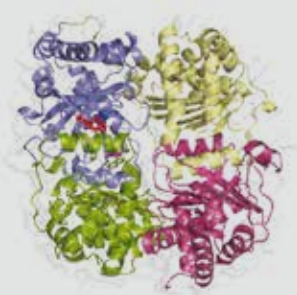

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Where cures begin.

Alan Saghatelian

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The Problem

Peptides and metabolites are two important classes of biological molecules, referred to as small molecules. Changes in the levels of these small molecules are known to cause prevalent diseases. For example, lower levels of the peptide insulin lead to diabetes, while higher levels of the metabolite cholesterol cause heart disease. There are thousands of small molecules in our bodies, so how do we find these disease-causing peptides and metabolites? Thanks to advances in a technology called mass spectrometry, scientists can now measure peptides and metabolites in a biological sample (cell, tissue or organism). By analyzing disease samples, researchers can identify those molecules that are changing during a disease. Just as the identification of insulin led to a new treatment of diabetes, these discoveries of disease-associated peptides and metabolites will likely pave the way for a new generation of therapeutics to improve human health.

The Approach

Alan Saghatelian's work touches on virtually all areas of human biology. He has developed and applied new mass spectrometry strategies that measure changes in small molecules overlooked by traditional biological methods, which typically focus on DNA, RNA and proteins. In particular, Saghatelian focuses on metabolites and peptides, which have been understudied because of technical challenges in their detection. Exploring this uncharted territory has enabled Saghatelian to make important discoveries, including the recent finding of a novel human lipid that reduces inflammation and reverses the symptoms of diabetes. Saghatelian hopes to use the knowledge gained from his lab's work to accelerate the development of new medicines in the area of diabetes. He is also collaborating with many laboratories at Salk to understand the roles of peptides and metabolites in cancer, neurodegenerative and immunologic disorders.

The Innovations and Discoveries

- By discovering how a gene associated with type 2 diabetes controls insulin levels, Saghatelian and colleagues developed a drug-like compound called 6bK—which improves blood glucose in mice—as a potentially new anti-diabetic therapeutic.
- With collaborators, Saghatelian analyzed changes in metabolite levels in mice that are resistant to diabetes, which led to the discovery of a lipid, called FAHFA. FAHFAs are also found in humans. Administration of these lipids to mice reduces inflammation and improves the symptoms associated with diabetes, making these interesting therapeutic candidates and revealing a new disease-associated metabolite.
- Saghatelian also identified a previously unknown cluster of human genes that produce peptides that control fundamental cellular processes, such as DNA repair, highlighting their potential importance in cancer.

For more information, please visit:
http://www.salk.edu/faculty/saghatelian.html

Cancer, Diabetes, Immunology, Metabolism, Neurological Disease