

## **HUPO-HAI: The Human Protein Atlas and HAI antibody catalogue.**

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The completion of the human genome sequence has opened up a possibility for global expression profiling of human tissues and cells, allowing for comparative studies between normal and disease tissues. A multi-disciplinary program has created a "Human Proteome Resource" by systematic exploration of the human proteome using antibody-based tissue proteomics, combining high-throughput generation of mono-specific antibodies (affinity-purified) with protein profiling in human tissues and cells using tissue microarrays. Recombinant protein fragments selected from unique regions called Protein Epitope Signatures Tags (PrESTs) were used as immunogens to generate antibodies. Analysis of protein expression patterns was performed on tissue and cell microarrays containing >700 spots of normal and cancer tissues as well as *in vitro* cultured cells.

We have used this strategy to construct a comprehensive, antibody-based protein atlas for expression and localization profiles in 48 normal human tissues and 20 different cancers. The results are presented in a publicly available database containing images and data from protein profiling using over 3,000 antibodies. Each image has been manually annotated and curated by a certified pathologist to provide a knowledge base for functional studies and to allow searches and queries about protein profiles in normal and disease tissue. Our results suggest that it should be possible to extend this analysis to a majority of all human proteins thus providing a valuable tool for medical and biological research. We believe that the presented approach combining immunohistochemistry and tissue microarray technology can be used as an effective strategy to identify and evaluate novel markers, with potential clinical importance, of cell lineages and tumors.

A subset of antibodies showing selective immunoreactivity were selected for an extended analysis in tumors from defined patient cohorts. Specially designed TMA's (tissue microarrays) contain over 100 different tumors from patients with a defined tumor type and an extended analysis has shown that for several potential biomarkers, protein expression levels correlates with various clinico-pathological parameters, including overall survival of respective patients. Using this strategy several new markers of potential clinical importance have been analyzed. One example includes a recently discovered transcription factor that was identified as a useful diagnostic marker, with 80% sensitivity and 95% specificity for colo-rectal carcinoma. When combined with an antibody recognizing keratin 20 sensitivity increased to 95%. In addition, the extended analysis showed that a group of patients with tumors lacking expression of this transcription factor had significantly poorer outcome.

### **References**

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