Towards a Systematic Characterization of NF-κB Dynamics

NF-κB is a family of transcription factors (the dimer p50-p65 being the most abundant) that coordinately control hundreds of genes involved in many steps of inflammatory processes, from microbial killing to cancer. Single-cell imaging experiments have previously shown that when inflammatory stimuli hit the cell surface, NF-κB undergoes several cycles of nucleus-to-cytoplasm translocations, resulting in oscillations of nuclear NF-κB concentration. The role of such oscillations, though, is still largely unknown. In order to have a deeper insight on NF-κB dynamics, we have performed in vivosingle-cell imaging of NF-κB dynamics in GFP-p65 knock-in cells when stimulated with concentrations of the cytokine TNF-a related with different inflammatory conditions. By using a precise imaging quantification method we have been able to collect data of the NF-κB translocation dynamics for hundreds of cells. Our experiments show that NF-κB dynamics in cells under the same conditions is very heterogeneous and that oscillatory behaviour is a common feature, but not the unique possible one. In particular, we observe that a fraction of the cells does not present oscillations and that NF-κB can be spontaneously activated in absence of external stimulations. We attempt to unveil the origin of these novel features by making use of mathematical models involving the main components of the NF-κB pathway.

Thursday, 6th of December at 3:00pm.
Room SV1717A

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