Human genome: the hunt continues for 'malicious proteins'

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This undated handout illustration shows the DNA double helix. Scientific advances of the past decade, such as the sequencing of the human genome, have opened up compelling new fields of research on the interaction of the body's 21,000 proteins, and the role they play in cancer and other diseases.

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This is the focus of the "International Interactome Initiative" ("Triple I") or as some researchers call it, "I Cubed," led by Canadian Benoit Coulombe, director of the Gene Transcription and Proteomics Laboratory at the Institut de Recherches Cliniques de Montreal -- the Clinical Research Institute of Montreal.

"Through genome sequencing, we obtained a list of all the proteins in the human body. We know their sequence through the DNA that encodes them, but for a large number of them, we had never seen them before and never studied them," he said.

We know even less about how they interact and what the biological outcomes are.

Proteins act not individually, but in "complexes" or groups, as they exert their influence on cells and on the human body, so researchers must map out their connections to understand their functions, Coulombe said.

To chart this, researchers select a protein, mark it or tag it, then yank it from its cell along with its "partners," after which it can be identified by mass spectrometry.

Studying certain proteins that we already knew to be involved in skin cancer, for example, allowed the discovery in the same grouping of a new protein responsible for a specific form of the disease -- research which is key to finding the right treatments one day.

While we may already know the culprit gene, it is impossible at the moment to modify the DNA in all cells. On the other hand, we can have an effect on the proteins with the right chemical molecule, the biologist explained.

A protein can become "malicious" because of a "bad" genetic code in its DNA, an evolution could be the result of something else, such as modification by an enzyme, in what is called an "epigenetic" event.

Charting the interactions of all of the body's 21,000 proteins is an immense task. Benoit Coulombe said laboratories currently use their own technologies to do so, but eventually will have to standardize their

procedures to obtain comparable results.

The "I Cubed" program involves for now American, Austrian, Canadian, Swiss and German laboratories. Its steering committee has already started to standardize their procedures. Each group of researchers conducts the same experiments with 30 proteins and then they compare the results.

"For a complete map (of protein interactions), the human interactome, we will need 100 million dollars, five to 10 laboratories and five years of work," said Coulombe, whose team is primarily interested in cancer and neuromuscular diseases.

"We have to move step by step," but the genome sequencing "formidably accelerated" the scientific effort, he said.

"Genomic specialists are interested in genes, medical doctors in diseases, our research fills a void between these two," he added. They may also someday discover drugs for use against "bad proteins."