Rare Genomics Institute

PROTEOMICS & MUTATIONS

A RARE-ED INFOGRAPHIC

Proteomics

an overview

Proteomics is the large-scale analysis and study of proteomes. It aims to create a "bigger picture" of proteins within a cell or organism.

SOME QUICK VOCAB!

- **Proteome**: a set of all proteins expressed in a cell, system, or biological context.
- **Protein**: chains of amino acids that perform specific functions in the cell.

what can proteomics do?

Our body relies on the proper function of proteins. Improper synthesis or amounts of proteins can have negative effects and lead to diseases. With proteomics, we can learn more about how the amount, structure, or interaction of proteins affects our biological system and health. This helps us better understand diseases and potentially treatment options.

how does it work?

Scientists will typically take a sample and separate out the protein by size, charge, or polarity. From there, they can take the isolated proteins and determine many things. They can identify the protein using a method called *mass spectrometry* and compare it to a known database. They can also quantify the amount of protein by tagging the protein with a recognizable fluorescent dye. Scientists can further study protein structure or protein interactions using *x-ray crystallography* or *NMR spectroscopy*.

Mutations

an overview

A **mutation** is a permanent change in the DNA sequence which alters the hereditary information contained in the building blocks of our genetic code.

Not all mutations cause disease. Some mutations may change the DNA, but do not alter protein function. Only a small percentage of mutations are disease causing. Disease causing mutations are called *pathogenic*.

types of mutations:

GERMLINE

Inherited from parents and present in every cell, including the ova for females and sperm for males.

SOMATIC

Acquired mutations, not inherited. Cannot be passed onto the next generation.

HOW DO MUTATIONS OCCUR?

SUBSTITUTION

A single (1) DNA base pair is changed. One amino acid in the base pair is substituted for another amino acid. This substitution can lead to a protein that has no function, or the wrong function.

DELETION

A piece or section of DNA is removed. This can range from a few base pairs to an entire gene, which may alter the function of the proteins.

INSERTION

A piece or section of DNA is added. This can range from a few base pairs to an entire gene. The protein function may be altered.

FRAMESHIFT

Amino acids, or the building blocks of our proteins, are typically "read" in blocks of 3 bases. When this "reading frame", or grouping of these amino acids is shifted, it generates a completely different and nonfunctional protein.

SPOTLIGHT: Menkes Disease

Menkes Disease is an X-linked neurological disorder caused by defects in the copper transporter protein *ATP7A* (also called Menkes' protein). This creates an imbalance in copper levels. It is characterized by kinky hair, failure to gain weight, and deterioration of the nervous system.

A study (Zlatic et al. 2018) used *genealogical proteomics* try and learn more about Menkes Disease. Researchers compared proteomes within a pedigree (family) of affected vs unaffected individuals. They were looking to identify protein traits that were specific to affected individuals.

Researchers discovered pathways that were affected by copper imbalances, such as mitochondrial function. They even found that copper metabolism defects in Menkes shared similar mechanisms with Parkinson's Disease.

Further study and use of geneological proteomics can be used to identify more mechanisms that will allow us to further understand the relationship between genes and diseases.

PUTTING IT ALL TOGETHER

Why does it all even matter?

The **central dogma** of biology is the flow of information from our DNA, to our RNA, to the creation of proteins.

Proteins are referred as the "molecules that make biology work". The function or dysfunction of proteins can create or cure diseases. Mutations within our DNA are often what dictates how these proteins are made and how they work.

With proteomics, we can learn more about how different amounts and even functions of proteins affects rare genetic diseases. This helps us better understand the impact of genetic mutations and treatment options for diseases.

REFERENCES

PROTEOMICS

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MUTATIONS

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