Glioblastoma (GBM) is an aggressive primary brain tumor affecting about 74,000 people worldwide each year. GBM has one of the lowest survival rates among all human cancers—most of the patients die within one year from the diagnosis and only 5% survive after 5 years. Treatment is initiated with a surgery to remove as much tumor as possible, followed by radiation and chemotherapy to slow the growth of the remaining tumor cells. Effect of chemotherapies remains limited due to poor blood-brain barrier (BBB) penetration, susceptibility to active efflux pump, hypoxic tumor environment and/or heterogeneous molecular biology… Despite progress (Figure 1) and emerging "out-of-the-box" alternatives to systemic therapies, GBM remains a notoriously difficult to treat cancer and new agents/new therapeutic modalities are actively sought to increase survival rate.

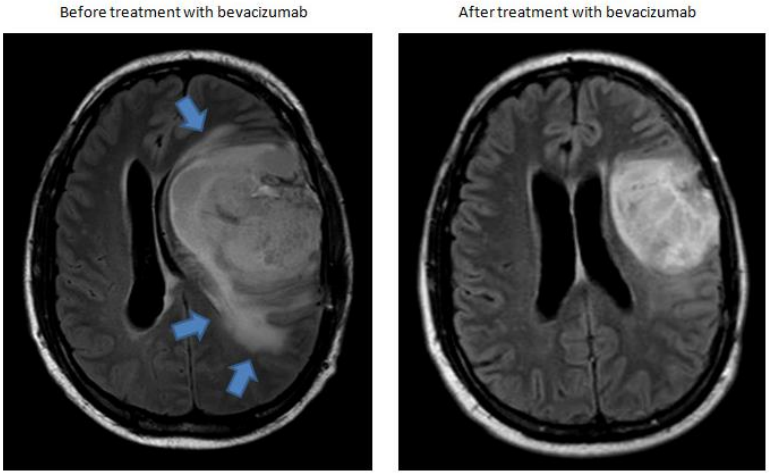

Figure 1: MRI images of recurrent GBM in a 44 y patient. Arrows indicate tumor associated vasogenic edema before bevacizumab treatment. Post treatment, edema significantly decreased showing a clinical benefit.

Immunotherapy emerged as a promising anti-cancer therapy in a broad range of indications. Preclinical evidences regarding the efficacy of different immunologic approaches (targeted immunotherapy, tumor vaccine, adoptive cell therapy, cytokines, virus…) support ongoing clinical trials in GBM. But developing an effective immunotherapy in GBM has been a considerable challenge due to the disease heterogeneity and hostile environment the tumor creates for the immune system (BBB, lack of organized lymphoid tissue or significant lymphatic drainage, down-regulation of MHC expression, immunoregulatory factors…).

Here we propose to collaborate with a world renowned expert lab in biomedical ultrasound and wave physics to study the potential of preclinical ultrasound in GBM treatment, leveraging on:

i- Ultrafast contrast ultrasound and ultrafast doppler imaging of preclinical GBM orthotopic models (with unprecedented spatial and temporal resolution)

ii- Focused Ultrasound (FUS) aided disruption of BBB for enhanced brain penetration of therapeutic agents and immune cells

iii- Focused Ultrasound (FUS) for GBM tumor ablation, inducing immunomodulation and boosting host anti-tumor response

Objective and specific aims: our focus is to study the potential synergistic interplay between ultrasounds and the immune system in preclinical GBM model and develop innovative and practical focused ultrasound solutions for treatment of GBM, in combination with existing immunotherapies. Our study will focus on optimization of the FUS treatment method and help better define its most effective use in combination with immunotherapy. In order to develop a translational model, we will work on a preclinical immunocompetent syngeneic GBM model established on rat after stereotactic injection of glioma cell lines into the brain.

Sponsor:
Sanofi Recherche et Developpement
Translational in vivo Models – BioImaging- Vitry sur Seine
Contact : erwan.jouannot @sanofi.com

Partner:
INSERM U979 laboratory "wave physics for medecine" directed by Mickael Tanter

Candidate:

Required skills:
- Basic knowledge in molecular & cellular biology
- Willingness to learn a range of biochemical and biophysical techniques
- Interest for in vivo pharmacology/bioimaging and ability to work with small animals
- Excellent skills in oral and written English
- Team spirit and ability to work in a multidisciplinary environment

Qualification and / or training desired:

MSc in biophysics, biology or pharmacology. Previous experience in ultrasound imaging will be a plus.

Experience required:

Laboratory experience (minimum 6 months) and previous training in *in vivo* pharmacology (working with rodents) are required.