Oren Ram PhD.

I joined the faculty of the Hebrew University in 2016. My lab uses epigenomics measurements of cells such as ChIP-seq and bisulfite-seq, existing single-cell technologies and our in-house technology developments, as well as bioinformatics to uncover fundamental principles of pluripotency, early differentiation, and cancer progression. Using sequential ChIP-bisulfite-sequencing, we observed global changes in CpG methylation in enhancer regions that regulate genes critical for differentiation (PLoS Genetics, 2021). Our CloneSeq technology combines clonal expansion inside 3D hydrogel spheres and droplet-based RNA-seq.

Using 3' digital RNA-seq, we showed that clonal cells maintain cell states and share similar transcriptional profiles. We demonstrated how clonal expansion within 3D soft microenvironments supports cellular stemness of ESCs and improves epigenetic reprogramming efficiency of mouse embryonic fibroblasts. We also showed that ESC differentiation decisions are made early following Oct4 downregulation and are kept during early clonal expansion (Developmental Cell, 2021; cover).

In another manuscript, we reveal a novel link between the cell-cycle state of pluripotent ESCs and differentiation potential. We demonstrate that G2/M ESCs are able to differentiate into extraembryonic endoderm cells (XEN), whereas G1 ESCs contribute only to the epiblast. Our data support a model in which Esrrb upregulation during ESCs G2/M phase and its binding to XEN-poised enhancers are key in promoting XEN differentiation (BioRxiv: doi: https://doi.org/10.1101/2020.08.03.234112, 2021). Together with Amnon Buxboim's lab, we identified distinct MSC subpopulations that are characterized by cellular mechanosensitivity, differentiation capacity, and proliferation activity. In particular, we identified tropomyosin-1 as a potent mechanosensor that mediates matrix cues that define cell-to-cell variability with implications for MSC-based therapy (PNAS, 2021). In an ongoing collaboration with Prof. Lukatsky (Department of Chemistry, Ben-Gurion University of the Negev), we are studying the molecular design principles responsible for specificity of transcription factor binding to DNA. We have found that certain short repetitive DNA sequence patterns substantially influence binding preferences and differentiation outcomes during early differentiation (Biophysical Journal, 2020; cover).