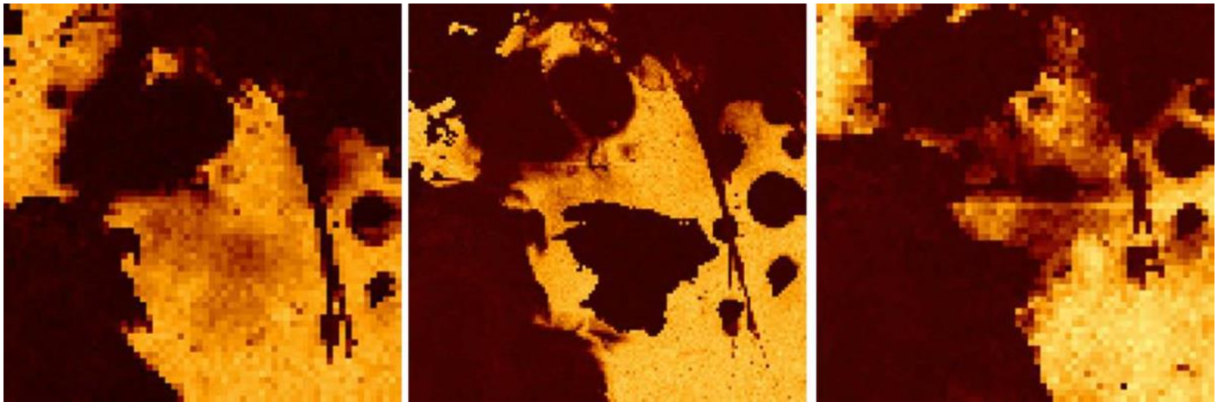

Fig. 2: Evolution of living neuroblastomas exposed to pharmaceutical stimulation

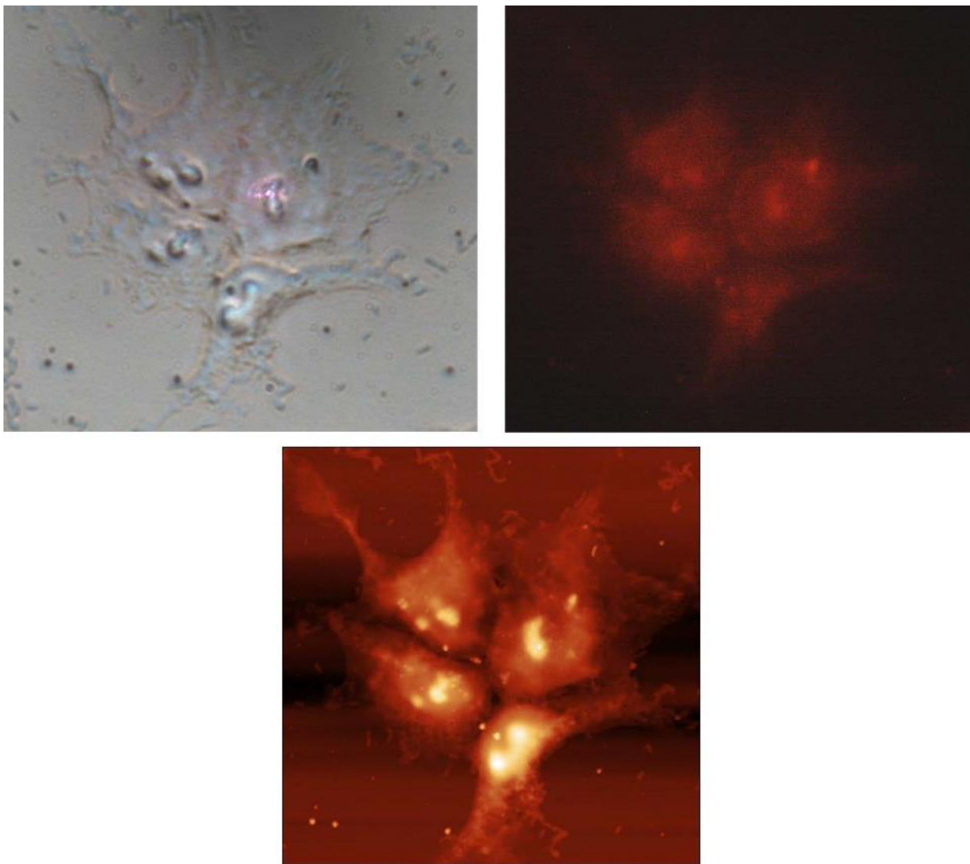

Fig. 3 Correlative Optical imaging/Fluorescence imaging/AFM morphology on HeLa cells