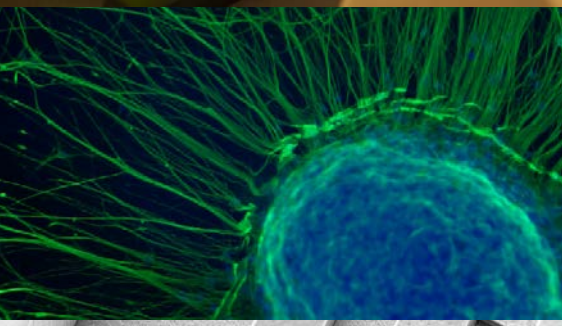

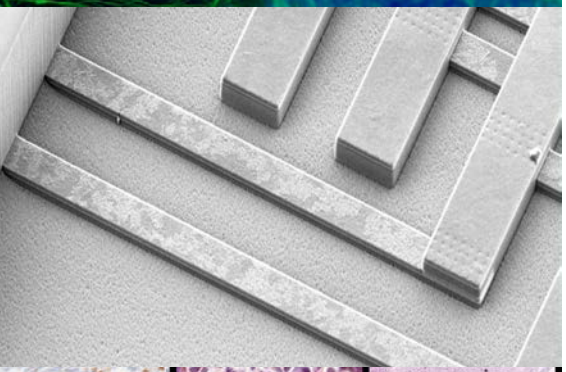

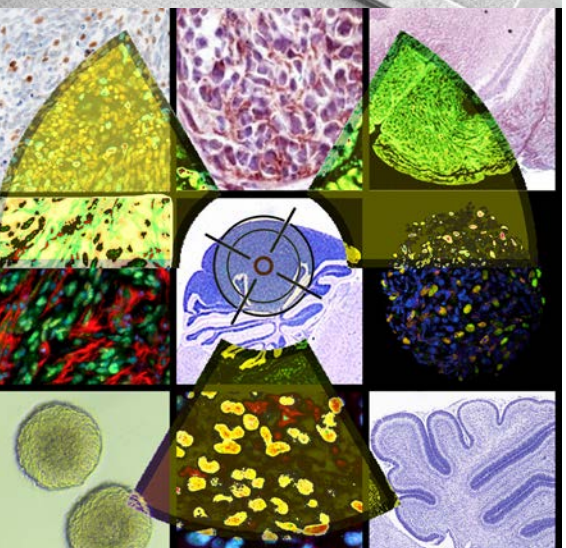

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European Commission

Sumcastec

PROJECT SUMMARY

SUMCASTEC explores radically new approach for **cancer stem cells** (CSCs) real time isolation (i.e. within minutes vs current 40 days) and **neutralization**. A novel **micro-optofluidic lab-on-chip** (LOC) platform will be developed through a joint and iterative efforts by biologists, clinicians and engineers. For the first time, a single LOC will be able to deliver ultra-wide broadband radiation to compare cell spectral signatures, image subcellular features, and hence modulate CSCs microenvironment conditions with unprecedent space and time resolution. It will be driven to isolate CSCs from heterogeneous differentiated and stem cell populations, and force CSCs differentiation, ultimately inducing sensitivity to anticancer treatments. In vitro and in vivo testing along with biophysical modelling will validate the approach and establish the proof-of-principle within the project life-time, while laying the ground work for further development of future electrosurgical tools that will be capable CSCs neutralization in tissue. This will not only establish a new line of treatment for brain cancers such as Gliobastoma Multiforme and Medulloblastoma, whose initiation and recurrence were linked to CSCs, and that claim tremendous human and economic tolls, worldwide.

All the required competences are gathered within a consortium of 6 partners:

1. Limoges University (France), involving EA 3842 and XLIM labs
2. Bangor University (UK),
3. IHP: Innovations for High Performance GMBH (Germany),
4. ENEA: Agenzia Nazionale per le Nuove tecnologie, l'Energia et lo sviluppo economico sostenibile (Italy),
5. Padova University (Italy),
6. CREO MEDICAL Limited (UK).

The SUMCASTEC project is planned over 42 months and started on January 1st 2017.

This project has received funding from the European Union's Horizon 2020 Framework Programme FET OPEN for Research and Innovation under grant agreement N° 737164

1. TARGETED BREAKTHROUGH

The targeted scientific breakthrough in SUMCASTEC is the world's first micro-optofluidic lab-on-chip platform enabling successively Cancer Stem Cells isolation (CSCs) via electromagnetic sensing and cell spectral signature identification, nanoscale imaging of targeted cells and their selective neutralization via electromagnetic radiations.

What we are going to characterize and selectively target CSCs, known to be deeply involved in cancer initiation and recurrence, through a technology capable of delivering individually broadband radiation to cells to establish their spectral signatures, imaging their subcellular features, and hence modulating their microenvironment conditions. Broadband EM radiation also delivered on-chip will be applied to achieve a selective neutralization of CSCs, notably by pushing their differentiation to enforce vulnerability to standard treatments.

2. LONG TERM VISION

The SUMCASTEC project is the first crucial step in a long term vision focusing on the development of new electrosurgical tools for in vivo therapeutic targeting of Cancer Stem Cells, thus preventing recurrence and ultimately treating cancers such as Glioblastoma Multiforme and Medulloblastoma. Successful CSC isolation from a mixed cell population and selective neutralization in a lab-on-chip environment constitute a quantum leap towards our long-term goal of electrosurgical treatment for brain tumors. It will take a further leap to overcome the huge heterogeneity of in vivo tissue conditions. Yet, the expected level of insight into CSCs function/response which will be possible through SUMCASTEC project will be essential to address these challenges.

3. SPECIFIC OBJECTIVES

CSCs will be detected and sorted on CMOS chip from a mixed differentiated and healthy cell population by a combination of microwave spectroscopy, nanoscale imaging and electromanipulation. Isolated CSCs will be selectively neutralized by delivering low-power ultra-wideband radiation to induce controlled depolarization of plasma/organelle membrane potential, trigger cell differentiation and enforce vulnerability to standard treatments. CSCs selective neutralization will be directly assessed by nanoscale imaging and though in vitro and in vivo validation protocols.

Within the duration of the project, we will target three main objectives.

- A novel Micro-optofluidic Lab-on-Chip platform build up with
  - Full integration of microfluidic channels and reservoirs, broadband high frequency sources and detectors, and nanoscale imaging modules into a Silicon Germanium (SiGe) CMOS environment;
  - EM stimulus tuned both in continuous wave (CW) format with 0.1 MHz-0.1THz frequency, 5 mW power, for low power CW sensing/stimulation, and in pulsed format with MV/m amplitude, ns-width, and KHz-repetition range, for membrane permeabilization and potential control;
  - Optical imaging with a 20 nm & 1ms resolution;
- Fast isolation, nanoscale imaging and selective neutralization
  - Detection, separation and mapping of intracellular properties and processes of CSCs;
  - Real time CSC isolation/neutralization from a mixed population;
- In vitro and in vivo validation
  - Demonstrate effective CSC neutralization with the absence of colony formation in vitro and the absence of tumour growth in vivo;
  - Demonstrate increased sensitivity of the neutralized CSCs to standard radiotherapy treatments by 30%