Alişya Anlaş
Postdoctoral Fellow
University of Pennsylvania

**Matrix stiffness suppresses growth, induces chromosome mis-segregation and increases genomic variation in cancer spheroids**

**Monday August 28th**
Lecture 4:00-5:00 p.m.  |  Physics/Astronomy
Auditorium (PAA) A110
Reception 5:00-6:00 p.m.  |  Benson Hall Lobby

**Bio**

Bio Alişya Anlaş is a postdoctoral researcher with Prof. Dennis Discher at the University of Pennsylvania. As a chemical and biological engineer, she uses engineered tissue culture models to uncover how the mechanical properties of the tissue microenvironment regulate hallmarks of cancer such as sustained proliferation, survival, genomic instability, and immune evasion. Her doctoral studies with Celeste Nelson revealed that autophagy is a mechanically-regulated cell survival mechanism that contributes to chemoresistance in breast cancer. Her postdoctoral work investigates how microenvironmental stiffness regulates cell division errors including chromosome missegregation. As a pilot grant awardee at Penn’s NSF Center for Engineering Mechanobiology, she also studies the impact of confined migration on macrophage-based immunotherapies. Alişya is committed to increasing public engagement with science, enhancing inclusivity, and expanding access to STEM education. She has taught college algebra with the Prison Teaching Initiative (PTI) at Princeton and has coordinated several community outreach events with Princeton Citizen Scientists, YWCA’s Breast Cancer Resource Center, and PTI including “The Prison and the Academy”, “The Day of Action”, and the workshop series, “Science and Intersectionality”.

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Abstract

Matrix stiffness suppresses growth, induces chromosome mis-segregation and increases genomic variation in cancer spheroids

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Genomic instability, the inability of a cell to pass on its genetic information accurately, is a hallmark of cancer. During cancer progression, the extracellular matrix stiffens to mechanically confine cancer cells, however it is not known whether such changes in the microenvironment contribute to chromosome loss. Here, we employed engineered tissue culture systems and cancer cell lines carrying chromosome reporters generated using the CRISPR/Cas9 system to investigate whether matrix stiffness regulates chromosome loss (Figure 1A). We cultured lung cancer spheroids in viscous methylcellulose or in agarose hydrogels of varying elastic moduli (Figure 1B-C, Figure 2A), then assessed cell division and chromosome loss. Our findings indicate that stiff microenvironments suppress cell division (Figure 2B) but enhance chromosomal aberrations such as micronuclei (Figure 2C-D) and chromosome loss (Figure 2E-F). We also show that stiff microenvironments induce genomic variation and increase tumor heterogeneity, which are known to reduce sensitivity to cancer therapeutics. In addition, our data suggest that cancer cells exhibiting chromosome loss are viable and can pass on these chromosomal aberrations to future generations (Figure 2G). Overall, our findings highlight that the mechanical properties of the tumor microenvironment regulate genomic instability - a major limiting factor in the treatment of solid tumors. Uncovering and targeting pathways that lead to chromosomal instability could help reduce resistance to therapy and improve patient outcomes.