Innovative brain/tumor interfaces technologies for the local theranostic deciphering of tumor complexity: from CLINATEC explorer project to Medimprint start up

Ali Bouamrani[3], Affif Zaccaria[2], Brieuc Turluche[2], Adrien Monbrun[3], M Dreyfus[1], L Selek[1], P Durand[1], S Chabardes[3], E Seigneuret[1], Frederic X. Gaillard[4], F Berger[1]
1 Clinatec Lab, U 1205, INSERM-UJF-Grenoble Hospital. France
² Medimprint-Grenoble-France
3 Clinatec- Leti- Grenoble-France
4Departement Technologies Silicium, CEA Léti, Grenoble, France
Contact : fberger@ujf-grenoble.fr- zaccaria.affif@gmail.com

Finding biomarkers to detect earlier and prevent human diseases, treating them specifically, in a personalized and nonlesional ways are key medical priorities. We are moving from anatomopathological medicine (detecting and treating pathology at the macroscopic level) to cellular and molecular medicine (detecting and treating at the micro-nano-level). The success of targeted therapies is now limited by the induction of molecular resistances, side effects related to systemic diffusion, tumor heterogeneity and the need for new peritumoral microenvironment targets.
Lack of adequate technology to catch the low concentrated theranostic biomarkers, inaccessibility of the peritumoral targets as well as the need for more relevant animal models probably explain the major delay observed in molecular annotation and therapy for brain diseases.
Deciphering the mechanisms of inaccessible Cancer/brain pathological areas and treating them locally with nonlesional technologies is mandatory.
The availability of a non-lesional micro-nano-invasive strategy to annotate and monitor tissue response to therapy is a crucial issue. In the medico-biological state of the art, this is performed by invasive lesional biopsies. In this context, the development of micro/nanotools devoted for tissue characterization is indispensable to annotate these inaccessible territories. Nanotechnologies introduced several high sensitivity devices, which should provide a micro-nano-invasive access to inaccessible human compartments.
We demonstrated that proteins could be captured from the microsurgery tools directly introduced into the human brain in area where it is impossible to implement a biopsy. We optimized the tool by the addition of specific chemical and micro/nanostructuration modifications. A small silicon chip was produced, and plugged on the metallic stylet. Surface modifications also provided the conservation of the spatial location of the molecular and cellular fingerprint inside the tissue. Extension to genomic as well as cell investigation was also validated as well alternative prototypes were developed to target other locations such as liver, lung, sarcoma, prostate and breast cancer. Multimodal imaging including MRI and *in situ* confocal imaging was also developed, unity to modify the local microenvironment. A pig glioblastome model was also developed.
More recently, we validate the first clinical efficacy of the GLIOPRINT technology in human glioblastoma patients paving the way for a new theranostic strategy. The completion of the translation at the bedside of this highly patented technology and the extension of the clinical application to phase II/III trials strongly supported the implementation of a company that will develop the industrial side of our research.

Ref: Zaccaria A, Bouamrani A, et al: A Micro-Silicon Chip for *in Vivo* Cerebral Imprint in Monkey. ACS Chem. Neurosci 2013, 4(3).