Immunology Seminar

Building Polymorphonuclear Cells

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Date: **April 9th** (Wed), 2025 Time: 16:00–17:30 (Talk; 1h, Q&A; 30min)
Venue: Seminar Room 134, 1st floor, No.1 Bldg., LiMe Inst. (Bldg. 31) (医生研1号館(構内マップ31番);1F 会議室) The seminar will be held on site only

It is established that swift migration through tight interstitial tissue spaces by an armamentarium of cell types is conducted by malleable nuclear structures. However, molecular programs that instruct nuclear shapes remain to be revealed. Here I will present our recent observations indicate that loss of loop extrusion rapidly converts macrophage/granulocyte progenitors into cells that display a myriad of nuclear shapes, including horse-shoe, ring and hyper-segmented nuclear morphologies. The conversion of mononuclear to polymorphonuclear cells was accompanied by massive chromatin remodeling at enhancers that harbored cis-elements associated with neutrophil-specific transcription factors. Halting loop extrusion acutely activated the expression of genes encoding for factors that instruct neutrophil development, activation, migration, extravascular migration, inflammation and respiratory bursts to neutralize phagocytosed bacteria. Additionally, cessation of loop extrusion in bone marrow hematopoietic progenitors enriched for cells that express a macrophage transcription signature. These data indicate that loop extrusion programs regulate nuclear shape and that halting loop extrusion acutely activates a neutrophil specific gene program. We propose that modulating loop extrusion programs facilitates the migration of cells through densely populated tissues by instructing the assembly of distinct nuclear shapes whereas aberrant loop extrusion programs instruct alterations in nuclear morphologies to promote metastatic cell migration, aging, cardiovascular disease and beyond.

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2. Murre C., et al. Constructing polymorphonuclear cells: chromatin folding shapes nuclear morphology. ***Trends Immunol.*** **2024** Nov;45(11):851-860. doi:10.1016/j.it.2024.09.012. Epub 2024 Oct 21.
3. Barajas-Mora EM, et al. Enhancer-instructed epigenetic landscape and chromatin compartmentalization dictate a primary antibody repertoire protective against specific bacterial pathogen. ***Nature Immunology***, **2023** Vol.24(2), 320-336
4. Zhou Y, Murre C. Bursty gene expression and mRNA decay pathways orchestrates B cell activation. ***Science Advance*** **. 2021** vol 7(49):eabm0819
5. Zhu Y, et al. Calcium signaling instructs NIPBL recruitment at active enhancers and promoters via distinct mechanisms to reconstruct genome compartmentalization. ***Genes and Development.*** **2021** Jan 1; 35(1-2):65-81
6. Denholts M., et al. Upon microbial challenge, human neutrophils undergo rapid changes in nuclear architecture and chromatin folding to orchestrate an immediate inflammatory gene program. ***Genes and Development.*** **2020** Feb 1; 34(3-4):149-165
7. Isoda T, et al. Non-coding transcription instructs chromatin folding and compartmentalization to dictate enhancer-promoter communication and T cell fate. ***Cell.*** **2017** Sep 21;171(1):103-119.e18.
8. Lucas JS, et al. 3D trajectories adopted by coding and regulatory DNA elements: first-passage times fro genomic interactions. ***Cell.*** **2014** Jul 17;158(2):339-352

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