

Clinical Proteomics Group's research projects:

The study of human proteome was shown to be complementary with the study of human genome for the analysis and understanding of complex pathological processes. The aim of the research carried out in our group is to apply proteomic tools – protein separation and identification techniques - to clinical questions: understanding of pathobiological mechanisms and search for new diagnostic, prognostic or therapeutic biomarkers. These objectives are reflected in the strong links existing with the Laboratory Medicine Service of the Geneva University Hospitals (HUG), in particular the Clinical Proteomics Laboratory, and in the numerous collaborations with medical units. Our main axes of research are exocrine pancreas diseases, renal diseases, toxicoproteomics and the bacterium *Staphylococcus aureus*.

The thematic of the exocrine pancreas is developed in collaboration with the Division of Gastroenterology of the HUG. We are studying animal models of acute pancreatitis in order to understand mechanisms controlling the course of the disease. Our objective is to identify factors responsible for the progression to severe, and potentially lethal, forms of the illness. The identification of such factors could allow the development of new prognostic biomarkers of acute pancreatitis. As part of our collaboration with the Division of Gastroenterology, we are also working on the proteomic analysis of bile. The goal is to identify in this biological fluid biomarkers of malignant etiologies of biliary duct strictures (pancreatic cancer and cholangiocarcinoma) using comparative proteomic analysis.

A second thematic, developed in collaboration with the Service of Pathology of the HUG, is the search for biomarkers of proteinuria of glomerular origin. As part of this study, we analyzed the proteome of vesicles produced by cells characteristic of the glomerular filter, the podocytes. The analysis of podocytes vesicles purified from healthy subjects and patients with various renal diseases allowed the detection of several proteins of interest that are currently in the process of validation.

In collaboration with the Genomic Research Lab at the HUG, we are also studying the bacterium *Staphylococcus aureus*. This germ, due to its potential virulence and its frequent resistance to numerous antibiotics, is a major actor of hospital-acquired infections. Several studies have then been performed to characterize *Staphylococcus aureus* proteome and investigate antibiotic resistance phenomena.

Finally, we recently started, in collaboration with the Swiss Institute of Bioinformatics, Microsoft-Research and the Service of Oncology of the HUG, a new project aiming at the identification of blood proteins post-translational modifications induced by xenobiotics. The finality of this project is the development of new analytical and bioinformatics tools that could be used in clinical applications for the diagnosis of acute or chronic intoxications and for therapeutic follow-up.

In addition to the understanding of biological processes and the identification of disease biomarkers, these projects imply continuous efforts for technological and methodological developments. Accordingly, we are working in collaboration with the Swiss Institute of Bioinformatics, Genebio SA and the Geneva Engineering School for developing tools to be applied at different steps of the proteomic workflows: fractionation of complex peptides mixtures, analysis of mass spectrometry data and multiplex immunoassays.

Group's publications:

How shall we use the proteomics toolbox for biomarker discovery?

JOURNAL OF PROTEOME RESEARCH

2007 vol. 6 pp. 3371-3376.

LESCUYER, P, HOCHSTRASSER, D, RABILLOUD, T

Proteomic approach to investigate MRSA

METHODS IN MOLECULAR BIOLOGY

2007 vol. 391 pp. 179-199

FRANCOIS, P, SCHERL, A, HOCHSTRASSER, D, SCHRENZEL, J

Using bioinformatic resources in the proteomic analysis of biological fluids

PROTEOMICS CLINICAL APPLICATIONS

2007 vol. 1 pp. 900-915

LISACEK, F, HOOGLAND, C, LESCUYER, P, HOCHSTRASSER, D, APPEL, RD

Impact of preanalytical variables on the analysis of biological fluids in proteomic studies

PROTEOMICS CLINICAL APPLICATIONS

2007 vol. 1 pp. 739-746

FERGUSON, RE, HOCHSTRASSER, DF, BANKS, RE

Correlation between cardiac biomarkers and right ventricular enlargement on chest CT in non massive pulmonary embolism

THROMBOSIS RESEARCH

2007 in press

VUILLEUMIER, N, RIGHINI, M, PERRIER, A, ROSSET, A, TURCK, N, SANCHEZ, JC, BOUNAMEAUX, H, LE GAL, G, MENSI, N, HOCHSTRASSER, D

State-of-the-art two-dimensional gel electrophoresis: a key tool of proteomics research

NATURE PROTOCOLS

2006 vol. 1 pp. 812-823.

CARRETTE, O, BURKHARD, PR, SANCHEZ, JC, HOCHSTRASSER, DF.

Exploring glycopeptide-resistance in *Staphylococcus aureus*: A combined proteomics and transcriptomics approach for the identification of resistance-related markers

BMC GENOMICS

2006 vol. 7 pp. 296-296

SCHERL A, FRANCOIS P, CHARBONNIER Y, DESHUSSES JM, KOESSLER T, HUYGHE A, BENTO M, STAHL-ZENG J, FISCHER A, MASSELOT A, VAEZZADEH A, GALLE F, RENZONI A, VAUDAUX P, LEW D, ZIMMERMANN-IVOL CG, BINZ PA

The molecular scanner in microscope mode

RAPID COMMUNICATIONS IN MASS SPECTROMETRY.

2006 vol. 20 pp. 3435-3442.

LUXEMBOURG, SL, VAEZADDEH, AR, AMSTALDEN, ER, ZIMMERMANN-IVOL, CG, HOCHSTRASSER, DF, HEEREN, RM

Gold coating of non-conductive membranes before matrix-assisted laser desorption/ionization tandem mass spectrometric analysis prevents charging effect

RAPID COMMUNICATIONS IN MASS SPECTROMETRY.

2005 vol 19 pp. 605-610.

SCHERL, A, ZIMMERMANN-IVOL, CG, DI DIO, J, VAEZZADEH, AR, BINZ, PA, AMEZDROZ, M, COCHARD R, SANCHEZ, JC, GLÜCKMANN, M, HOCHSTRASSER, DF

Prostaglandin D2 synthase and its post-tranlational modifications in neurological disorders

ELECTROPHORESIS

2005 vol. 26 pp. 4563-4570

LESCUYER P, GANDINI A, BURKHARD P, HOCHSTRASSER D, SANCHEZ JC

Correlation of proteomic and transcriptomic profiles of *Staphylococcus aureus* during the post-exponential phase of growth

JOURNAL OF MICROBIOLOGICAL METHODS

2005 vol. 60(2) pp. 247-257

SCHERL A, FRANCOIS P, BENTO M, DESHUSSES J, CHARBONNIER Y, CONVERSE V,
HUYGHE A, WALTER N, HOOGLAND C, APPEL RD, SANCHEZ JC, ZIMMERMANN C,
CORTHALS G, HOCHSTRASSER D, SCHRENZEL J

MSight: An image analysis software for liquid chromatography-mass spectrometry

PROTEOMICS

2005 vol. 5 pp. 2381-2384

PALAGI P, WALTHER D, MANFREDO Q, CATHERINET S, BURGESS J, ZIMMERMANN-
IVOL CG, SANCHEZ JC, BINZ PA, HOCHSTRASSER D, APPEL RD