THE HUMAN CELL

Cells are the machinery of life. Much of the bustling activity in the human cell results from proteins performing specific tasks in designated compartments, the organelles. This poster describes the results and ongoing creation of an image-based atlas of the subcellular distribution of the human proteome. Explore it further at **www.proteinatlas.org**.

THE HUMAN PROTEIN ATLAS

The Human Protein Atlas presents the translated human genome captured in millions of images collected using high-resolution microscopy. The Cell Atlas, Tissue Atlas, and Cancer Atlas provide a comprehensive overview of gene expression–together with the spatial distribution of corresponding proteins–across organs, tissues, and cell lines at subcellular resolution.

ORGANELLE PROTEOME

The cellular function of proteins is dictated by their location and interactions with other proteins or substrates. Revealing the human proteome's spatial distribution is thus essential to understanding cell biology. By visualizing the nonsecreted human proteome using high-resolution confocal microscopy, the molecular composition of organelles and substructures has been determined.

MULTILOCALIZING PROTEOME

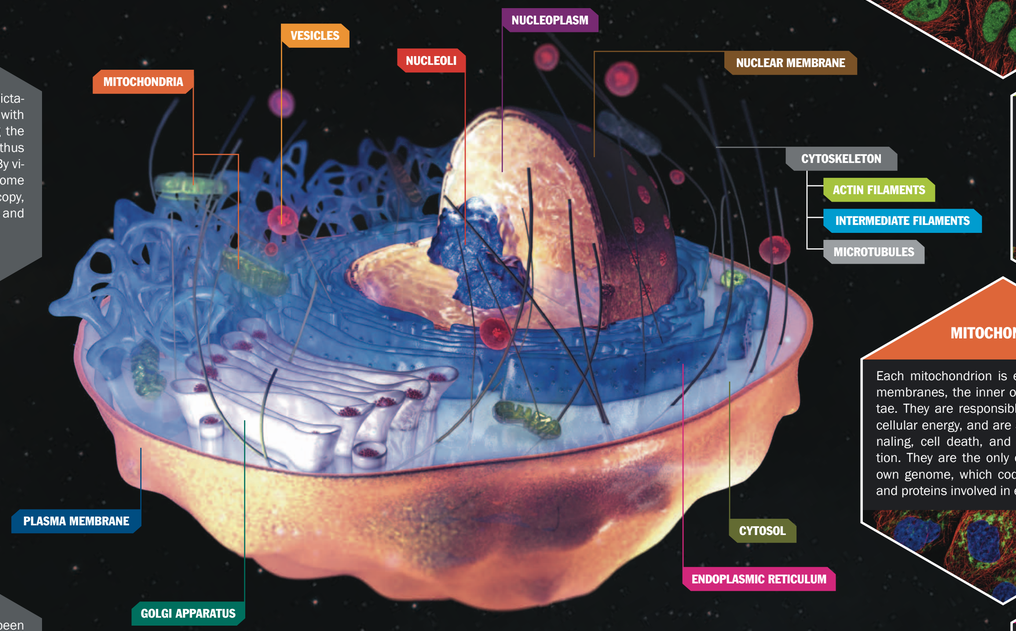
Over one-third of human proteins are found in multiple organelles. The presence of a single protein at several locations may reflect its dynamic distribution, and suggests multiple roles in cell physiology. Understanding the multilocalizing proteome is key for discovering novel pathways underpinning cellular dynamics and developing a holistic view of the human cell.

CELL CYCLE-DEPENDENT PROTEOME

The cell cycle describes the process by which cells grow and divide. This dynamic and tightly regulated process drives changes in abundance and spatial redistribution of many proteins. Cell cycle dysregulation can lead to diseases such as cancer. Knowledge about the cell cycle proteome is therefore essential for understanding health, aging, and disease.

CELL LINE TRANSCRIPTOME

Expression of protein-coding genes has been analyzed in a large set of human cell lines of different cellular origins. One-third of all genes are differentially expressed, indicating cell type-specific functions related to the origin of the cell line. The majority of genes are expressed in all cells and drive rudimentary processes such as metabolism or proliferation.



NUCLEOPLASM

The nucleoplasm is enclosed by the nuclear membrane and embeds the nucleoli to form the nucleus. It surrounds the chromatin and nuclear substructures, the nuclear bodies. The nucleoplasm is the site of DNA replication and transcription, tightly regulated processes controlling cellular growth and division.

NUCLEOLI

The nucleoli are nonmembrane-bound structures in the nucleus. They are the sites of ribosome synthesis, processing, and assembly. These are complex processes controlled in nucleolar substructures such as the fibrillar center. Nucleoli also comprise proteins involved in cell cycle regulation and cell stress responses.

NUCLEAR MEMBRANE

The nuclear membrane physically isolates the DNA in the nucleus from the cytoplasm. The inner membrane is the anchoring site of nuclear chromatin, while the outer membrane is continuous with the endoplasmic reticulum. Nuclear pores are scattered throughout the membrane, regulating large molecule transport in and out of the nucleus.

ACTIN FILAMENTS

The actin filaments are polarized filaments that are part of the cytoskeleton and provide structure to the cell. They interact directly with focal adhesions and membrane-bound proteins, allowing the cell to respond to extracellular stimuli and control cellular motility. This dynamic remodeling ability also makes them essential for cellular division.

INTERMEDIATE FILAMENTS

The intermediate filaments are part of the cytoskeleton and provide physical support and stabilization to the cell, enabling it to withstand mechanical stress and tension. They also participate in chromatin organization by anchoring the DNA to the nuclear lamina, which lines the inner part of the nuclear membrane.

MICROTUBULES

The microtubules are the stiffest of the cytoskeleton components and are essential for maintaining the internal architecture and polarity of the cell. They are involved in spindle formation during mitosis, and also form a network facilitating intracellular transport. Cell motility requires rapid rearrangement of microtubules.

MITOCHONDRIA

Each mitochondrion is enclosed by double membranes, the inner one folding into cristae. They are responsible for production of cellular energy, and are also involved in signaling, cell death, and cellular differentiation. They are the only organelle with their own genome, which codes for rRNA, tRNA, and proteins involved in energy metabolism.

CYTOSOL

The cytosol is the semifluid substance within the cell that, together with all nonnuclear organelles, forms the cytoplasm. It is composed mainly of proteins, ions, and amino acids. Several cellular processes, including protein synthesis, interorganelle transport, and many metabolic reactions occur in the cytosol.

CENTROSOME

The centrosome is a small and distinct organelle responsible for organizing microtubules in the cell. It consists of two centrioles, which are surrounded by a matrix of proteins named the "pericentriolar material." The centrosome is a key regulator of cell division and also important for cell shape, polarity, and mobility.

ENDOPLASMIC RETICULUM

The endoplasmic reticulum (ER) is a membranous network consisting of sheets and tubules that span the cytoplasm. The rough ER is covered with ribosomes that translate most of the transmembrane and secreted proteins. The smooth ER lacks ribosomes, but contains the machinery for synthesis of lipids and other biomolecules.

GOLGI APPARATUS

The Golgi apparatus consists of stacks of interconnected membranous disks, cisternae, in a ribbon-like structure close to the nucleus. It plays a central role in the secretory pathway, since it is involved in the modification and sorting of proteins that are transported to other organelles in the cell, as well as to the extracellular space.

VESICLES

The small membrane-bound organelles, known collectively as vesicles, include endosomes, lysosomes, peroxisomes, lipid droplets, and transport vesicles including secretory granules. The diversity of vesicles is reflected in their plethora of functions, such as specialized metabolic reactions, transport, secretion, and degradation of biomolecules.

PLASMA MEMBRANE

The plasma membrane physically separates the cell's interior from the surrounding environment. It is the site of cell–cell interactions and communications, and anchors the cell to neighboring cells or the extracellular matrix. Transmembrane proteins in the cell membrane are important for signal transduction and transportation of molecules.

SECRETED

Secreted proteins can often be identified by the presence of a signal peptide. This localization signal results in active transport out of the cell, predominantly via the secretory pathway. They play a crucial role for inter- and intracellular communication and include antibodies, peptide hormones, coagulation factors, growth factors, and other signaling molecules.

HIGHLIGHTS OF CELL BIOLOGY AND MICROSCOPY

1595-1610 The first compound microscopes made

1665 Robert Hooke coins the term "cell"

1673 Antonie van Leeuwenhoek manufactures single lens microscope

1833 Robert Brown describes the cell nucleus

1838-39 Matthias Schleiden and Theodor Schwann formulate "cell theory"

1852 George Stokes describes wavelength change between fluorescent absorption and emission (Stokes shift)

1873 Ernst Abbe describes resolution limit for light microscopes

1890 Richard Altmann describes bioblasts (later mitoehondria) in muscle of beetle, *D. marginalis*

1891 Paul Ehrlich describes antibodies (Nobel Prize 1908)

1898 Camillo Golgi describes internal reticular apparatus later known as the Golgi apparatus (Nobel Prize 1906)

1933 Ernst Ruska develops first electron microscope (Nobel Prize 1986)

1941 Albert Coons is first to use antibodies coupled to fluorescent molecules

1945 Keith Porter, Albert Claude, and Ernest Fullam describe organization of cell using TEM (A. Claude Nobel Prize 1974)

1935 Frits Zernike develops phase contrast microscopy (Nobel Prize 1953)

1955-56 Christian de Duve describes lysosome and peroxisome vesicles; George Palade describes ribosomes on endoplasmic reticulum (Nobel Prize 1974)

1957 Marvin Minsky patents principles of confocal microscopy

1962 Osamu Shimomura describes GFP isolated from jellyfish, *A. victoria* (Nobel Prize 2008)

1975 Günter Blobel elucidates role of signal peptide for subcellular localization of proteins (Nobel Prize 1999); Georges Köhler and César Milstein develop first monoclonal antibodies (Nobel Prize 1984)

1985 Nils Åslund publishes first 3D stack from confocal laser scanning microscope

1989 William Moerner detects single fluorophore (Nobel Prize 2014)

1995-96 Martin Chalfie develops GFP as gene expression marker; Roger Tsien creates multicolored mutants of GFP (Nobel Prize 2008)

1994 Stefan Hell develops STED microscopy (Nobel Prize 2014)

2001 First draft of the human genome completed (Human Genome Project and Celera Genomics)

2006 Eric Betzig develops PALM (Nobel Prize 2014)

2015 Tissue-based human proteome published (Human Protein Atlas)

CELL BIOLOGY HIGHLIGHTS

MICROSCOPY HIGHLIGHTS

GFP = Green fluorescent protein
TEM = Transmission electron microscopy
STED = Stimulated emission depletion microscopy
PALM = Photoactivated localization microscopy

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