

SEMINAR

Prof. Amnon Buxboim

The Hebrew University of Jerusalem

“How does ageing-related stiffening of brain tissue microenvironments affect the regenerative capacity of CNS progenitor cells”

12th June 2023

15:00 – 16:00

Venue: Conference Hall, Center for Biomedical Technology (CTB) Universidad Politécnica de Madrid (UPM), Campus Montegancedo M-40 km. 38, 28223 Pozuelo de Alarcón, Madrid.

How to arrive: <http://www.ctb.upm.es/contact/>

Zoom link: <https://upm.zoom.us/j/88633567364>

Speaker: Prof. Amnon Buxboim

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Abstract: Ageing-related stiffening of neuronal microenvironments in the brain generates potent signals that attenuate the regenerative capacity of oligodendrocyte progenitor cells (OPCs) to proliferate and differentiate. We find that ageing drives substantial remodeling of the nuclear lamina in OPCs, in which A-type lamin levels increase and B-type lamin expression decreases. Owing to the ubiquitous role of lamins in anchoring mostly heterochromatic sections at the nuclear envelope known as lamina associated domains (LAD's), we hypothesized that ageing effects are mediated via altered genomic organization and regulation. In this study, we isolate OPCs from neonate and aged rats and study the effects of ageing-related tissue stiffening by designing and optimizing hydrogel-based matrices that mimic the extracellular elasticity and adhesion signals of neonate and aged microenvironments. Indeed, the differences in cellular morphologies and lamina compositions between neonate and aged cells are recapitulated by matrix elasticity. To characterize differences in the structural organization of the nuclear lamina, we combine high-resolution optical and electron microscopies and perform micropipette aspiration based rheology to define the viscoelastic properties of OPC nuclei within intact cells. LAD mapping is performed using optimized CUT&RUN assays that target endogenous lamin-B1, thus avoiding the effects of ectopic expression of nuclear envelope proteins, which is a prerequisite by standard methodologies. Downstream effects on transcriptional regulation are studied via single-cell RNA sequencing (scRNA-seq), thus providing insight into cell-to-cell variations. In summary, our work-in-progress highlights the mechanobiological component of ageing on progenitor cells of the CNS that can stimulate potential therapeutic strategies.

Dr. Amnon Buxboim: is a professor of biology and bioengineering at the Hebrew University of Jerusalem, Israel. Trained as a biophysicist, he opened the Buxboim Lab for Mechanobiology in 2013. Dr. Buxboim research aims at understanding how physical and mechanical inputs combine with parallel signaling pathways to direct cell-fate decision-making processes. The Buxboim Lab studies oocyte maturation, preimplantation embryo development, stromal bone marrow immunomodulation, and CNS stem/progenitor cell ageing. Dr. Buxboim also studies mechanisms of nuclear mechanotransduction, as mediated via nuclear lamins and associated nuclear envelope proteins. The Buxboim Lab combines established assays, advanced computational tools, newly designed device-based technologies, and integrates single-cell level genomics with micro-rheological measurements. Based on his research findings, Dr. Buxboim develops assisted reproductive technologies to advance and improve medical care.