



Université Claude Bernard



## HABILITATION A DIRIGER DES RECHERCHES

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Titre de la thèse : « Bioprocédés de culture cellulaire: Application à la production de virus et à la médecine régénérative »



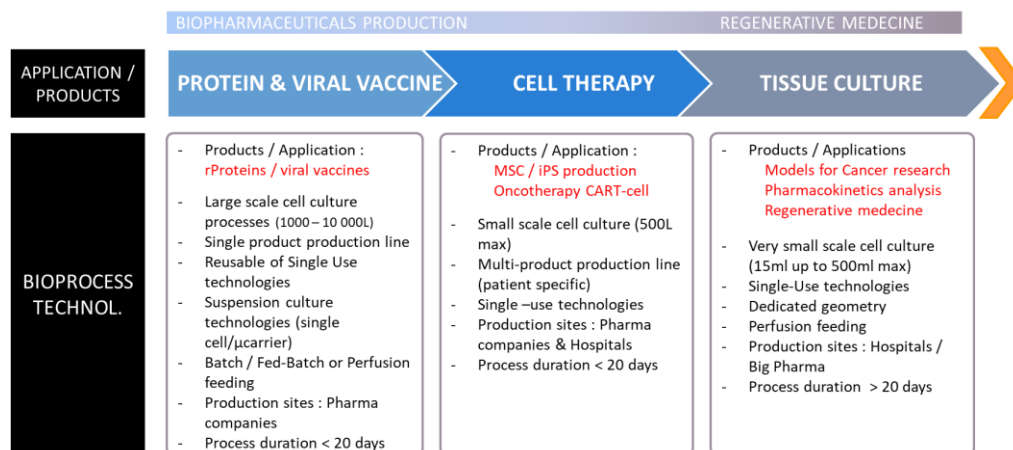
### Résumé

Cell-culture based bioprocesses are in-use at large scale since the 80's for bio-manufacturing operations. They now concern a wide range of applications including the production of therapeutic molecules (recombinant protein, monoclonal antibody) or vaccines (viral vaccine), the cell-based therapies (stem cells, CART cells with viral vectors), and more recently the production of living tissues for regenerative medicine. In general, cell-based processes are highly technological and necessitate a large range of expertise to allow for controlled production of qualified products. Science and expertise underlying the development of such processes are thus several and imply multi-disciplinarity.

Nowadays, multi-scale approaches are necessary to link cell physiology with metabolism, product interaction with the intracellular behaviours (ex. viral replication kinetics), cell differentiation with the process and equipment operated/implemented to provide and maintain optimal cells culture conditions. On the top of such considerations, analytical tools and methodologies allowing the characterization and quantification of both cell fate and generated product, are critical to reach high quality bioprocesses and understanding the fundamental biological mechanism. This approach is mostly described in FDA, and regulation agencies institution as the Quality by Design and Process Analytical Technology.

The proposed manuscript described the research strategy and applications I developed over the last 10 years on cell-based production processes applied to several application fields; vaccinology field with viral vaccine bioprocesses, cell-therapy/oncotherapy with viral vectors production bioprocesses and regenerative medicine field with tissue production and maturation bioprocesses.

The objective is to present and obtain a French Habilitation to conduct research (HDR) to pursue such research activities and to form a publishing group around these aspects within my current research team.



**Figure 1 \_ Cell based bioprocesses: development history.**

## 5 significant publications:

1. Pourchet L, Petiot E, Loubière C, Olmos E, Dos Santos M, Thépot A, Loïc BJ, Marquette CA, L. Pourchet, E. Petiot, C. Loubière, E. Olmos, M. Dos Santos, A. Thépot LBCM, Pourchet L, et al.: **Large 3D bioprinted tissue : heterogeneous perfusion and vascularization.** *Bioprinting* 2019, **13**:e00039.
2. Petiot E, Guedon E, Blanchard F, Geny C, Pinton H, Marc A, Gény C, Pinton H, Marc A: **Kinetic characterization of vero cell metabolism in a serum-free batch culture process.** *Biotechnol Bioeng* 2010, **107**:143–153.
3. Petiot E, Bernard-Moulin P, Magadoux T, Gény C, Pinton H, Marc A: **In situ quantification of microcarrier animal cell cultures using near-infrared spectroscopy.** *Process Biochem* 2010, **45**:1427–1431.
4. Petiot E, Ansorge S, Rosa-Calatrava M, Kamen A: **Critical phases of viral production processes monitored by capacitance.** *J Biotechnol* 2017, **242**.
5. Petiot E, Proust A, Traversier A, Durous L, Dappozze F, Gras M, Guillard C, Balloul J-M, Rosa-Calatrava M: **Influenza viruses production: Evaluation of a novel avian cell line DuckCelt®-T17.** *Vaccine* 2017, doi:10.1016/j.vaccine.2017.03.102.