# Cologne Seminar Series on Ageing


## Duygu Ucar

The Jackson Laboratory for Genomic Medicine, Farmington, CT


**Wednesday, 4 December, 2019, at 16:00**

CECAD Research Center
Joseph-Stelzmann-Str. 26
Lecture hall, ground floor

Host: Andreas Beyer (CECAD)
Dario Valenzano (MPI Age)

**Scientific Background:**

2013-Present Assistant Prof, The Jackson Laboratory for Genomic Medicine, Farmington, CT
2010-2013 Post-doctoral fellow, Genetics Department, Stanford University, Stanford, CA
2009-2010 NSF Computing Innovation fellow, Internal Medicine, University of Iowa, Iowa City, IA
2003-2009 Graduate Student, Department of Computer Science, Ohio State University, Columbus, OH
2008 Guest Researcher, Technical University of Denmark, Copenhagen, Denmark
2006 Research Intern, Bristol Myers Squibb, Hopewell, NJ

# Chromatin accessibility signatures of immune system aging

**About Prof Ucar's talk:**


Aging is linked to deficiencies in immune responses and increased systemic inflammation. To unravel regulatory programs behind these changes, we profiled peripheral blood mononuclear cells (PBMCs) from young and old individuals (n=77) using ATAC-seq and RNA-seq technologies and analyzed these data *via* systems immunology tools. First, we described an epigenomic signature of immune system aging, with simultaneous systematic chromatin closing at promoters and enhancers associated with T cell signaling. This signature was primarily borne by memory CD8+ T cells, which exhibited an aging-related loss in IL7R activity and IL7 responsiveness. More recently to uncover the impact of sex on immune system aging, we studied PBMCs from 194 healthy adults (100 women, 94 men) ranging from 22-93 years old using ATAC-seq, RNA-seq, and flow cytometry technologies. These data revealed a shared epigenomic signature of aging between sexes composed of declines in naïve T cell functions and increases in monocyte and cytotoxic cell functions. Despite similarities, these changes were greater in magnitude in men. Additionally, we uncovered male-specific decreases in expression/accessibility of B-cell associated loci. Trajectory analyses revealed that age-related epigenomic changes were more abrupt at two timepoints in the human lifespan. The first timepoint was similar between sexes in terms of timing (early forties) and magnitude. In contrast, the latter timepoint was earlier (~5 years) and more pronounced in men (mid-sixties versus late-sixties). Unexpectedly, differences between men and women PBMCs increased with aging, with men having higher monocyte and pro-inflammatory activity and lower B/T cell activity compared to women after 65 years of age. Our study uncovered which immune cell functions and molecules are differentially affected with age between sexes, including the differences in timing and magnitude of changes, which is an important step towards precision medicine in older adults.


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