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# Study of MicroRNA Helps Scientists Unlock Secrets of Immune Cells

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(PhysOrg.com) -- With the rapid and continuous advances in biotechnology, scientists are better able to see inside the nucleus of a cell to unlock the secrets of its genetic material. However, what happens outside of the nucleus has, in many ways, remained a mystery.

Now, researchers with the National Institutes of Health are closer to understanding how activity outside of the nucleus determines a cell's behavior. They looked at mouse immune cells and examined the types, amount, and activity of microRNAs, genetic components that help regulate the production of proteins. Their study provides a map to the variety of microRNAs contained within mouse immune cells and reveals the complexity of cellular protein regulation. The study appears online in the journal *Immunity*.

An organism is made up of cells containing genetic material in the form of deoxyribonucleic acid (DNA) residing within the nucleus. An organism's entire collection of DNA is called its genome and consists of genes, short segments of DNA that code for proteins, and many long segments of DNA that do not contain genes. While each cell contains the entire genome, not all of a cell's genes are making proteins all of the time. Which genes are turned on and which are turned off, and when, determine the behavior of a cell, such as the type of cell it becomes, where it goes, and what it does.

"A plethora of cellular functions, ranging from development, differentiation, metabolism, and host defense, are impacted by protein

levels," said Rafael Casellas, Ph.D., the study's principal investigator from the Genomics and Immunity Group of the NIH's National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS). " We were interested in discovering how microRNAs contribute to the regulation of these functions."

A cell makes proteins through a process called transcription, in which genes are copied from DNA into messenger ribonucleic acid (RNA), which travels from the nucleus into the body of the cell. Not all RNA transcribed from DNA are messenger RNA, however. There are many other forms of RNA that do not code for proteins. MicroRNAs (miRNAs), for example, are small strands of RNA that modulate the production of proteins from messenger RNA, thereby helping to regulate protein levels in the cell. Previous studies have shown that cells are very sensitive to fluctuations in miRNA levels, which require tight control in order to regulate protein activity effectively.

In the current study, the NIH scientists used a new microsequencing technology to comprehensively identify all of the different miRNAs existing in mouse immune cells. In addition to increasing the number of known miRNAs, the scientists also discovered several cellular mechanisms that regulate miRNA abundance. The study found that some miRNA constructs exist in a dormant state within the nucleus until they receive signals from the epigenome to become active. The epigenome regulates transcription and comprises all of the non-genetic material in the nucleus. Other miRNAs, the researchers determined, are not hampered by these epigenetic mechanisms and are controlled simply through transcription. However, for some of these miRNAs, abundance depends upon the amount of target messenger RNA available in the cell.

According to NIAMS Director Stephen I. Katz, M.D., Ph.D., "The data generated from this study represent a useful tool for immunologists and cell biologists to use for future studies on functional aspects of the

immune system and basic miRNA biology."

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