Discuss how proteomic tools can be used to identify and understand a specific disease in a given population.

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From the start of our scientific education we are told proteins are the building blocks of life, so we know they are a wide range of complex molecules that are critical for the normal function of our cells and body. All the proteins being expressed at a given time in a particular cell, tissue, or organism is known as the proteome. Protein expression changes can result in very different cellular actions and upregulation or downregulation of certain proteins can cause and show disease. Expression proteomics can identify the level of proteins in two or more states like in disease vs normal, so we can find proteins that are associated with disease, thereby diagnosing or finding targets to treat disease. Functional proteomics allows for the understanding of a given proteins function through identify interaction between proteins, which in the case of diseases means we can understand the actual reasons behind a disease. This essay will discuss how proteomic tools including 2D gel electrophoresis, high performance liquid chromatography (HPLC), matrix-assisted laser desorption/ionisation – time of flight mass spectrometry (MALDI-TOF MS), liquid chromatography and tandem mass spectrometry (LC-MS/MS), and protein microarrays to identify and understand a disease in a given population using Alzheimer's disease (AD) as an example.

Two-dimensional gel electrophoresis separates proteins by charge and mass, and thus identify proteins by differences in these. It involves putting an SDS-PAGE gel onto the other end of another gel running perpendicular based on charge. SDS has be been stripped off the protein so it goes back to its original charge. It can be used to assess changes to protein levels in response to certain drugs or identify proteins that cause harmful effects. In the context of AD a study that took 15 AD temporal cortex brain samples and compared it to 15 control samples, found 28 proteins that were significantly decreased in AD brains, 5 proteins that were significantly increased in AD brains, and 9 proteins that were only found in AD brain samples, which with now identified will allow for targeted future research of the pathogenic protein changes. HPLC allows for the precise separation of similar proteins, by pumping a given sample through a tube filled with beads/gels, separating them by charge or mass or both or a given property such as phosphorylation. It has been used to screen for sickle cell anaemia by identifying haemoglobin variants. In the context of AD HPLC coupled with Tandem Mass Spectrometry can detect Amyloid beta 1-40 peptide in blood samples to incredible accuracy which has been previously implicated with the development of AD, and can therefore open it up as a possible biomarker for the detection and diagnosis or mark it as a significant molecule to research and understand the process of AD opening up possible treatment strategies.

MALDI-TOF MS gives mass : charge ratios of samples as the samples on a metal plate are hit with a laser, vaporised and charged ions are accelerated along an electrical gradient and timed, the larger particles hit the detector later and usually the more positively charged the more it is pulled in X direction allowing identification of proteins. This can again be used to identify biomarkers either in blood or cerebrospinal fluid that could catch the disease early, or identify proteins implicated with a given disease. In the case of AD, MALDI-TOF MS with tandem mass spectrometry (see paragraph below) has been used to study and characterise proteins isolated from senile plaques (a structure in AD brains), assisting with the understanding of the formation and growth of these plaques, which opens up areas of research for potential future therapies. LC-MS/MS uses liquid chromatography to separate them then mass spectrometry to identify them and tandem mass spectrometry lets you pick a substance and use only that mass for mass spectrometry again as it passes the sample through argon gas and they are detected and separated by individual amino acid differences. In the case of AD, ultra performance LC-MS has been used to identify 9 potential biomarkers for AD when comparing the plasma metabolic profiling of AD vs control, it also showed a correlation between the severity of AD.

This was then narrowed down further to potential LPCs, sphingosine and tryptophan, which could be used to catch AD early and start treatment.

Protein microarrays use antibodies on the array and can use proteins that bind to other proteins to find binding partners or protein complexes. In the case of AD this has been used to identify AD blood biomarkers with a high sensitivity (96.0 percent) and specificity (92.5 percent) distinguishing it clearly from other cancers that share overlapping markers. This again potentially opening up opportunities for early diagnosis and treatment. In conclusion the above has described how different proteomic tools can be used for the identification and understanding of a specific disease by comparing samples from different populations. This essay used AD as an example for each of the techniques, but this could just as easily be almost any other disease pretty much always will change protein expression. We all simply have to love these building blocks of life/disease and the proteomic techniques that have saved lives.