Mapping proteins key to human health and immune system

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Proteins, the building block for all living organisms, are the ultimate transformers – able to splice and switch roles and functions within the human body. But when these changes go wrong, diseases such as cancers and arthritis may result, says University of British Columbia researcher Chris Overall.

"Scientists have made great advances since mapping the human genome 10 years ago, but our next frontier is mapping and understanding the function of all proteins in the human body," says Dr. Overall, Canada Research Chair in Metalloproteinase Proteomics and Systems Biology and professor in the Dept. of Oral Biological and Medical Sciences at the Faculty of Dentistry.

He points to the "Human Proteome Project," a global initiative to unravel the "protein code of life." "The task is immense – 20,244 human genes hold the instructions for up to 5,000,000 protein forms in man!"

Overall's groundbreaking research has led to a seismic shift in the understanding of immune response. All innate immunity – or the body's first response to injury or disease – is controlled by a family of enzymes called metalloproteinase.

Overall and his team discovered a protein that acts like a molecular beacon or a green traffic light capable of directing white blood cells – or leukocytes – to the site of injury or bacterial infection, such as gingivitis or periodontitis.

In the process, they found that instead of just chewing up and destroying the collagen matrix, these enzymes were also cutting the protein, "biting off" the first four amino acids at the end of the molecule.

This resulted in a profound change in the behaviour of the protein, effectively turning the green traffic signal to red, and stopping the cascade of leukocytes to the site of inflammation.

"What we discovered was the off signal for inflammation," Overall explains. "Without this off signal, inflammation becomes chronic and causes destruction of cells and tissues."

Overall has also shed light on "moonlighting" proteins. These proteins show up in unexpected places within a cell, or are intracellular proteins that venture outside a cell, but take on completely different functions depending on their new homes.

What causes these proteins to suddenly change roles can be traced to their start and end points, or their "termini,'" says Overall. He explains that specialized proteins – enzymes called proteases – have the job of precisely cutting into proteins. In so doing, new termini are generated and often start to perform new functions depending on the nature of their new ends.

"The termini at each end of a protein can have distinct jobs that are often critical for the function of the whole protein," notes Overall.

The Human Proteome Project

Dr. Chris Overall and his team are taking part in the Human Proteome Project, launched in 2010 – a decade after the Human Genome Project was completed.

The international collaboration aims to map all the proteins in the human body, dividing the challenge into 24 chapters on for each of the 22 pairs of chromosomes plus X and Y. Researchers will identify the proteins coded by each of the genes on each chromosome, deciphering their role in cells and tissues.

Each country will be tackling a certain number of proteins on a specific chromosome. Canadian investigator teams have selected chromosomes 6 and 21, and are seeking funds to proceed with the work.

Provided by University of British Columbia

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