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**NYU Bioinformatics and Genetics Team Maps An Immune Cell's Development**

Each cell in the human body contains the same genomic code, yet cells use this information in different ways to develop into various cell types. The process, known as differentiation, is perhaps most evident in the immune system, where a cell can become a B cell and produce antibodies or differentiate into one of several types of T cells. Some of those ward off disease by promoting inflammation and some alleviate inflammation. Each cell’s fate depends on a complex interplay between genes and the factors that regulate them.

A concerted effort among geneticists, immunologists, and computational biologists at New York University together with colleagues from around the world recently generated one of the largest maps ever of such a complex regulatory network. Using techniques reminiscent of the recently published [ENCODE](http://www.genome.gov/10005107) project, the study combined gene expression profiles, RNA sequencing, and chromatin immunoprecipitation ([ChIP](http://en.wikipedia.org/wiki/Chromatin_immunoprecipitation)) data to answer a specific question: How do T cells differentiate into a type of cell known as Th17?

According to NYU bioinformaticist and study author [Richard Bonneau](http://biology.as.nyu.edu/object/RichardBonneau), the beauty of the research, which was [published recently in Cell](http://www.cell.com/abstract/S0092-8674%2812%2901123-3), is that it addresses key biological questions about cell differentiation while also providing medically useful information.

When immune cells differentiate into Th17 cells, they promote inflammation. That can be good for fighting off a bacterial infection or a virus. But if cells differentiate when they aren’t supposed to, autoimmune disorders such as Crohn’s disease and multiple sclerosis can develop. Teasing out the chain of events that occurs when immune cells differentiate and pinpointing the genes and proteins that are unique to certain types of immune cells could help identify drug targets for some of these immune diseases, the scientists hope.

Previous studies investigated differentiation in Th17 cells, but focused on only one or two genes and discovered approximately 50 regulatory interactions. Bonneau and his colleague have discovered over 2,400 more interactions and mapped them onto a complex web that demonstrates how genes and proteins interact during the differentiation of Th17 cells. Some interactions were already known to be important; others were previously unknown and offer new clues to the biology of cell differentiation.

As with all large-scale genomic studies, this one produced a vast amount of data that must now be sifted through to separate valuable from useless information. [Aviv Madar](https://files.nyu.edu/am2654/public/), a post-doctoral fellow in Bonneau’s lab who was involved in much of the study’s computational work, explains that comparing the results of different experimental methods filters out noise and false hits while providing more confidence that positive hits are real. A gene that shows up in ChIP, microarray, and RNA sequencing results, for instance, is more likely involved in the network than a gene that shows up in only one of the assays. But integrating data produced by different techniques remains a computational challenge, he says.

Bonneau says that understanding the pathways involved in genetic regulation is key to future genetics and bioengineering research. He sees regulatory network maps like the one his team has produced becoming invaluable resources. For example, if a scientist is interested in a particular transcription factor, she could search established networks to identify candidate targets or regulators.

Further down the road, these maps could also help researchers and even the average curious citizen scientist to interpret genome sequencing results. While many single nucleotide polymorphisms—including those delivered to individuals who pay to have their own genomes sequenced—have been linked with specific diseases, there is often no mechanistic insight that explains how or why. Linking SNP data to a regulatory network could explain why that aberration might lead to disease.