Looking at proteins to make new medicines and better wine

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Proteins hold keys to making more effective medicine. Credit: Jeff Fillmore, Flickr, CC BY-SA

The Human Genome Project was completed in 2003, mapping out all of the genes of the human genome. When the first draft of results were published many were surprised that we had only 24,000 genes. This seemed like an unremarkable amount considering fruit flies had about 14,000 genes.

Clearly the total number of genes does not account for the marked difference in complexity in humans and fruit flies. This can be partly explained by the fact that genes encode for proteins, the functional entities in cells, which can be considered as the business end of bioengineering.

Proteins carry out functional roles interacting with each other as well as other cellular components. The same gene can code different proteins and after being produced, proteins can be activated and deactivated.

Proteomics is a subject that has emerged because of our growing knowledge of genomics. While genomics aims to understand how a human works at the gene level, proteomics aims to reveal this at the protein level, measuring protein expression at precise moments in specific conditions and in either cells, tissues or organs.

Proteomics is tricky because there is no current technology to amplify proteins and this means that detecting all expressed proteins is not possible. But rapid advances in technology have helped improve the field and now thousands of proteins can be identified and quantified with different experimental techniques.

Our ability to understand how proteins operate and how cells behave through proteomics is being increasingly applied in a variety of fields – from developing new drugs for medicinal uses to better understanding how ecosystems are changing. A study even came out this week on how to make red wine taste better through manipulating the bacteria involved in its fermentation process using proteomics.

Developing better drugs

E. coli is not just the bacteria that makes you horribly sick after catching it in contaminated chicken. Many of its strains are harmless and they

grow well in laboratories, so the *E. coli* organism is commonly used in scientific research. When manipulated, it helps produce about 30% of therapeutic drugs on the market today.

The breakthrough that made this possible came about 30 years ago when genetically engineered *E. coli* was used to make human insulin. This is not only a cheaper method, but also more effective than obtaining it from the pancreas of dogs and pigs, as was common practice then.

Insulin is a relatively simple protein drug. More complex drugs involve specific modifications to the protein, such as the addition of sugars to specific amino acids in a process called glycosylation. This features in more than two-thirds of therapeutic protein drugs and increases their effectiveness. But the production process of these more complex drugs is more costly than making simpler ones in *E. coli*.

Genetic engineering can be used for adding the cellular machinery to *E. coli* cells so that they can attach specific sugars to protein targets. But it is very inefficient at this process. Through mapping protein expression changes in cells grown in different conditions and working out differences in *E. coli* cellular processes, research I'm involved in is working out how to enable protein drugs to be modified more efficiently .

Understanding the environment

Proteomics can also be used to help uncover the way different ecosystems work and how changes to the environment, for example, through mining activity, can affect the ecosystem. By looking at the proteins expressed in a small sample of soil, water or air, it is possible to gain a snapshot of how an environment functions at a local level. This field is called metaproteomics.

The challenges involved in metaproteomics are huge as the diversity and complexity of proteins increases in these types of samples. But it is a powerful tool as it provides insight into the natural state of the biology of a system compared to examining proteins in the laboratory, which relies on culturing cells in a way that does not truly represent their natural state in a community.

By merging metaproteomics findings with traditional ecology and environmental chemistry measurements, we aim to better understand the microbial processes and metabolic pathways that are central to the functioning of an ecosystem. Essentially, we can gain a window into what the microbes in our ecosystems are doing. Microorganisms are often sidelined in ecology experiments, although changes to the system, for example, due to climate change or man-made disasters like oil spills, can have significant effects.

Recently, we have been looking into measuring changes in bacterial and algal proteins in natural water systems. As the human population grows so does the demand for food, and increasing fertiliser use is leading to nutrient run-off into lakes, rivers and oceans. Some are so badly affected by this nutrient enrichment that they are considered dead zones. Metaproteomics is a new field that can help us understand the changing microbial components of these systems and how they react to the technologies designed to remedy their decline.

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