



# Technological innovation around protein and cell biochip for diagnosis: a translational research from nanoworld to patient

Céline Elie-Caille, Alain Rouleau, Benoit Simon, Céline Heu, Géraldine Lucchi, W. Boireau, P. Ducoroy

## ► To cite this version:

Céline Elie-Caille, Alain Rouleau, Benoit Simon, Céline Heu, Géraldine Lucchi, et al.. Technological innovation around protein and cell biochip for diagnosis: a translational research from nanoworld to patient. Nanobiotechnology International Workshop: protein-surfaces interactions, Dec 2009, Ispra, European Union. hal-00447438

**HAL Id: hal-00447438**

**<https://hal.science/hal-00447438>**

Submitted on 15 Jan 2010

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

## Technological innovations around protein and cell biochip for diagnosis: a translational research from nanoworld to patient

**Céline Elie-Caille**<sup>1</sup>, Alain Rouleau<sup>1</sup>, Benoit Simon<sup>1</sup>, Céline Heu<sup>1</sup>, Géraldine Lucchi<sup>2</sup>,  
Wilfrid Boireau<sup>1</sup>, Patrick Ducoroy<sup>2</sup>

Clinical & Innovation Proteomic Platform:

<sup>1</sup>FEMTO-ST Institute, Université de Franche-Comté, CNRS, ENSMM, UTBM - 25044 Besançon, F.

<sup>2</sup>Centre Hospitalier Universitaire Dijon -CGFL – 21000 Dijon, F.

A great challenge in biosensors and diagnosis devices relies on the way to reconstitute relevant biological mechanisms on surface of the biochips and which analytical tools are convenient to provide accurate and rapid information on the structures and function of molecules attached to this surface. A better control in the realization of biochips can be obtained in combining different complementary approaches while always keeping in mind the biological key point. Researches in CLIPP are focused towards this objective.

Conception, realization and characterization of protein and cell chips are presented. We detail different strategies of materials engineering<sup>1,2,3</sup>, chemical functionalizations and biomolecular graftings<sup>4</sup>, molecular and cellular characterization in physiological conditions<sup>5,6</sup>, which lead to the optimization of “biorecognitions events” at the surface of the chip.

We present herein an original interdisciplinary approach, consisting to carry out in parallel a micro-scale analysis (SPR, fluorescence microscopy) and nano-scale characterizations (AFM, XPS, TOF-SIMS).

Concerning protein interfaces, we demonstrated in particular that the molecular orientation in a protein monolayer can be determined based on the specific fragment ions from the protein in TOF-SIMS spectra<sup>7</sup>. These developments have also contributed to the establishment of a new biomolecular interaction analysis/mass spectrometry (BIA-MS) combination based on an entire “on-a-chip” procedure<sup>8</sup>. We report a low-cost approach combining Biacore 2000 analysis with homemade chips and MS and MS/MS identification directly onto the chips without elution step. Using this technique, identification of protein complexes were routinely obtained giving the opportunity to the “on-a-chip” processing to complete the BIA-MS approach in the discovery and analysis of protein complexes in biological fluids.

Our interest is also focused on cell/surface interaction. The cell biochips we are developing consist either of circulating or adherent cells, that we characterized in terms of cell capture on biofunctionalized surface or growth with substrate dependency respectively. Parameters such as cell spreading, growth, morphology, and topography are particularly investigated and controlled by atomic force microscopy in physiological conditions<sup>6</sup>.

With the aim to increase the throughput of analysis, we are currently working on cell and protein micro-arrays. Our expertise in cell and protein biochip preparation, and competences in micro- to nanoscale characterization in liquid conditions, represents precious assets enabling a relevant clinical proteomic research, thanks to deeply controlled steps of biosensor development and use.

<sup>1</sup>Elie-Caille C, Rauch J-Y, Rouleau A, Boireau W (2009). Preparation of flat gold terraces for protein chip developments. *Micro & Nano Letters*, 4(2), 88-94.

<sup>2</sup>A. Renier, T. Mangeat, H. Benalia, C. Elie-Caille, C. Pieralli and B. Wacogne (2010). Gold/Silica thin film for biosensors applications: Metal Enhanced Fluorescence. *Laser Physics* issue 3, (To be published).

<sup>3</sup>T. Mangeat, A. Berthier, C. Elie-Caille, M. Perrin, W. Boireau, C. Pieralli and B. Wacogne (2009). Gold/Silica biochips: applications to surface plasmon resonance and fluorescence quenching. *Laser Physics*, 19, 252-258.

<sup>4</sup>Berthier A., Elie-Caille C., Lesniewska E., Delage-Mourroux R., Boireau W. (2008). Nanobioengineering and characterization of a novel estrogen receptor biosensor. *Sensors*, 8, 4413-4428.

<sup>5</sup>Elie-Caille C, Severin F, Helenius J, Howard J, Muller DJ, Hyman AA (2007). Straight GDP-Tubulin Protofilaments Form in the Presence of Taxol. *Current Biology*, 17 (20), 1765-1770.

<sup>6</sup>Elie-Caille C, Heu C, Guyon C, Nicod L (2009) Morphological damages of a glyphosate-treated human keratinocyte cell line revealed by a micro- to nano-scale microscopic investigation. *Cell Biol Toxicol.* (submitted).

<sup>7</sup>Aoyagi S, Rouleau A, Boireau W (2008). TOF-SIMS structural characterization of self-assembly monolayer of cytochrome b5 onto gold substrate. *Applied Surface Science* 255(4), 1071-1074.

<sup>8</sup>Boireau W, Rouleau A, Lucchi G, Ducoroy P (2009). Revisited BIA-MS combination: entire "on-a-chip" processing leading to the proteins identification at low femtomole to sub-femtomole levels. *Biosens Bioelectron.* 4(5):1121-1127.