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Single-cell dissection of immune system aging and acute myeloid leukemia

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Curriculum Vitae

Onur was born in Soma, Turkey, on July 8th, 1994. He attended primary school in Kastamonu and later ranked 266th among more than 900,000 students in the nationwide high school entrance examination in 2008, earning admission to A.U. Fen Lisesi, a private science high school in Ankara.

In 2012, he ranked 1,044th nationwide in the YGS, taken by more than 1.8 million candidates, and was admitted to the Electrical and Electronics Engineering program at Bilkent University in Ankara. He later pursued a Master's degree in Computer Science at Bilkent University, where his research focused on predicting cancer biomarkers from H-NMR spectroscopy data acquired during brain surgery. This project marked his first introduction to bioinformatics.

Following his Master's studies, he moved to the United States to join The Jackson Laboratory, where he worked on deciphering the molecular mechanisms of immune system aging. During this time, he contributed to multiple publications and gained extensive experience in single-cell transcriptomics and epigenomics.

Driven by a desire to deepen his expertise in computational biology, Onur then relocated to the Netherlands to pursue a PhD at Leiden University Medical Center. His doctoral research focused on characterizing hematopoietic aging and acute myeloid leukemia using single-cell multi-omics technologies, integrating multiple omics modalities with functional data. His work aimed to uncover the transcriptional and epigenetic mechanisms governing immune system aging and malignant transformation, with the broader goal of improving precision medicine strategies for acute myeloid leukemia.

Currently, Onur works as a postdoctoral researcher in the group of Dr. Erik van den Akker at Leiden University Medical Center. He leverages his expertise in myeloid malignancies and machine learning to investigate the cellular and molecular mechanisms of lymphoid cancers, with the aim of identifying novel biomarkers and therapeutic targets.

Acknowledgments

A PhD is a war with many mental battles. You win some and lose some. In the end, what matters is winning the war, and that is impossible without the help of many people.

Starting with my supervisors: first, you need one with limitless optimism and a desire to learn anything new (Erik), one with an ever-positive attitude and seemingly unlimited revision capabilities (Marieke), and one highly rational thinker who can effortlessly play the devil's advocate when you really need it (Marcel). This combination makes you revise things many times, but it also prepares you to fight any battle. Thank you all for trusting in me; it was a pleasure to work with you. I would also like to thank other great commanders, Duygu, Eline, Marian, Ahmed, and Hendrik for always being kind and understanding.

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Ramin, you joined the campaign late, but you made my days better and funnier. I envy your enthusiasm for *every* single story you tell. Alper, you are a rock-star researcher. Jeppe, you are truly one of a kind. I do not remember a single time you did not make me laugh; thank you. Dani, you are one of the highlights of my PhD. We have a word in Turkish that does not have an exact one-word equivalent in English: *dost*. You are one. Emily, I hope you get your PhD as soon as possible and make him your paranymp one more time.

Anneciğim ve babacığım, sizden daha iyi insanlar hayal edemiyorum. Verdiğiniz tüm emekler ve fedakarlıklarınız için teşekkür ederim. Sizi çok seviyorum, iyi ki varsınız ve sizin evladınızım. Bu tez size armağanımdır.

My dear mother and father, I cannot imagine better people than you. Thank you for all your efforts and sacrifices. I love you very much; I am so grateful that you are in my life and that I am your child. This thesis is my gift to you.

Acknowledgments

Veni, vidi, vici.

List of Publications

1. **Karakaslar, E. O.**, Argiro, E. M., Struckman, N. E., Shirali, R. H. Z., Severens, J. F. *et al.* Resolving inter- and intra-patient heterogeneity in *NPM1*-mutated AML at single-cell resolution. *Leukemia* (2025).
2. Tajer, P., **Karakaslar, E. O.**, Canté-Barrett, K., Naber, B. A. E., Vloemans, S. A. *et al.* Utilizing epigenetic regulators to improve HSC-based lentiviral gene therapy. *Blood Adv.* **8**, 4936–4947 (2024).
3. Severens, J. F., **Karakaslar, E. O.**, van der Reijden, B. A., Sánchez-López, E. *et al.* Mapping AML heterogeneity–multi-cohort transcriptomic analysis identifies novel clusters and divergent ex-vivo drug responses. *Leukemia* **38**, 751–761 (2024).
4. Ravichandran, S.*, Erra-Diaz, F*, **Karakaslar, E. O.***, Marches, R. *et al.* Distinct baseline immune characteristics associated with responses to conjugated and unconjugated pneumococcal polysaccharide vaccines in older adults. *Nat. Immunol.* **25**, 316–329 (2024).
5. **Karakaslar, E. O.**, Severens, J. F., Sánchez-López, E., van Veelen, P. A., Zlei, M. *et al.* A transcriptomic based deconvolution framework for assessing differentiation stages and drug responses of AML. *NPJ Precis. Oncol.* **8**, 105 (2024).
6. **Karakaslar, E. O.***, Katiyar, N.*, Hasham, M., Youn, A., Sharma, S., Chung, C. *et al.* Transcriptional activation of Jun and Fos members of the AP-1 complex is a conserved signature of immune aging that contributes to inflammaging. *Aging Cell* **22**, e13792 (2023).
7. Cheong, J. G., Ravishankar, A., Sharma, S., Parkhurst, C. N., Grassmann, S. A., Wingert, C. K., Laurent, P., Ma, S., Paddock, L., Miranda, I. C., **Karakaslar, E. O.** *et al.* Epigenetic memory of coronavirus infection in innate immune cells and their progenitors. *Cell* **186**, 3882–3902.e24 (2023).
8. **Karakaslar, E. O.** & Ucar, D. cinaR: A comprehensive R package for the differential analyses and functional interpretation of ATAC-seq data. *bioRxiv* 2021.03.05.434143 (2021).
9. Cakmakci, D., **Karakaslar, E. O.**, Ruhland, E., Chenard, M. P., Proust, F., Piotto, M. *et al.* Machine learning assisted intraoperative assessment of brain tumor margins using HRMAS NMR spectroscopy. *PLoS Comput. Biol.* **16**, e1008184 (2020).
10. **Karakaslar, E. O.**, Coskun, B., Outilaft, H., Namer, I. J. & Cicek, A. E. Predicting carbon spectrum in heteronuclear single quantum coherence spectroscopy for online feedback during surgery. *IEEE/ACM Trans. Comput. Biol. Bioinform.* **17**, 533–544 (2019).