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## **Expression of Interest**

### **Contact Person/Scientist in Charge**

- **Name and surname:** Javier Martin-Broto
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## **INSTITUTO DE BIOMEDICINA DE SEVILLA**

### **Department / Institute / Centre**

- **Name:** Advanced Therapies and Biomarkers in Oncology, Institute of Biomedicine of Seville (IBIS)
- **Address:** Avda. Manuel Siurot s/n. IBIS Building University Hospital Virgen del Rocío. 41013, Seville
- **Province:** Sevilla

### **Research Area**

- Life Sciences (LIF)

### **Brief description of the institution:**

The Institute of Biomedicine of Seville is a high quality joint research centre established in 2006 as a health research, being participated by the Andalusian Regional Ministry for Innovation, Science and Enterprise, the Andalusian Regional Ministry of Health, the Spanish National Research Council, the University of Seville and the Andalusian Health Service, having these entities a common interest in fostering collaboration and cooperation and in joining efforts in the field of health research. It is one of the 18 health research institutes accredited in Spain by the Spanish Research Council (Instituto de Salud Carlos III).

IBIS is a multidisciplinary biomedical research centre, with the aim to undertake high quality and competitive research at international level on the most prevalent diseases. IBIS is based on fundamental research at the molecular and cellular level with a view to promote the rapid transfer of knowledge to the clinical setting, at the same time improving the quality of clinical and epidemiological research. It is focused on most prevalent diseases and organized in 4 research areas: Neurosciences, Cardiovascular & Respiratory pathology, Oncohematology & Genetics, and Infectious diseases & Immune system.

### **Brief description of the Centre/Research Group (including URL if applicable):**

The research lines of the group (Advanced Therapies and Biomarkers in Oncology) focus on a translational research that accompanies numerous clinical trials in sarcoma, lung, GU, GI and breast cancer patients, both nationally and internationally, and in the molecular biology and preclinical models setting. Bi-directional synergy between biomedical research of a more fundamental nature and clinical research in patients is promoted.

#### **In this context, our main objectives are:**

1. To study cell signaling pathways and molecular mechanisms of resistance to antitumor drugs in order to design therapeutic strategies.
2. Preclinical analysis of drugs *in vitro* and *in vivo* to determine expression profiles in response to these drugs. This information can support the design of clinical trials in patients.
3. To define molecular prognostic and predictive biomarkers of response to different antitumoral therapies.

The project PI, Dr. Javier Martin-Broto has led several national and international research projects in sarcomas. In the last five years, he chairs the Spanish Group for Research in Sarcoma (GEIS) that involves more than 350 researchers and over 120 hospitals. Within GEIS, Dr. Martin-Broto conducts several clinical and translational research projects. He has participated in clinical trials and research projects within the GEIS since 1994 which represents 35 projects in clinical research and more than 50 international articles.

<https://www.ibis-sevilla.es/investigacion/oncohematologia-y-genetica/terapias-avanzadas-y-biomarcadores-en->

### **Project description:**

**Phase I-II trial of sunitinib plus nivolumab after standard treatment in advanced soft tissue and bone sarcomas. *EudraCT Number: 2016-004040-10***

Sarcoma incidence is 50-60 new cases/year per million. 20% are metastatic at diagnosis and other 40% will have distant metastases. For locally advanced or metastatic disease, no curative attempt might be offered. In metastatic setting, complete responses to chemotherapy are very rarely seen and the median survival is 1 year.

New therapeutic approaches are urgently needed to increase survival. One attractive strategy focuses on immune modulation. There are solid arguments supporting this combination in sarcoma: immune modulation as innovative strategy for treatment.

Sunitinib plus nivolumab has been combined in the context of metastatic renal cell carcinoma showing encouraging antitumor activity and a manageable safety profile. The impact of immune modulation on the efficacy of sunitinib via its potential synergy with anti PD-1 deserves to be explored in the context of sarcomas.

### **Clinical study endpoints**

**Primary:** Progression-free survival rate: Efficacy measured at 6 months

**Secondary:**

- Overall survival
- Objective Response Rate
- Efficacy
- Safety profile
- Clinical outcomes

### **Population, sample size**

Patients with confirmed soft tissue/bone sarcoma with metastatic and measurable disease. 75 patients-up to 43 in STS cohort and 32 in bone sarcoma cohort.

### **Translational objectives**

1. PD-L1 analysis
2. To test immune modulation biomarkers
3. Immunohistochemical analysis of different antigens
4. T-cell R sequencing
5. Gene expression profiling
6. To test immuno-response components
7. Cytokine secretion analysis
8. *In vitro* osteosarcoma cell lines cytotoxicity (sunitinib)

## **Applications**

### **Documents to be submitted**

- Complete CV
- Contact information of two researchers familiar with the candidate
- Motivation letter

Expertise in Soft Tissue Sarcomas will be positively considered.

Deadline: 31/08/2017