

Damon Runyon Cancer Research Foundation Awards Quantitative Biology Fellowships to Four Cutting-Edge Scientists

The award program was created to encourage quantitative scientists to pursue careers in cancer research.

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Damon Runyon has announced its 2024 Quantitative Biology Fellows, four exceptional early-career scientists who are bringing cutting-edge computational tools to bear on some of the most important questions in cancer biology. From the packaging of DNA to mechanisms of chemotherapy resistance, their projects aim to shed light on these fundamental questions through large-scale data collection, mathematical modeling, and quantitative analysis.

“In the five years since we named the first class of Quantitative Biology Fellows, it has only become more evident that these scientists bring fresh perspectives and creative approaches to cancer research in addition to their computational skills,” said Yung S. Lie, PhD, President and CEO of the Damon Runyon Cancer Research Foundation.

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 award program 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.

2024 Quantitative Biology Fellows

Isabella N. Grabski, PhD, with mentors David A. Knowles, PhD, and Rahul Satija, PhD, at New York Genome Center, New York

Only 3% of cancer drugs in clinical trials ultimately receive FDA approval, compared to 15-33% of drugs for other types of diseases. Recent studies have suggested that many drugs being explored

for cancer treatment do not actually target their intended molecule in the cell. This has important implications for efficacy and safety and could be a key contributor to the low FDA approval rate. Dr. Grabski has created a novel experimental and computational framework to identify drug mechanisms of action at molecular resolution by leveraging CRISPR-based technologies. With this framework, she hopes to more precisely identify how a given cancer drug functions in the cell. This could serve as a powerful tool for preclinical evaluation and even potential discovery of new cancer therapeutics.

Computational Methodology:

Dr. Grabski's project aims to identify drug targets by modeling drug transcriptional response as a sum of genetic perturbation responses. She will perform this deconvolution in two steps. First, she will use a multi-condition latent factor model to produce denoised estimates of perturbation effects. Second, she will leverage sparse Bayesian regression techniques to map drug responses to these perturbation effects, in a way that can summarize complex patterns of uncertainty among related perturbations.

Jeremy A. Owen, PhD, with mentors Tom W. Muir, PhD, and Ned S. Wingreen, PhD, at Princeton University, Princeton

Chromatin remodelers are complex protein machines responsible for packaging DNA and regulating gene expression. Their dysfunction is strongly implicated in cancer. For example, certain types of sarcoma and ovarian cancer are driven by mutations in a chromatin remodeler called BAF. Combining experiments with theoretical work, Dr. Owen's research aims to understand how remodelers recognize their target sites in the cell's nucleus. By expanding our understanding of chromatin remodeling, the findings of this research will provide the groundwork for more effective cancer treatments—suggesting how drugs might target chromatin remodelers—as well as enhance our understanding of how existing drugs that target remodeler-adjacent mechanisms might work.

Computational Methodology:

A central aim of this project is the development of new, quantitative models to explain the behavior of chromatin remodelers seen in experiments. Dr. Owen will achieve this by successive rounds of passing between theory and experiments repeatedly—measuring, modeling, then measuring again. For comparison to experiments, model predictions will be extracted computationally (e.g., numerically solving ODEs, or by exact stochastic simulation using Gillespie's algorithm) or analytically (e.g., by the King-Altman procedure, and variants), as appropriate.

Ahmed Roman, PhD [Leslie Cohen Seidman Fellow], with mentors Eliezer M. Van Allen, MD, and Andrew J. Aguirre, MD, PhD, at Dana-Farber Cancer Institute, Boston

Dr. Roman aims to develop mathematical tools to determine which genes are associated with resistance to chemotherapy. Given genomic information from pancreatic cancer patients whose tumors are resistant or sensitive to chemotherapy, this tool will identify genes that distinguish the

two populations. These genes can then be explored as potential drug targets that can sensitize chemotherapy-resistant tumors to treatment.

Computational Methodology:

Dr. Roman's research relies on the use of information theory to improve the ability of neural networks to find genes whose RNA expression distinguishes chemotherapy-sensitive from resistant patients. Another research direction is to leverage prior knowledge, accumulated over decades about gene-gene interactions in the laboratory, to inform the architecture of the neural networks or use large foundation models training on millions of cells to study cancer.

Jakob Wirbel, PhD, with mentors Ami S. Bhatt, MD, PhD, and Michael C. Bassik, PhD, at Stanford University School of Medicine, Stanford

Certain cancers of the blood are treated by transplanting stem cells that can regenerate all kinds of blood cells from healthy donors. Even though this procedure has the potential to cure the cancer, common complications such as bloodstream infections or graft-versus-host disease (when the body rejects the donor cells) can lead to major side effects and even death. There is substantial evidence that these complications are linked to the microbes residing in the gut, collectively termed the gut microbiome, but the exact mechanism for this interaction is unknown. To address this knowledge gap, Dr. Wirbel will study how the genomes of gut microbes change over time in a large cohort of blood stem cell transplantation patients, using modern DNA sequencing techniques and developing novel analyses pipelines. He will then investigate whether the genes that are changing in microbial genomes might influence the human immune system and thereby contribute to these clinical complications.

Computational Methodology:

Dr. Wirbel plans to develop a computational tool for the reference-free analysis of microbial genomes over time based on long-read sequencing. By comparing newly assembled genomes across different sampling time points, the tool will detect structural variation (deletion or insertions into the genome) in microbial genomes. Additionally, genomic inversions ("flipping" of the orientation of DNA) and genes associated with these changes will also be identified.

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