Scientists uncover how immune cells sense who they are

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Scientists at the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), a part of the National Institutes of Health, have demonstrated that DNA previously thought to be "junk" plays a critical role in immune system response. The team's findings were published in *Cell* and may lead to the identification of new therapeutic targets for the treatment of immune-related disorders.

There are 3.2 billion DNA base pairs in the human genome, but only 2 percent are in the regions we call genes, which provide the code for proteins. Up until recently, the role of the rest of the genome was mostly unknown and overlooked.

NIH researchers used whole genome DNA sequencing technology that allowed them to "see" which part of the genomic DNA is actively engaged in supporting various cellular functions. The investigators found that members of the signal transducers and activators of transcription (STAT) protein family play a major role in shaping the identity of the immune system's T helper cells. Importantly, when studying the impact of "junk" DNA, they saw that this greater than expected role was made possible by the STAT proteins' regulation of enhancer activity. Enhancers are short DNA regions that are outside the genes, but regulate gene transcription. While enhancers do not directly code for proteins, they regulate the protein production process.

This work provides an example of how the cellular environment helps determine cell identity. Specifically, the research team demonstrated that

STAT proteins act as cellular environmental sensors that, by regulating enhancers residing in the "junk" region of the genome, determine what subtype a T cell becomes. The present work should help clarify how these switches may relate to genetic risk of immune diseases.

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