

THE HUMAN PROTEIN ATLAS

The Human Protein Atlas contains a wealth of expression and localization data on the majority of protein-coding genes. It is divided into four parts: normal tissue, subcellular, cell lines, and cancer. Transcriptomics data provides gene expression information across different tissues and organs, while antibody-based protein profiles show cell-level localization for the corresponding protein. The Human Protein Atlas (version 13.0) contains protein data for 85% of the translated human genome and includes 13 million images with primary data from immunohistochemical and immunofluorescent studies.

THE TISSUE-SPECIFIC PROTEOME

The expression of all human protein-encoding genes has been measured in samples representing all major tissues and organs in the human body. Approximately one-third showed some level of elevated expression in at least one of the analyzed tissues, but few showed strict tissue-specific expression. Functional analysis has shown that the role of such proteins with a tissue-elevated expression correlates with the tissue/organ function. For example, the liver produces large numbers of secreted proteins, while the kidney expresses many membrane-bound transport proteins, and the brain harbors a preponderance of neurological proteins.

THE HOUSEKEEPING PROTEOME

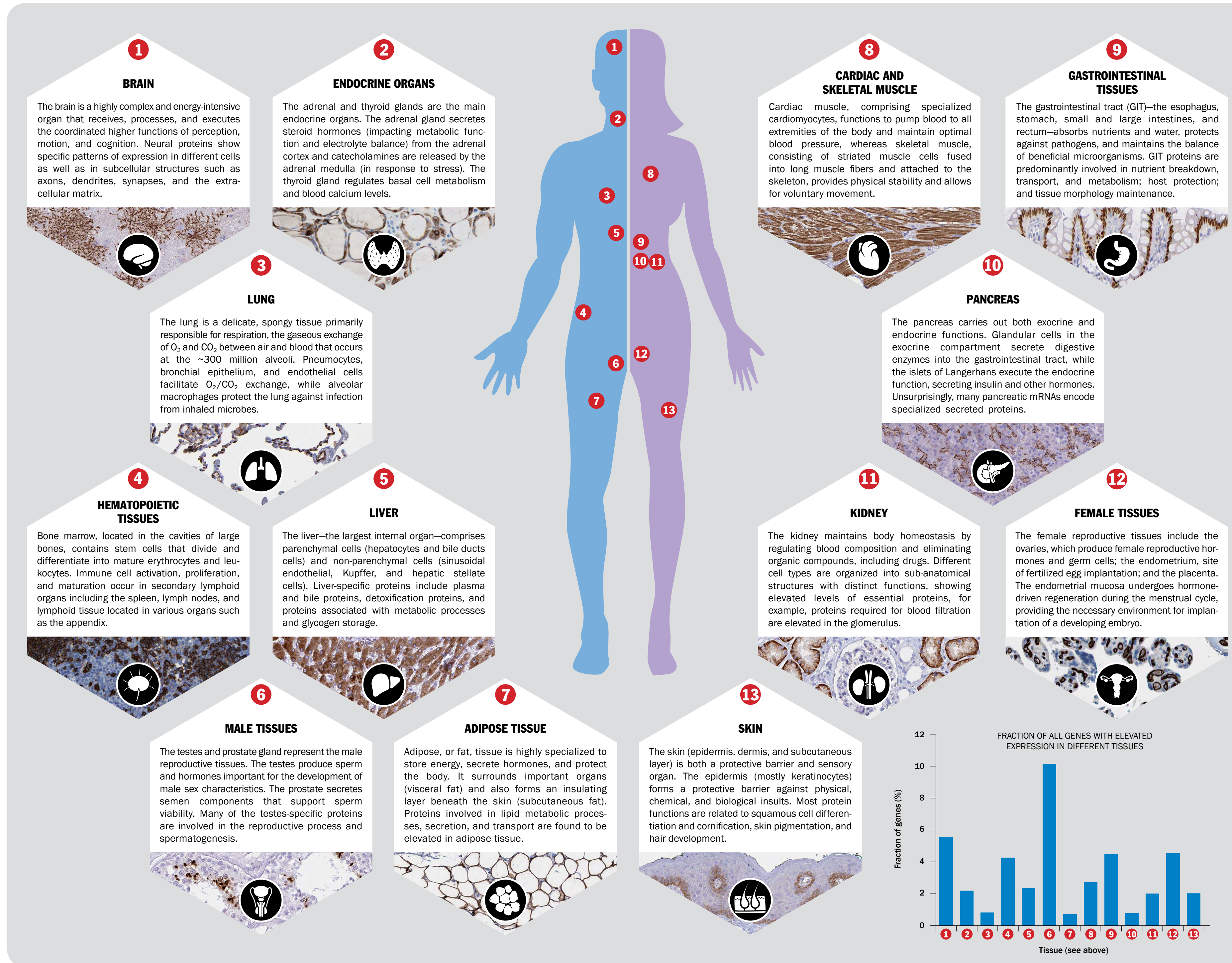
Transcriptomics analysis suggests that some 9,000 genes code for so-called housekeeping proteins, located in every cell, that maintain the normal cellular structure and basic functions for life. These include ribosomal proteins involved in protein synthesis, enzymes essential for cell metabolism and gene expression, and mitochondrial proteins needed for energy generation as well as structural proteins responsible for building and maintaining the physical integrity of the cell.

THE REGULATORY PROTEOME

All processes within a living cell are highly regulated, including cell proliferation, differentiation, and death. Regulatory mechanisms include the control of gene expression as well as posttranslational modifications that can regulate protein activity, stability, localization, or degradation. Transcription factors, of which 1,500 human proteins have been identified, are an especially important class of regulatory proteins as they function as the on/off switch for gene expression.

THE HUMAN PROTEOME

The Power of Proteins. The human genome consists of approximately 20,000 protein-coding genes. If DNA can be equated with the blueprint for a home, then proteins can be thought of as the bricks and mortar, plumbing, and paint—essentially everything that makes up the house. This poster summarizes the multiple ongoing antibody- and transcriptomics-based proteome projects and where in the human body this research is focused. For more detailed information, visit: www.proteinatlas.org



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To explore the human proteome in more depth, visit:

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THE SECRETOME AND MEMBRANE PROTEOME

Both secreted and membrane-bound proteins play crucial roles in many physiological and pathological processes. Important secreted proteins include cytokines, coagulation factors, and growth factors, among others, while membrane proteins include ion channels or molecular transporters, enzymes, receptors, and anchors for other proteins. Approximately 3,000 human genes are predicted to encode secreted proteins, with another 5,500 encoding membrane-bound proteins.

THE ISOFORM PROTEOME

The existence of a variety of protein isoforms in each cell endows the structural space of the human proteome with breadth and complexity. Isoforms are produced through posttranslational modifications, proteolytic cleavage, or somatic recombination. Variations in the amino acid sequence also result from local genetic variations in protein-coding regions. Additionally, a large proportion of protein-coding genes have splice variants that yield protein products of different sizes. The almost limitless variety of posttranslational modifications combine to create thousands of additional variants, contributing to a rich and diverse proteome.

THE CANCER PROTEOME

Over 500 genes have been implicated in the tumorigenesis process. Normal expression of these genes is essential for orderly growth, survival, and function. However, overexpression, loss of expression, or expression of a defective protein can contribute to dysfunction and tumor growth. Dysregulated expression results from large structural rearrangements, chromosomal duplication, specific gene amplifications, or silencing of transcription through mutations or epigenetic mechanisms. Furthermore, point mutations or small insertions or deletions can lead to loss or gain of function in the affected protein.

THE DRUGGABLE PROTEOME

Most pharmaceutical drugs act by targeting proteins and modulating their activity. Target proteins belong to four main families: enzymes, transporters, ion channels, and receptors. The U.S. Food and Drug Administration has approved drugs targeting approximately 600 human proteins, with most acting on signal transduction proteins that convert extracellular signals into intracellular responses. Antibody-based drugs usually cannot penetrate the plasma membrane and therefore target cell surface proteins such as receptors, while small molecule drugs are able to act on both intracellular and extracellular targets.