BioMEMS – Integrative bio-engineering

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Differentiation of human iPS cells into hepatocyte-like cells in microfluidic bioreactors

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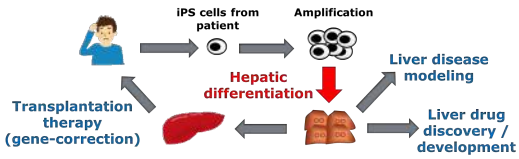
Host Professor: **Pr. Y. Sakai**

Keywords: **hepatocytes, hiPS cells, microfluidics**

Context



Potential applications of hiPS technology

Specific aim 1: Optimization of the maturation of hepatocyte-like cells derived from hiPS cells

Specific aim 2: Zonation of hepatic microtissues in microfluidic bioreactors

Status of consensus problems:

- Important demand for clinical, pharmacological, and fundamental research
- Current models not suitable for many applications

Objectives

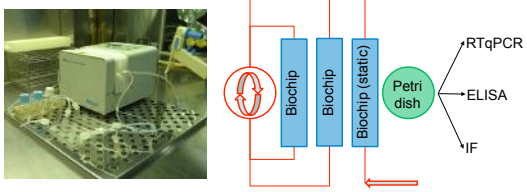
- Improve the functionality of hepatocyte-like cells
- Develop a model mimicking the liver tissue organization

Step	Growth factor	Cell differentiation	Protocol 1 (Si-Tayeb, 2010)	Protocol 2 (Kido, 2015)
0		iPS	Change medium daily	Change medium at D0, D1 and D3
1 (5 days)	Activin A	Definitive endoderm		
2 (5 days)	bFGF/BMP-4	Hepatocyte progenitor		
3 (5 days)	HGF	Hepatoblast progenitor		
4 (biochip, 7 days)	OSM	Mature like hepatocyte		

Differentiation protocols and associated commitment

Methods

Combination of technologies
1) cell model 1: human iPS cells
2) cell model 2: hepatocarcinoma cells
3) microfluidic bioreactor
4) dynamic culture



Microfluidic bioreactors connected to peristaltic pump and schematic of the general strategy

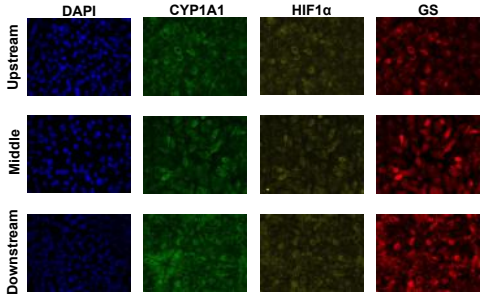
Results

Concerning specific aim 1

Optimization of the differentiation protocol for an improved maturation of hiPS cells towards adult hepatocyte profile.

Concerning specific aim 2

Zonation of the liver microtissue derived from hepatocarcinoma cells in a controlled manner.



Modification of the expression of specific markers along the bioreactor

Perspectives

(i) Development of a relevant model for translational research
(ii) Application in drug screening and detoxification for pharmaceutical industry
(iii) Promising strategy for personalized medicine

Publications

Submitted

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