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THE HUMAN PROTEIN ATLAS

Knut och Alice Wallenbergs Stiftelse

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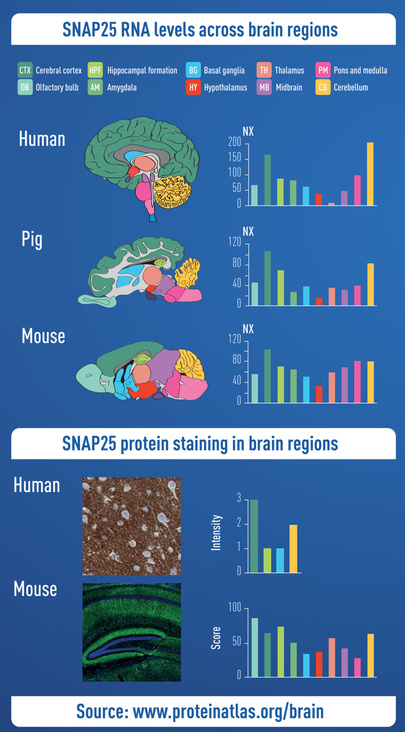
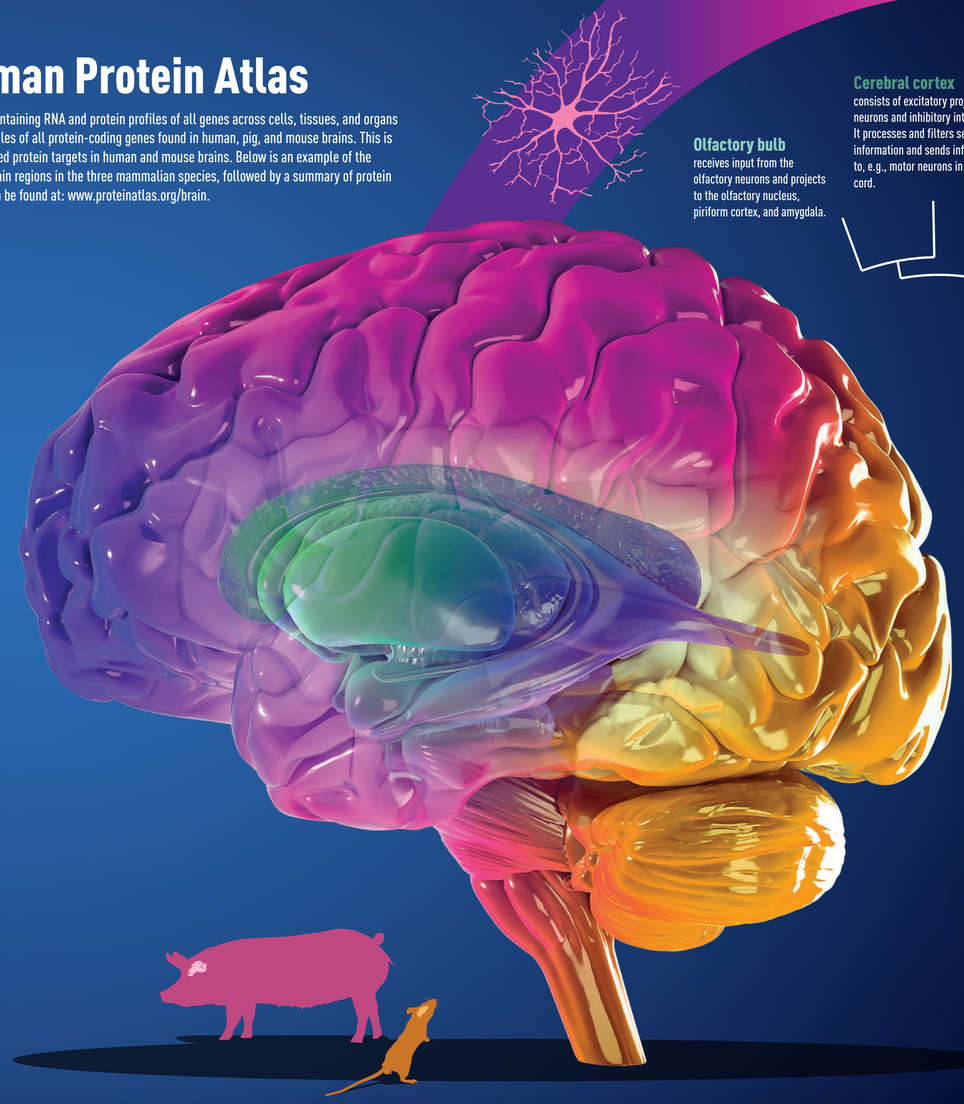
THE HUMAN BRAIN

Introduction to the Human Protein Atlas

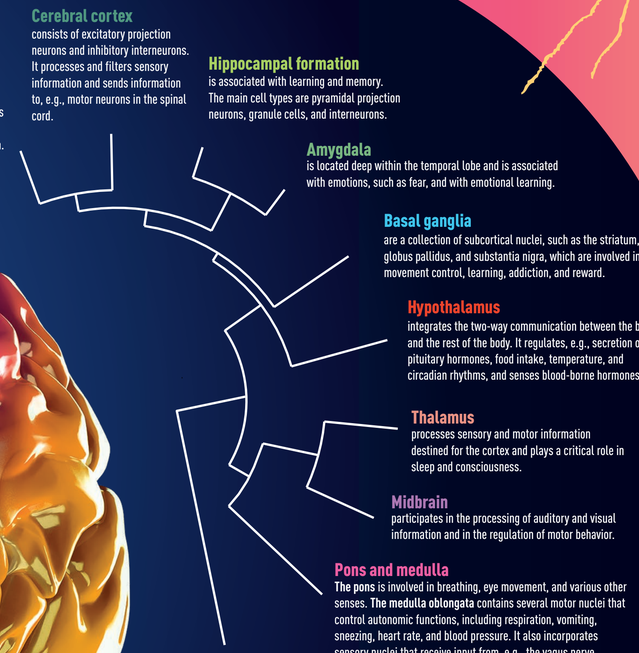
The Human Protein Atlas (www.proteinatlas.org) is an open access database containing RNA and protein profiles of all genes across cells, tissues, and organs in the human body. The Brain Atlas subsection contains genome-wide RNA profiles of all protein-coding genes found in human, pig, and mouse brains. This is complemented by antibody-based protein-localization data collected for selected protein targets in human and mouse brains. Below is an example of the summary page for one gene (SNAP25), showing RNA levels across the major brain regions in the three mammalian species, followed by a summary of protein staining in human and mouse brains. The brain profiles for all human genes can be found at: www.proteinatlas.org/brain.





Brain regions

The brain consists of a complex, interconnected net of neurons organized in regions, subregions, nuclei, and layers. The different regions of the brain are separated anatomically as well as functionally. Below, a dendrogram illustrates the relationship between genome-wide RNA profiles found in different regions in the human brain, using data from the Human Brain Atlas.
Source: www.proteinatlas.org/brain



Olfactory bulb
receives input from the olfactory neurons and projects to the olfactory nucleus, piriform cortex, and amygdala.

Cerebral cortex
consists of excitatory projection neurons and inhibitory interneurons. It processes and filters sensory information and sends information to, e.g., motor neurons in the spinal cord.

Hippocampal formation
is associated with learning and memory. The main cell types are pyramidal projection neurons, granule cells, and interneurons.

Amygdala
is located deep within the temporal lobe and is associated with emotions, such as fear, and with emotional learning.

Basal ganglia
are a collection of subcortical nuclei, such as the striatum, globus pallidus, and substantia nigra, which are involved in movement control, learning, addiction, and reward.

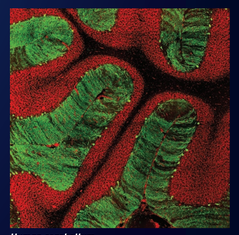
Hypothalamus
integrates the two-way communication between the brain and the rest of the body. It regulates, e.g., secretion of pituitary hormones, food intake, temperature, and circadian rhythms, and senses blood-borne hormones.

Thalamus
processes sensory and motor information destined for the cortex and plays a critical role in sleep and consciousness.

Midbrain
participates in the processing of auditory and visual information and in the regulation of motor behavior.

Pons and medulla
The pons is involved in breathing, eye movement, and various other senses. **The medulla oblongata** contains several motor nuclei that control autonomic functions, including respiration, vomiting, sneezing, heart rate, and blood pressure. It also incorporates sensory nuclei that receive input from, e.g., the vagus nerve.

Cerebellum
contains large Purkinje cells and is associated with motor control, motor learning, and coordination, and is also believed to be important for certain cognitive functions.



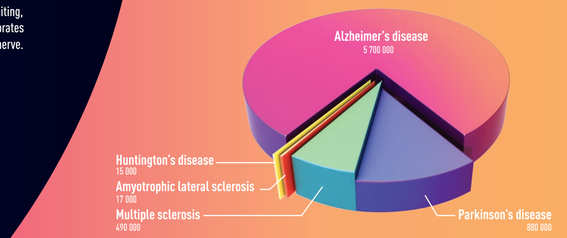
Human cerebellum

Cell types

Neurons are the main signaling units in the brain, communicating with each other via synapses. The two main subclasses of neurons are interneurons (local interconnections between neurons) and projection neurons.

Non-neuronal cells support and promote the proper function of neurons. These include **endothelial cells** lining blood vessels, **ependymal cells** lining the ventricular walls, and **glial cells**. Glial cells include **oligodendrocytes** (insulating neuronal axons for faster signal conduction), **microglia** (brain macrophages with a hematopoietic origin), and **astrocytes** (involved in numerous functions, such as maintaining the blood brain barrier, homeostasis, neuronal growth, and neurotransmitter recycling).

Neurodegenerative disorders



Number of patients in USA suffering from selected neurodegenerative disorders. Source: www.proteinatlas.org/brain

Approximately 1 billion people worldwide suffer from neurological disorders, defined as progressive loss of neurological functions, including dementia, stroke, multiple sclerosis, epilepsy, migraines, brain injuries, cancer, and neuroinfections. The neurodegenerative disorders (see figure above) include Alzheimer's disease (AD), the tremor-associated Parkinson's disease (PD), caused by death of dopaminergic neurons, amyotrophic lateral sclerosis (ALS), involving neuronal death and loss of motor function, the inherited disorder Huntington's disease (HD), and multiple sclerosis (MS), an immune-mediated disorder that affects myelination of neuronal axons. Source: www.proteinatlas.org/brain.

A Century of Advances in Neuroscience
reflected in discoveries awarded the Nobel Prize

1906 — **Camillo Golgi and Santiago Ramón y Cajal**
Structure of the nervous system and the definition of the neuron

1914 — **Robert Bárány**
Inner ear structures controlling balance

1932 — **Edgar Douglas Adrian and Charles Scott Sherrington**
Nerve impulses from single axons and reflexes; the synapse

1936 — **Henry Dale and Otto Loewi**
The first chemical transmitter, acetylcholine

1944 — **Joseph Erlanger and Herbert Gasser**
Threshold of axon excitability and impulse velocity

1949 — **Walter Rudolf Hess and António Egas Moniz**
Brain areas critical for autonomous bodily functions; leucotomy therapy

1961 — **Georg von Békésy**
Inner ear structures and mechanisms essential for hearing

1963 — **Alan Hodgkin and Andrew Fielding Huxley**
Propagation of the nerve impulse along the axon, the axon potential, the Hodgkin-Huxley equations
John Eccles
Inhibition and the first neurotransmitter, acetylcholine

1967 — **Ragnar Granit, Haldan Keffer Hartline, and George Wald**
Vision: impulses in single optic nerves, contrast and color

1970 — **Bernard Katz, Ulf von Euler, and Julius Axelrod**
Acetylcholine signaling at the neuromuscular junction; noradrenaline transmitter and its reuptake

1973 — **Karl von Frisch, Konrad Lorenz, and Nikolaas Tinbergen**
Basic principles underlying animal behavior

1976 — **Carleton Gajdusek**
Slow spread of virus in the brain

1977 — **Roger Guillemin and Andrew Schally**
Brain neurohormones controlling anterior pituitary hormone secretion

1981 — **Roger Sperry, David Hubel, and Torsten Wiesel**
Different functions of left and right brain; the cortical circuitry underlying vision

1986 — **Stanley Cohen and Rita Levi-Montalcini**
Discovery of nerve growth factor (NGF)

1991 — **Erwin Neher and Bert Sakmann**
Patch-clamp method for analysis of single-ion channels

1997 — **Stanley Prusiner**
Discovery of prions, self-reproducing protein pathogens

2000 — **Arvid Carlsson, Paul Greengard, and Eric Kandel**
Dopamine and serotonin—modulatory neurotransmitters in motor behavior or memory

2002 — **Sydney Brenner, H. Robert Horvitz, and John Edward Sulston**
Programmed cell death

2003 — **Peter Agre and Roderick MacKinnon**
Water channels and potassium channels

2004 — **Axel Richard and Linda B. Buck**
Odorant receptors and the organization of the olfactory system

2012 — **Brian K. Kobilka and Robert J. Lefkowitz**
G-protein coupled receptors

2013 — **James E. Rothman, Randy Schekman, and Thomas C. Südhof**
Machinery regulating neurotransmitter release

2014 — **Edvard I. Moser, May-Britt Moser, and John O'Keefe**
Positioning systems in the brain

2017 — **Jeffrey C. Hall, Michael Rosbash, and Michael W. Young**
Molecular mechanisms of circadian rhythms