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Draft of human proteome maps: Significant milestones from India

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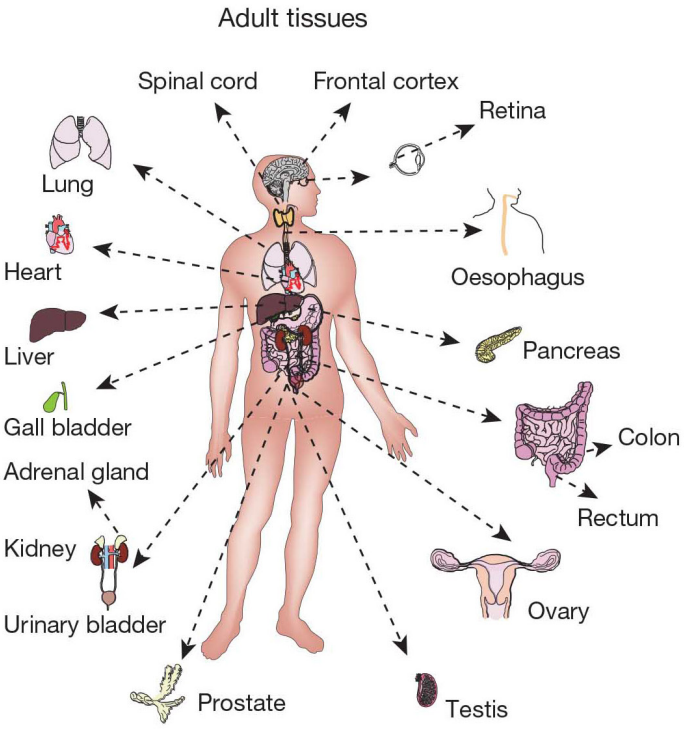
Human genome sequencing was a very important milestone that transformed biological research. The human proteome was the next frontier in the post-genomics era. Three different research groups have now completed this milestone independently[1,2,3]. Of these, two groups employed mass spectrometry-derived proteomics while the third used protein specific antibodies. Interestingly, two of these three studies involved two independent research teams from India.

Scientists at the Institute of Bioinformatics (IOB) in Bangalore played a major role in mapping the human proteome by employing Fourier transform mass spectrometry. They carried out an unbiased survey of human proteins across 17 adult tissues, 7 fetal tissues and 6 purified primary hematopoietic cells (**Figure 1**). The expression pattern of the identified proteins across these 30 human tissues/



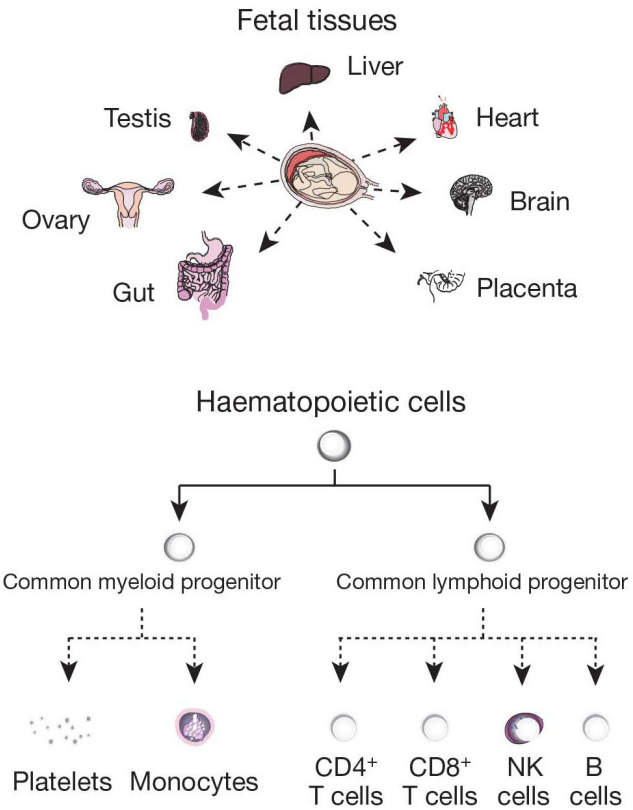


Figure 1: Human tissues and cell types that were analysed by mass spectrometry based proteomics to generate draft map of the human proteome..

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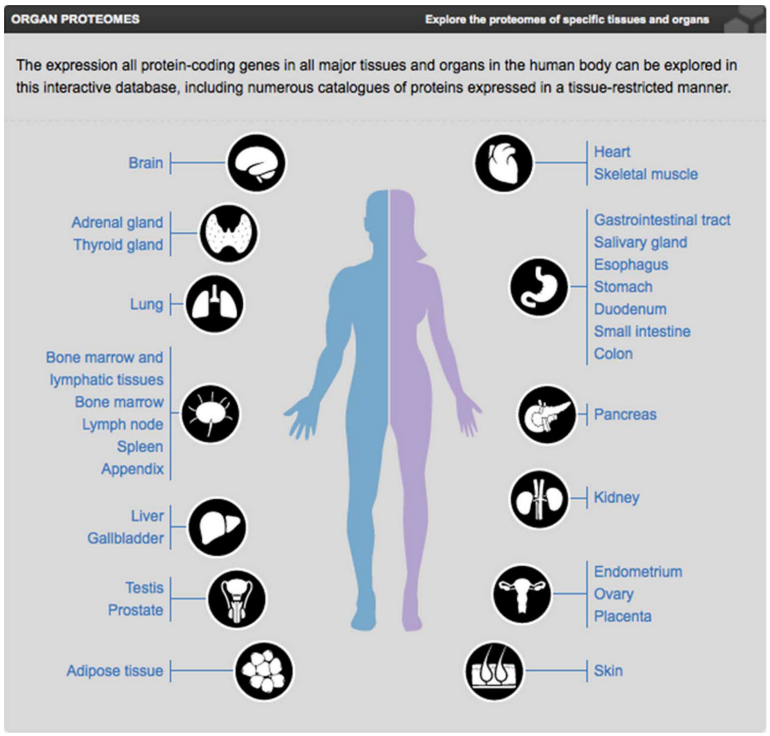

Figure 2: Human tissues analysed by protein specific antibodies to generate draft map of the human proteome.

cell types can be accessed through a web-based resource (www.humanproteomemap.org).

A research group at Lab Surgpath in Mumbai played a major role in mapping the human proteome using an antibody based approach. The tissue-based analysis detected more than 90% of the putative protein-coding genes. This approach was used to explore the human secretome, the membrane proteome, the druggable proteome, the cancer proteome, and the metabolic functions in 32 different tissues and organs. All the data were integrated in an interactive web-based database that allows exploration of individual proteins, as well as navigation of global expression patterns, in all major tissues and organs in the human body.

The Lab Surgpath pathology group has annotated more than 13 million images following immunohistochemical labeling of tissue sections of all major organs in the human body, at the rate of 8,000 images being evaluated every day (**Figure 2**). This includes 44 normal human tissues, 20 cancer types and 46 human cell lines. All images with their detailed annotations are freely accessible at 'The Human Protein Atlas' portal (www.proteinatlas.org). This interactive portal is aimed at researchers interested in human biology, translational medicine and surgical pathologists with interest in immunohistochemistry.

Together, these efforts to map the human proteome, which included a significant contribution from India, provided evidence of protein expression for nearly 90% of the annotated genes in the human genome. They also provided first protein level evidence for hundreds of proteins that were designated "missing proteins" by the research community due to lack of protein level evidence. For example, a unique proteogenomics strategy developed by IOB led to identification of 193 novel protein coding regions in the human genome that were not reported earlier. A large majority of these novel regions are annotated as pseudogenes or regions that code for non-coding RNAs.

In addition, this study also reported identification of more than 100 novel coding exons and novel open reading frames for some of the annotated genes in the human genome. The Human Protein Atlas portal allows exploration of tissue-elevated proteomes in specific tissues and organs. In addition, it allows analysis of tissue expression profiles for specific protein classes, including proteins involved in housekeeping functions in the human body, such as cell growth, energy generation, and metabolic pathways; groups of proteins involved in diseases; and proteins targeted by pharmaceutical drugs. The impact of these studies on basic research as well as biomedical research will become evident in the coming years. Methods used in these studies will also be embraced by the scientific community for further exploration of the human proteome.

The contribution of Indian scientific groups in these seminal studies to characterize the human proteome holds enormous significance for Indian science. These studies have clearly demonstrated that India has the talent, infrastructure and capability to be a major player in global science. It also highlights the ability of researchers from India in carrying out large scale collaborative international research projects that have global impact.

Both research groups from India, which participated in this global effort, are from private institutions. Institute of Bioinformatics is a 13-year-old private non-profit organisation engaged in biological research. The institute, besides publishing over 200 papers in international journals, has developed several world-class biological databases that are extensively used by the global scientific community. Lab Surgpath is the first private surgical pathology laboratory in India to have participated as a major collaborator in an international project with the annotated images resulting in more than 300 publications. Lab Surgpath offers both research and diagnostic services.

Given that strategic initiatives are being enacted in most countries, this makes a strong case for enhanced support by Indian funding agencies to institutions based on their scientific productivity and excellence regardless of their governmental affiliation. Such an approach is likely to foster parallel development of novel research ecosystems in India in addition to government research institutions.

The United States of America has successfully nurtured such an ecosystem for several decades with the Broad Institute being one such example. To keep the momentum going in proteomics, India needs bold initiatives with funding that supports scientific projects where India can make a global impact. This will not only help the country build human resource required for successful execution of such large scale projects but will also make Indian scientists a scientific force to contend with in the international arena.

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