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

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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[1,2,3], chemical functionalizations and biomolecular graftings[4], molecular and cellular characterization in physiological conditions[5,6], 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[7]. 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[8]. 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[6].

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.

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