

## **TITLE: Investigating inflammatory components across multiple diseases**

·Estimated hours per week:**5-10 hours**

·Department:**CSAIL**

·**Required Skills/Classes:** coding, general understanding of molecular biology and genetics

·**Preferred Skills/Classes:** bioinformatics, ML, single-cell omics, disease genetics, network biology

### **Description:**

The MIT CompBio lab ([compbio.mit.edu](http://compbio.mit.edu)) headed by Prof. Manolis Kellis is looking for talented UROP students for computational projects to investigate inflammatory components across multiple diseases. Expertise in programming, data analysis, and machine learning, as well as motivation to understand diseases genetics will be great factors for a successful project. Our team is truly interdisciplinary, working at the interface of computational biology and high-throughput genomics. We seek to systematically understand genetic and epigenetic regulation at single cell resolution, in order to dissect the mechanisms underlying human disease genetics, and to enable development of new therapeutics in the context of precision medicine. With 93% of genetic associations from genome-wide association studies (GWAS) lying in non-coding regions, a big focus of our lab is on developing new statistical/ML methods and experimental techniques for systematically mapping gene-regulatory regions, linking them to their target genes, inferring causality through mediation analysis of intermediate phenotypes, and testing our predictions in cellular and organoid systems. In our previous work, we created the most comprehensive map of the human epigenome by large-scale data generation and integration, and the most comprehensive maps of evolutionary constraint in the human genome. We used these to gain new insights about many diseases, including Alzheimer's Disease, Obesity, Bipolar disorder, Schizophrenia, Immune Disorders, and Cancer. Our results have often challenged the way we see common disorders: for example, we found that genetic variants contributing to Alzheimer's act and Bipolar disorder through immune processes, rather than neuronal processes; for obesity, we found that the strongest genetic association acts via a master switch controlling energy storage vs. energy dissipation in our fat cells, rather than through the control of appetite in the brain, and we were able to manipulate these circuits to reverse the phenotypic signatures of obesity in human cells and in mice. We have recently generated some of the largest collections of single-cell datasets of human disease, across Alzheimer's, Schizophrenia, Bipolar disorder, Down Syndrome, Heart Disease, Obesity,

Exercise, and other brain, metabolic, and cardiac tissues and disorders. We seek computational UROP students to help analyze these datasets and previous epigenomic datasets in close collaboration with researchers in our team in the context of a truly interdisciplinary team, where highly-talented computational postdocs and students work side-by-side with each other, and with leading experimental scientists to design the next generation of statistical techniques, computational tools, experimental datasets, integrative models, and validation experiments. You'll be working with state-of-the-art tools for analyzing single-cell genomics and epigenomics datasets, developing new methods for their integration, and working with other scientists in the group to understand their biological implications.

To get an overview of our recent results in these areas, here's a recent talk by Professor Kellis: <https://www.youtube.com/watch?v=MEFQvHYLWB4>

and the corresponding slides:

[https://www.dropbox.com/s/nfkq5g2pd1cl14d/679\\_UCL\\_MedTech\\_ManolisKellis.pdf?dl=0](https://www.dropbox.com/s/nfkq5g2pd1cl14d/679_UCL_MedTech_ManolisKellis.pdf?dl=0)

and a link to papers by our group: <http://compbio.mit.edu/papers.html>

To learn more about our ongoing activities, you can find a list of our current NIH grants and Industry funds here: <http://compbio.mit.edu/funding.html>

Please complete the form and instructions here: <http://compbio.mit.edu/positions.html> and email [kellis-admin@mit.edu](mailto:kellis-admin@mit.edu) with a copy of your CV and a few introductory paragraphs on your background, interests, and goals.

Looking forward to meeting you soon! Manolis