

# Explore Proteins with Unknown Function

By the Use of Prestige Antibodies®





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## Creation of a Whole Genome-based Human Protein Atlas

The human genome sequence was first published 2001 and an ambitious effort was initiated in 2003 to create a comprehensive human protein atlas based on the genome sequence. This effort resulted in an impressive resource of human protein expression profiles in a multitude of normal tissues, cancer cells, and cell lines with validated Prestige Antibodies as reagents. Today, more than 11,200 human genes have been analyzed within this effort and the results are publicly available on the Human Protein Atlas web portal ([proteinatlas.org](http://proteinatlas.org)).<sup>1,2</sup> Each year, protein expression and localization data of approximately 2,500 new proteins are added to the portal. By 2015, a first draft of the localization of the full human proteome will be ready.

## Antibodies for Proteins with Unknown Function

Prestige Antibodies are unique in the way they are developed by a strategy originating from genome sequence and not from knowledge about defined proteins. Bioinformatics tools were developed to select 50-150 amino acid antigen regions from coding parts of the genome and exclude regions with high sequence identity to other human proteins.<sup>3</sup>

Today, 2,959 (26%) out of 11,348 published Prestige Antibodies on the Human Protein Atlas are directed against target proteins with no "evidence at protein level" according to the Universal Protein Resource (UniProt) database. The Prestige Antibody catalog is thus unique by containing so many antibodies towards proteins with unknown function and the Human Protein Atlas can assist in learning more about these proteins.

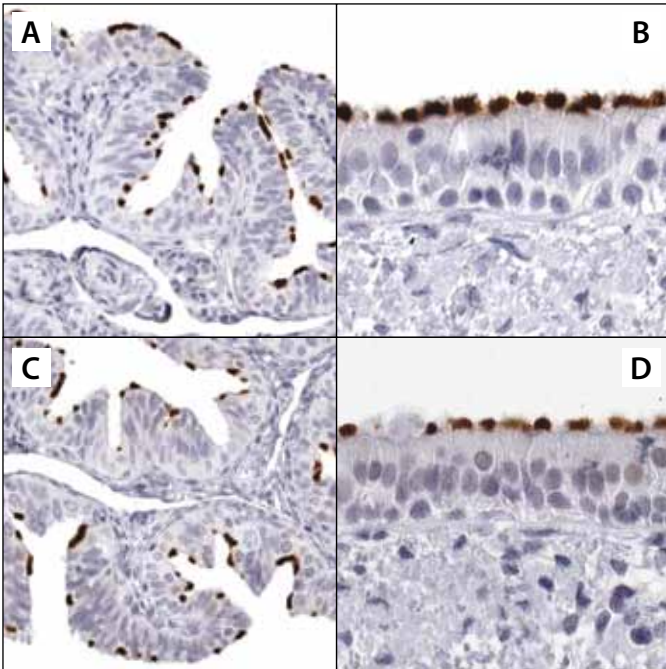
The Human Protein Atlas database can be searched for specific proteins using a string of queries including protein expression patterns, protein classes, validation of antibodies etc. Protein expression data are presented from 46 normal human tissue samples, 432 human cancer samples covering the 20 most common cancer types, and from 59 different human cells and cell lines.<sup>4</sup> By narrowing search criteria, proteins with selective or cell type-specific expression patterns can be found. The three examples shown in **Figure 1, 2, and 3** were found using the new and advanced search functions in the Human Protein Atlas database.

In version seven of the Human Protein Atlas (November 2010), annotated protein expression was introduced with the presentation of the combined results from several independent antibodies directed against the same protein target. Similar protein expression profile results from several Prestige Antibodies towards non-overlapping regions of the same target strengthen the annotation of unknown targets.<sup>2</sup>

## Location Information Enhances Understanding

Data on where proteins are localized within tissues and cells provide important information as to what basic functions a protein may have, as well as a possibility to map possible other interacting proteins.

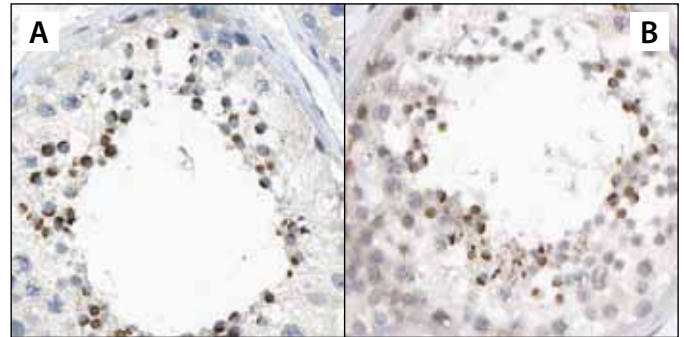
In **Figure 1**, Prestige Antibodies generated towards the putative protein encoded by the C1orf114 gene show a distinct and highly specific immunoreactivity in ciliated cells from different tissues. Four different antibodies towards non-overlapping regions of this alleged protein have been generated and all four show the same pattern of immunostaining. The results from two of these (HPA027281 and HPA027189) are shown in fallopian tube and nasopharyngeal mucosa. The corresponding images display a localized expression of the C1orf114 protein in cilia of surface epithelial cells, indicating this protein is involved in cilia function.



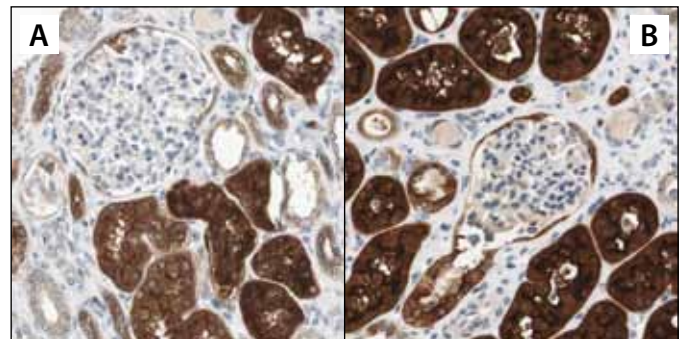
**Figure 1.** Immunohistochemical staining using Anti-C1orf114 antibodies HPA027281 (A, B) and HPA027189 (C, D) in human fallopian tube tissue (A, C) and human nasopharyngeal tissue (B, D) shows strong immunoreactivity of ciliated epithelia. Recognition of target antigen is represented by brown color.

In **Figure 2**, two different Prestige Antibodies generated towards a putative protein encoded by the C9orf11 gene, for which there is only evidence of existence on a transcript level, show a highly specific immunoreactivity in the innermost layer of maturing cells in the seminiferous ducts of testis. The localization of immunoreactivity is well in accordance with the acrosome and thus these results indicate that this protein is involved in sperm maturation and function.

In **Figure 3**, two different Prestige Antibodies generated towards a putative protein encoded by the PDZK1 gene show immunoreactivity in cells from normal kidney. A clear cytoplasmic expression pattern is displayed in cells of proximal tubules with a tendency to accentuated expression in the luminal brush border. Distal tubules show only a weak signal and cells of the glomerulus appear negative.



**Figure 2.** Immunohistochemical staining using Anti-C9orf11 antibodies HPA015089 (A) and HPA015504 (B) in human testis tissue shows highly selective expression in acrosomes on spermatids. Recognition of target antigen is represented by brown color.



**Figure 3.** Immunohistochemical staining using Anti-PDZK1 antibodies HPA005755 (A) and HPA006155 (B) in human renal tissue shows strong specific expression in proximal tubules. Recognition of target antigen is represented by brown color.

## Prestige Antibodies for Well Known Targets

In parallel to the analysis of proteins with unknown function, well characterized proteins are also targets for Prestige Antibody production. The reliable results achieved from these act as the optimal quality control for the whole Human Protein Atlas project.



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## Summary

- Prestige Antibodies are developed from a genome-based strategy and 1/4 of the Prestige Antibodies are directed against not yet characterized protein targets
- Several independent Prestige Antibodies against different regions of the same target protein verify the specific expression pattern of the target
- Proteins with selective or cell type-specific expression patterns can be found using the search tools in the Human Protein Atlas database
- More than 500 IHC images from normal and diseased human tissues and cells are presented for each Prestige Antibody on the Human Protein Atlas portal ([prote atlas.org](http://prote atlas.org))

## References

- (1) Uhlén M, Björling E, Agaton C, Szgyarto CA, Amini B, Andersen E, Andersson AC, Angelidou P, Asplund A, Berglund L, Bergström K, Hansson M, Hober S, Kampf C, Pontén F, et al. A Human Protein Atlas for Normal and Cancer Tissues Based on Antibody Proteomics. *Mol Cell Proteomics* **2005** 4(12):1920-1932.
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- (4) Pontén F, Jirstrom K, Uhlén M. The Human Protein Atlas – a tool for pathology. *J Pathology* **2008** 216(4):387-93.

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