

## The Human Protein Atlas – implications for human biology, drug development and precision medicine

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Science for Life Laboratory (KTH and KI)  
Stockholm, Sweden

### Disclaimer



- Director of the Human Protein Atlas consortium
- Director of KTH Center for Applied Precision Medicine
- Co-founder of Atlas Antibodies, Antibodypedia, ScandiBio Therapeutics, Abclon (South Korea), Affibody, ScandiEdge Therapeutics
- Collaboration with AstraZeneca (Human Secretome Project)

### Science for Life Laboratory

**SciLifeLab**

#### A national infrastructure for next-generation life science

##### Global trends:

- Need for major infrastructures
- Technology evolving rapidly
- Big data



Founding Director: Mathias Uhlen

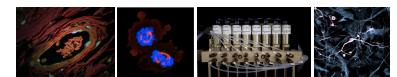
### Science for Life Laboratory (Stockholm) - 2010

**Vision:** Center for high-throughput bioscience with focus on genome, protein profiling, bioimaging and bioinformatics with relevance for human diseases



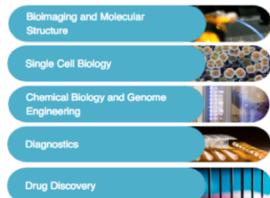
**SciLifeLab**  
STOCKHOLM

Science 328:805 (14 May 2010)



### Infrastructure resource for integrative omics

**SciLifeLab**

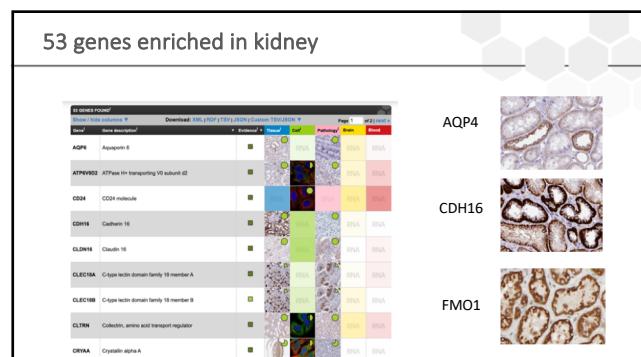
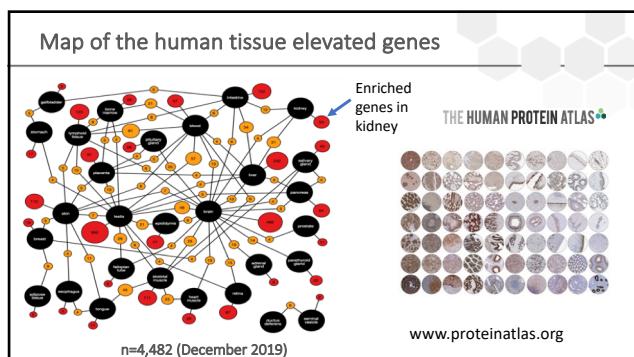
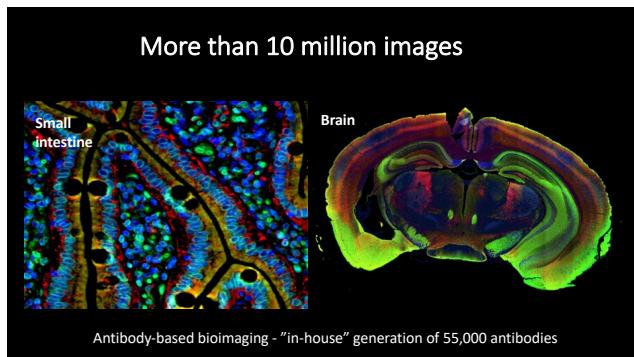
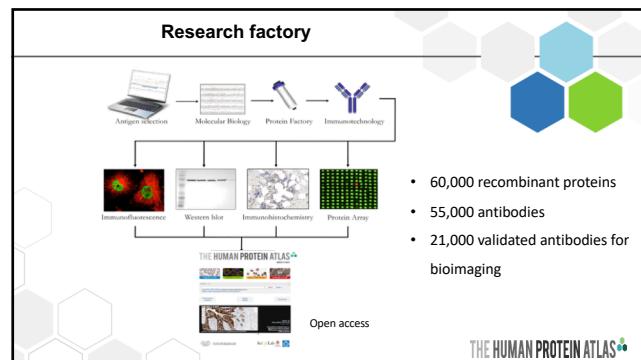
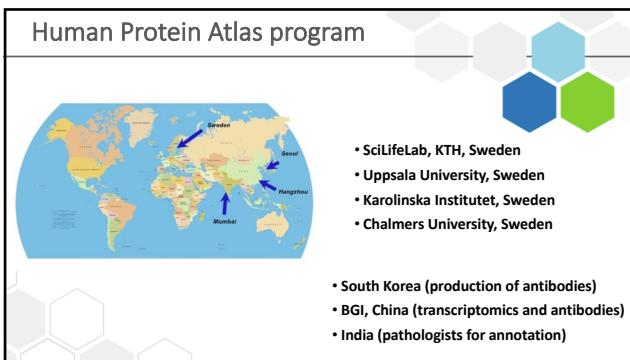


- Started in 2010
- 1 200 researchers
- More than 2000 projects in 2019



1.

The Human Protein Atlas



**Cell Atlas - Subcellular profiling (2017)**

**Science** AAAS

Thul et al (2017) "A subcellular map of the human proteome" Science 347: 394

**RESEARCH ARTICLE SUMMARY**  
A subcellular map of the human proteome

• Subcellular resolution (confocal)  
• Single cell variation

**THE HUMAN PROTEIN ATLAS**

**Pathology Atlas (2017)**

**Science** AAAS

Uhlen et al (2017) "A pathology atlas of the human cancer proteomes" Science 357(6352)

**RESEARCH ARTICLE SUMMARY**  
A pathology atlas of the human cancer proteomes

**Adil Mardinoglu**  
**Fredrik Ponten**

**THE HUMAN PROTEIN ATLAS**

**Science** AAAS

**The Human Blood Atlas**

December 20, 2019

**RESEARCH ARTICLE SUMMARY**  
A genome-wide transcriptomic analysis of protein-coding genes in human blood cells

**CONCLUSION** Our study of the blood transcriptome identifies a large number of genes that are differentially expressed between blood and other tissues. This analysis provides a detailed view of the gene expression landscape in blood and identifies a set of genes that are highly expressed in blood cells. These findings will help to improve our understanding of the biology of blood and its role in disease processes.

**Figure 1** shows a network of human blood cell types. Nodes represent individual genes, and edges represent interactions between genes. The network is color-coded by cell type, with nodes for neutrophils, monocytes, and macrophages being red, nodes for erythrocytes and platelets being orange, and nodes for T cells, B cells, and NK cells being purple. The network also includes nodes for mast cells, dendritic cells, and myeloid DCs.

**Analysis of single blood cell types**

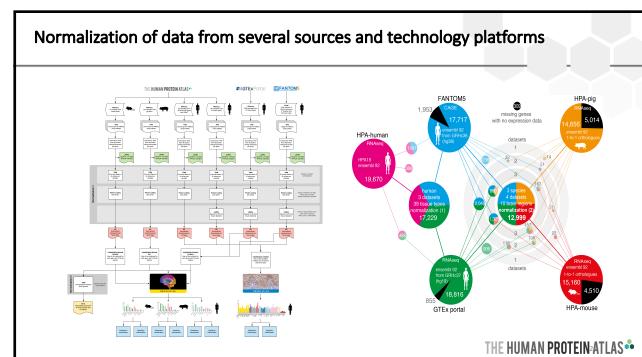
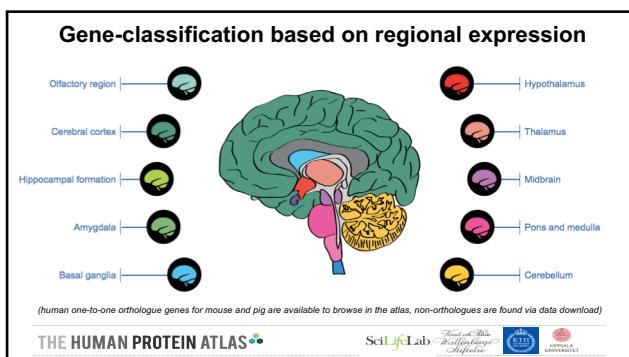
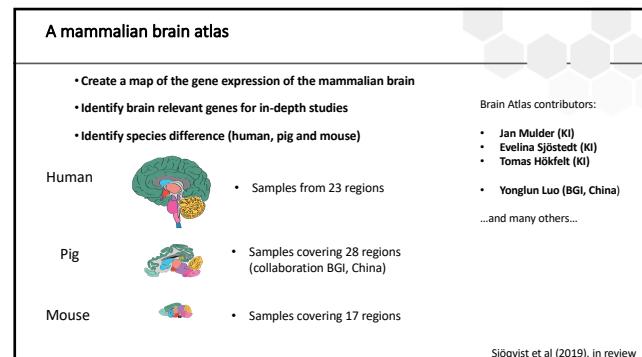
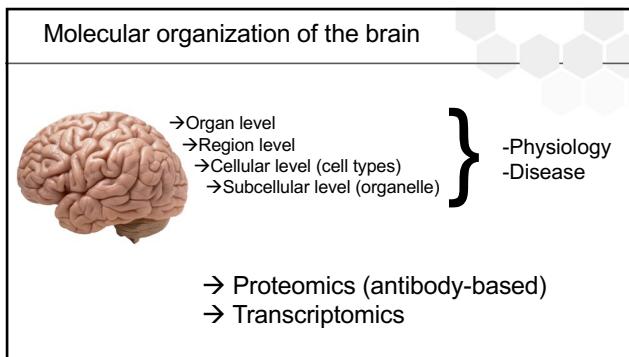
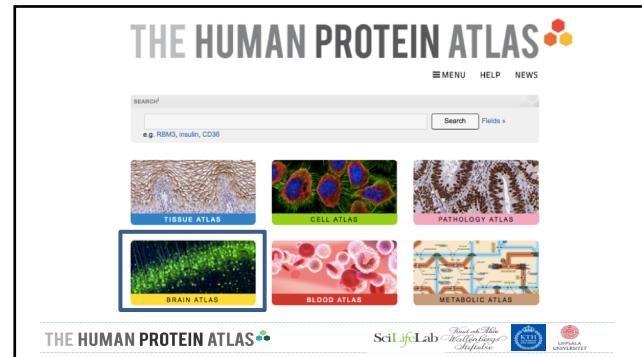
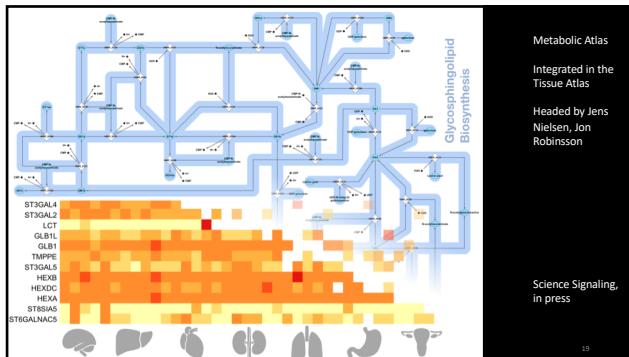
**A**

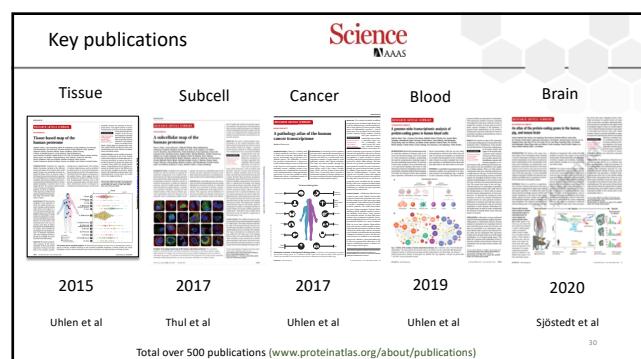
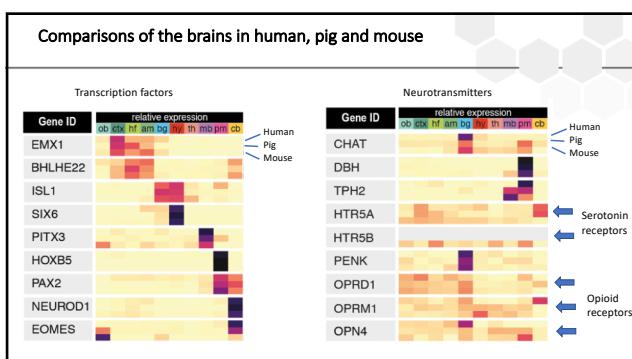
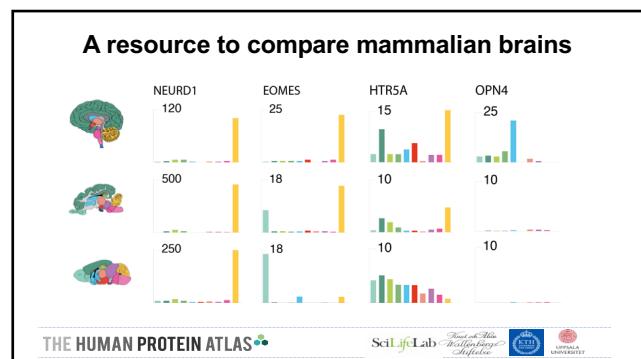
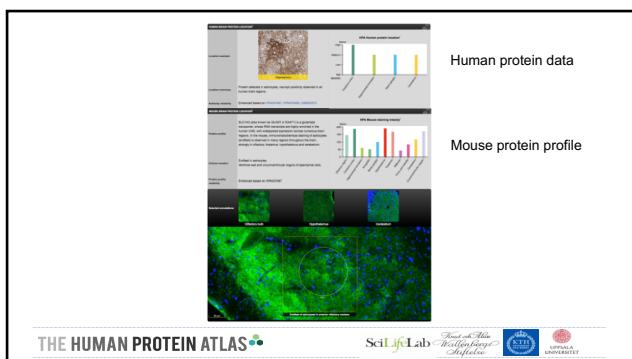
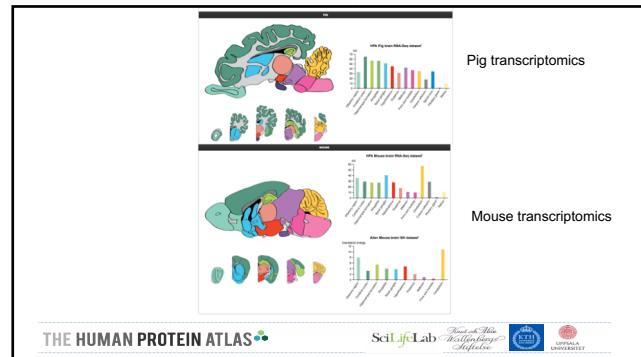
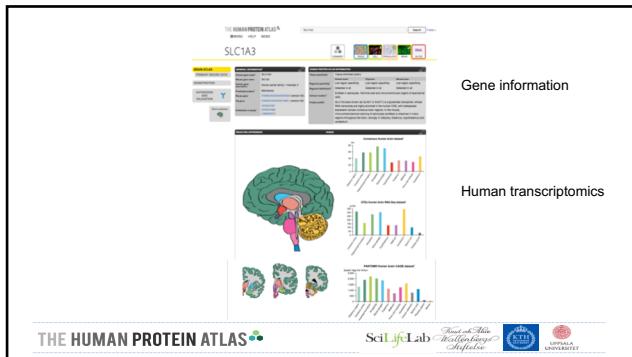
**B**

**Blood specific genes**

**Regulatory T-cell enriched genes**

Genes include CTLA4, FOXP3, CCR8, BFSP2, and C1orf53.





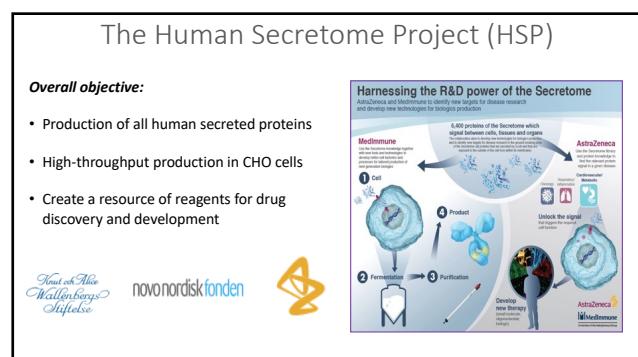
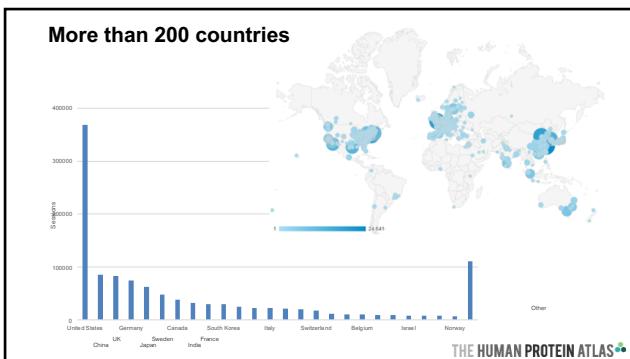
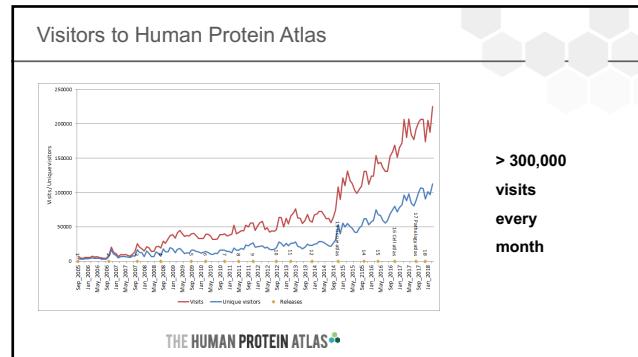
**Version 19.2 launched this week**

New summary page

CD19

Disease involvement included in the summary

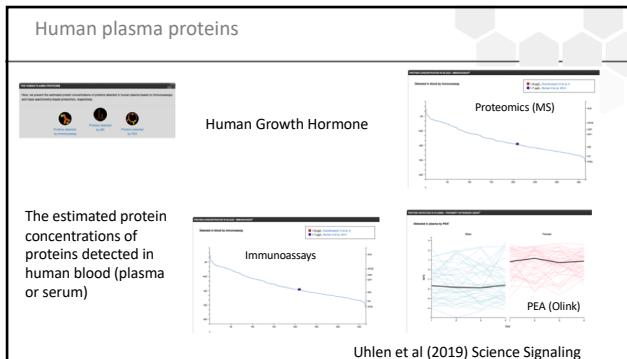
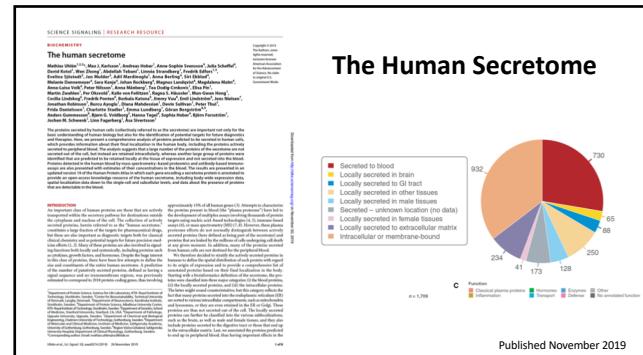
THE HUMAN PROTEIN ATLAS



**Human Secretome Project**

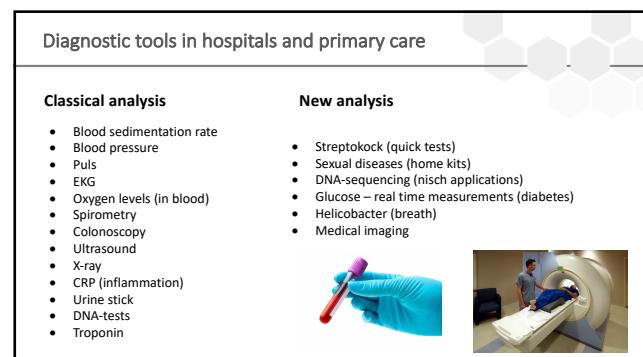
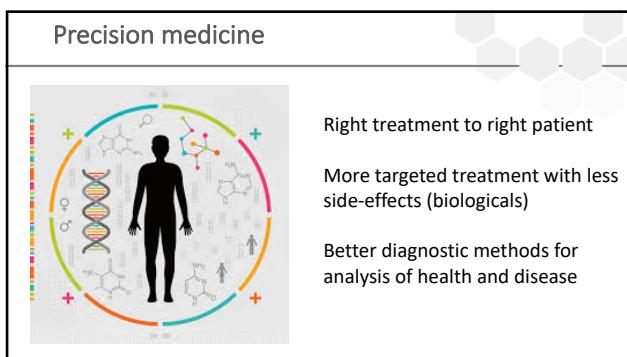
- 3017 genes have been generated with synthetic biology
- 1600 bioactive proteins have been produced in CHO cells.
- Phenotypic assay have been run in collaboration with AstraZeneca

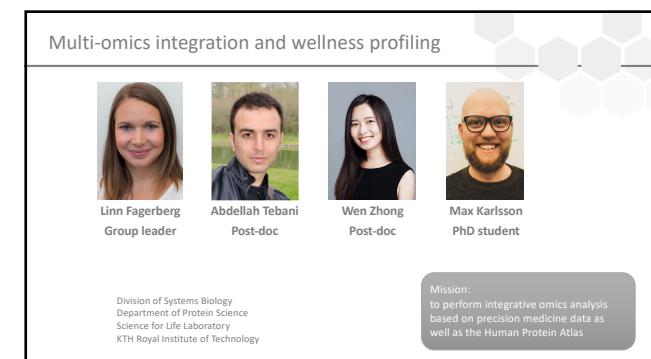
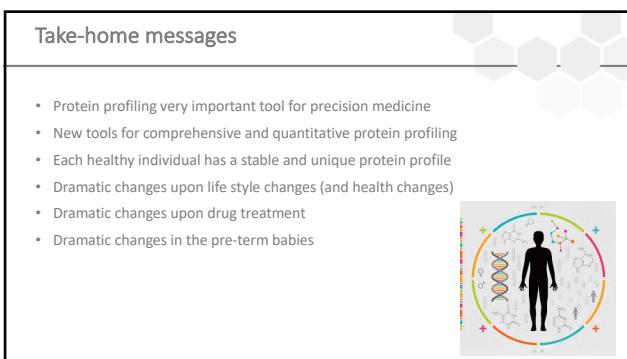
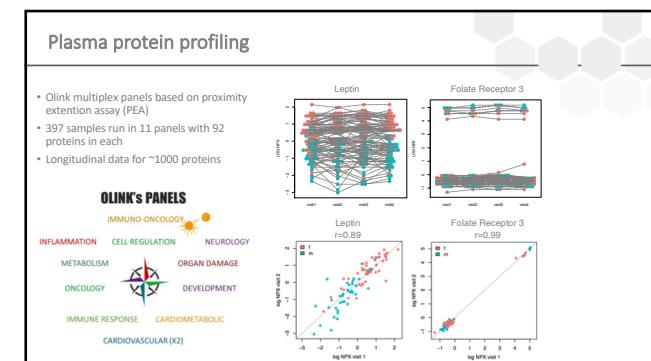
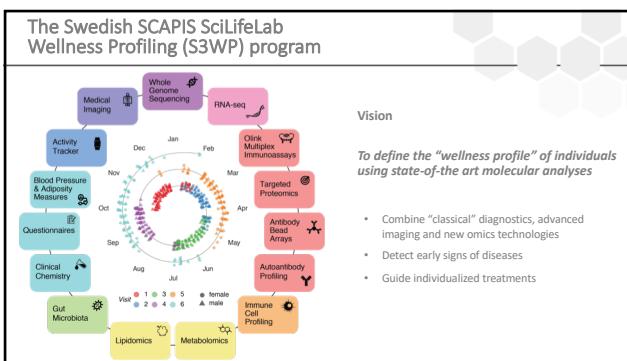
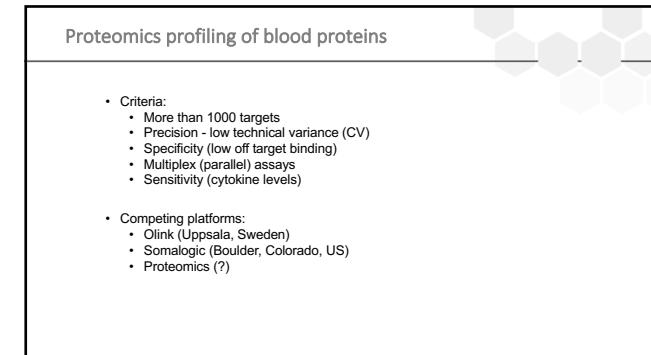
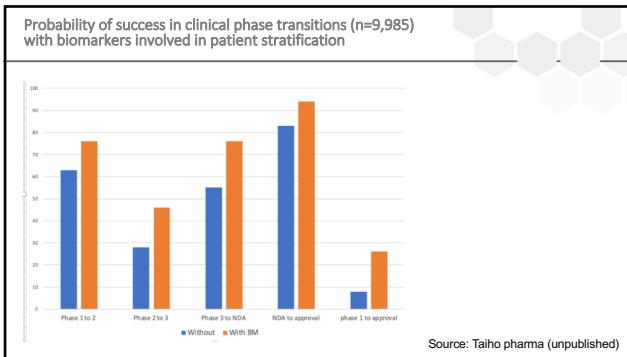
KTH Royal Institute of Technology, Novo Nordiskfonden, AstraZeneca IMED Biotech Unit



3.

Precision medicine





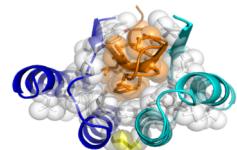
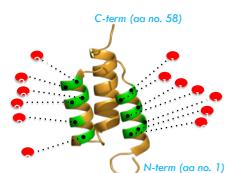
# 5.

## Biological drugs

### Next generation antibody therapeutics



Next generation scaffold binders to targets of pharmaceutical interest



Affibody binding to beta-amyloid

### Affibody - the advantage of small size



### Psoriasis – A Severe Disease

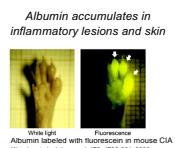
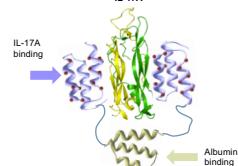


Psoriasis Area Severity Index (PASI)

### Ligand trap – Complete Blocking at Disease Site



Tri-specific ligand trap completely captures IL-17A homodimer



Complete blocking at the right site enables molecular healing

# 6.

## Concluding remarks

How many proteins in humans ?		
Type	Number	Comment
Protein-coding genes	19,670	The protein existence confirmed for 17,723 genes (90%)
Splice variants (isoforms)	82,271	So far, few examples of new functionalities (but interesting to explore)
Protein modifications	>200,000	Modulate activity in enzymes and signal pathways
Somatic re-arrangements	>20,000,000	The creation of immunological memory (IgG and T-cell receptors)

Evidence for protein-coding genes

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Altogether 19,670 predicted protein-coding genes (September 2019)

- 17,723 with evidence on the protein level (mainly antibody-based)
- 1,833 with evidence on transcriptional level
- 114 with no evidence (keratins, olfactory receptors and AC genes)



## Evidence for protein existence – chromosome summary

**PROTEIN EVIDENCE**

**Legend:**

- Green: Evidence at protein level
- Yellow: Evidence at transcript level
- Grey: No evidence

**Data from:**

- UniProt
- HPA
- NextProt
- PeptideAtlas (MS)

Chromosome	Protein ID	Protein Name	Gene ID	Gene Name	Protein Existence Summary
1	P00001	ATP5A	ATP5A	ATP5A	High (Protein Level)
2	P00002	ATP5B	ATP5B	ATP5B	High (Protein Level)
3	P00003	ATP5C	ATP5C	ATP5C	Medium (Protein Level)
4	P00004	ATP5D	ATP5D	ATP5D	Medium (Protein Level)
5	P00005	ATP5E	ATP5E	ATP5E	Medium (Protein Level)
6	P00006	ATP5F	ATP5F	ATP5F	Medium (Protein Level)
7	P00007	ATP5G	ATP5G	ATP5G	Medium (Protein Level)
8	P00008	ATP5H	ATP5H	ATP5H	Medium (Protein Level)
9	P00009	ATP5I	ATP5I	ATP5I	Medium (Protein Level)
10	P00010	ATP5J	ATP5J	ATP5J	Medium (Protein Level)
11	P00011	ATP5K	ATP5K	ATP5K	Medium (Protein Level)
12	P00012	ATP5L	ATP5L	ATP5L	Medium (Protein Level)
13	P00013	ATP5M	ATP5M	ATP5M	Medium (Protein Level)
14	P00014	ATP5N	ATP5N	ATP5N	Medium (Protein Level)
15	P00015	ATP5O	ATP5O	ATP5O	Medium (Protein Level)
16	P00016	ATP5P	ATP5P	ATP5P	Medium (Protein Level)
17	P00017	ATP5Q	ATP5Q	ATP5Q	Medium (Protein Level)
18	P00018	ATP5R	ATP5R	ATP5R	Medium (Protein Level)
19	P00019	ATP5S	ATP5S	ATP5S	Medium (Protein Level)
20	P00020	ATP5T	ATP5T	ATP5T	Medium (Protein Level)
21	P00021	ATP5U	ATP5U	ATP5U	Medium (Protein Level)
22	P00022	ATP5V	ATP5V	ATP5V	Medium (Protein Level)
X	P00023	ATP5W	ATP5W	ATP5W	Medium (Protein Level)
Y	P00024	ATP5X	ATP5X	ATP5X	Medium (Protein Level)

*Chromosome 1 Protein Evidence Summary:*

Protein ID	Protein Name	Gene ID	Gene Name	Protein Existence Summary
P00001	ATP5A	ATP5A	ATP5A	High (Protein Level)
P00002	ATP5B	ATP5B	ATP5B	High (Protein Level)
P00003	ATP5C	ATP5C	ATP5C	Medium (Protein Level)
P00004	ATP5D	ATP5D	ATP5D	Medium (Protein Level)
P00005	ATP5E	ATP5E	ATP5E	Medium (Protein Level)
P00006	ATP5F	ATP5F	ATP5F	Medium (Protein Level)
P00007	ATP5G	ATP5G	ATP5G	Medium (Protein Level)
P00008	ATP5H	ATP5H	ATP5H	Medium (Protein Level)
P00009	ATP5I	ATP5I	ATP5I	Medium (Protein Level)
P00010	ATP5J	ATP5J	ATP5J	Medium (Protein Level)
P00011	ATP5K	ATP5K	ATP5K	Medium (Protein Level)
P00012	ATP5L	ATP5L	ATP5L	Medium (Protein Level)
P00013	ATP5M	ATP5M	ATP5M	Medium (Protein Level)
P00014	ATP5N	ATP5N	ATP5N	Medium (Protein Level)
P00015	ATP5O	ATP5O	ATP5O	Medium (Protein Level)
P00016	ATP5P	ATP5P	ATP5P	Medium (Protein Level)
P00017	ATP5Q	ATP5Q	ATP5Q	Medium (Protein Level)
P00018	ATP5R	ATP5R	ATP5R	Medium (Protein Level)
P00019	ATP5S	ATP5S	ATP5S	Medium (Protein Level)
P00020	ATP5T	ATP5T	ATP5T	Medium (Protein Level)
P00021	ATP5U	ATP5U	ATP5U	Medium (Protein Level)
P00022	ATP5V	ATP5V	ATP5V	Medium (Protein Level)
P00023	ATP5W	ATP5W	ATP5W	Medium (Protein Level)
P00024	ATP5X	ATP5X	ATP5X	Medium (Protein Level)

Initiative	Funding
Human Protein Atlas (Europe/Asia)	Wallenberg Foundation
Allen Brain and Cell Atlas (USA)	Paul Allen (Microsoft)
Human Cell Atlas (US and Europe)	Chan-Zuckerberg (Facebook)
Project Baseline - Verily (USA)	Google
Watson Health (USA)	IBM

# Funding



 **Knut and Alice Wallenberg Foundation**

 **VINNOVA**

 **Novo Nordisk Foundation**

 **THE ERLING PERSSON FAMILY FOUNDATION**

 **Hjart & Lungfonden**

 **ELIXIR**

- ⌚ **Wallenberg Foundation (Human Protein Atlas project)**
- ⌚ **VINNOVA (CellNova)**
- ⌚ **Novo Nordisk Foundation (Center for Biostainability) – until end of 2020**
- ⌚ **Erling Persson Foundation (Precision medicine) – until end of 2020**
- ⌚ **Heart and Lung Foundation (Biobank profiling)**
- ⌚ **ELIXIR – sharing of data resources**

