

Meet Three Cutting-Edge Scientists Awarded Quantitative Biology Fellowships

The Damon Runyon Cancer Research Foundation highlights exceptional early-career scientists making a difference in cancer research.

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Damon Runyon has announced its 2023 Quantitative Biology Fellows, three exceptional early-career scientists who are applying the tools of computational science to generate and interpret cancer research data at extraordinary scale and resolution. Whether constructing synthetic synapses to study cellular communication or engineering tumor models to predict treatment response, their projects seek to extend the boundaries of what is possible in cancer research by approaching fundamental biology questions from a new direction.

Each postdoctoral scientist selected for this unique three-year award will receive independent funding (\$240,000 total) to train under the joint mentorship of an established computational scientist and a cancer biologist. The grant was created to encourage quantitative scientists (from fields such as mathematics, physics, computer science, and engineering) to pursue careers in cancer research. By investing in research that combines techniques from “wet” and “dry” labs, Damon Runyon aims to highlight the importance of these specially trained scientists in the era of precision medicine.

“Nowadays, we’re not even limited by computational power but by our creativity in how we apply these frameworks to research questions,” explains 2022 Quantitative Biology Fellow Tal Einav, PhD. “The fun part is seeing ideas that have been around for a while come into contact with newer technologies, like machine learning—what emerges are questions that people have not asked before and which are going to change the way we understand the field.”

2023 Quantitative Biology Fellows

Nicholas C. Lammers, PhD, with mentors Cole Trapnell, PhD, and David Kimelman, PhD, at University of Washington, Seattle

In both embryonic development and disease, the same genetic mutation can lead to highly variable outcomes in different individuals. Dr. Lammers aims to shed light on the drivers of this nongenetic variability using the developing zebrafish embryo as a model system. By combining

fluorescence microscopy and single-cell sequencing, he will test whether subtle differences in gene expression within individual cells can explain why some embryos with a given genetic mutation survive to adulthood, while others perish within the first 24 hours of their development. His findings will provide a quantitative foundation for understanding the genetic and molecular basis of cancer outcomes in human patients where, for instance, tumors with the same underlying mutations often exhibit dramatically different disease courses.

Computational Methodology:

Dr. Lammers will train Variational Autoencoders to learn low-dimensional latent space representations of whole-embryo transcriptomes and grayscale images depicting embryonic morphology. He will then train a third neural network to translate from transcriptional latent space to morphological latent space. Together, these three networks will comprise a new computational method, morphSeq, that takes single-cell transcriptomes of mutant and wildtype embryos as input and produces predictions for corresponding embryo morphologies as its output.

Youngmu (Nick) Shin, PhD, with mentors Wendell A. Lim, PhD, and Rohit V. Pappu, PhD (Washington University, St. Louis), at University of California, San Francisco

Cells in our body communicate with each other in a highly selective manner. These cell-cell interactions form the basis of numerous physiological functions, such as neuronal wiring and immune recognition. Dr. Shin plans to explore the general principles of cell-cell communication by constructing a synthetic synapse and studying its organization and functional diversity. His findings will elucidate the mechanisms that organize cell-cell interfaces involved in immune cell recognition of cancer and in the cell-type transitions associated with cancer and metastasis. This work will also provide a platform for engineering highly customized cell-cell interfaces, which may prove useful in engineering immune cell therapeutics.

Computational Methodology:

This project employs the stickers-and-spacers model adapted from polymer physics. Macromolecules such as proteins and nucleic acids are described as a sequence of attractive domains called “stickers” and flexible, non-interacting domains called “spacers.” Dr. Shin will use his lab’s Monte Carlo simulation engine LaSSI (Lattice simulation engine for Sticker and Spacer Interactions) to calculate the average interactions between macromolecules and analyze their mesoscopic organization and phase properties.

Carolina Trenado-Yuste, PhD, with mentors Celeste M. Nelson, PhD, and Ned S. Wingreen, PhD, at Princeton University, Princeton

Breast cancer is the most frequent cancer in women and the second-leading cause of cancer deaths in women worldwide. Triple-negative breast cancer is among the most aggressive subtypes; its name refers to the fact that it lacks all three primary markers of breast cancer, making it particularly challenging to detect and treat. Although our ability to detect early-stage breast cancer has improved substantially over the past few decades, anticipating whether and

how fast a tumor will progress to metastatic disease remains challenging. Dr. Trenado-Yuste aims to improve our ability to predict a tumor's disease course and response to therapy by creating a new framework of biomathematical models and experimentally engineered tumors, which may aid in prognostication and decrease cancer-related deaths.

Computational Methodology:

Experimental research in cancer biology also drives a need for new computational models. This project focuses on mathematical modeling, with an emphasis on developing agent-based and pharmacokinetic models, to help clarify how tumor spheroids progress and respond to drug treatments. The importance and innovation of the proposed theoretical and computational methods lie in their potential to identify the optimal combinations of personalized treatment schedules for individual patients.

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