We are looking for a graduate student willing to conduct a PhD biomedical research program in our research line on Fibrodysplasia ossificans progressiva (FOP). FOP is an ultra-rare musculoskeletal disorder caused by specific genetic mutations in the *ACVR1* gene, which encodes for the Bone morphogenetic protein (BMP) type I receptor ALK2. Patients with FOP, also termed the ***Stone Man syndrome***, experience episodes of extra-skeletal ossification in response to inflammation (for example, muscle damage or fatigue, vaccinations, or trauma), leading to the formation of a secondary (ectopic) skeleton and progressive immobilization of joints (such as jaws, neck, hips, shoulders), resulting in lethal disorders in the majority of cases. Unfortunately, there is no approved curative treatment. To carry out the work in the research line, a **highly motivated** individual with a **Bachelor's degree in Biochemistry, Biology, Biotechnology, or a similar field,** with an academic record of an average grade equal to or higher than 8.0 and proficiency in English, is required.

The tasks will involve cultivating and differentiating induced pluripotent stem cells (iPSC) into disease-relevant cell types. The differentiated cells will be subjected to mechanical forces (i.e., shear stress, mechanical loading, matrix stiffness) that recapitulate the microenvironment of lesions in FOP patients, using various organ-on-chip models. The candidate will join a recently established group in Oviedo (Asturias, Spain) and become part of an international team, allowing for regular interactions with other members remotely, including regular meetings in English. There is a possibility of short stays in other European laboratories and participation in international conferences.

RELATED PUBLICATIONS

- Gonzalo Sanchez-Duffhues, Eleanor Williams, Marie-José Goumans, Carl-Henrik Heldin, Peter Ten Dijke. Bone morphogenetic protein receptors: structure, function and targeting by selective small molecule kinase inhibitors. *Bone,* (2020). 138: 115472. https://doi.org/10.1016/j.bone.2020.115472 .

- Jerome Fortin, Ruxiao Tian, Ida Zarrabi, Graham Hill, Eleanor Williams, Gonzalo Sanchez-Duffhues, Midory Thorikay, Parameswaran Ramachandran, Robert Siddaway, Jong Fu Wong, Jillian Haight, Annick You-Ten, Bryan Snow, Drew Wakeham, Daniel Schramek, Alex N Bullock, Peter ten Dijke, Cynthia Hawkins, Tak W Mak. A Diffuse Intrinsic Pontine Glioma-Driving ACVR1 Mutation Causes Oligodendroglial Lineage Cell Expansion and Differentiation Arrest. Cancer Cell, (2020). 37(3): 308-323 e312. https://doi.org/10.1016/j.ccell.2020.02.002**.**

- G. Sánchez-Duffhues, E. Williams, P. Benderitter, V. Orlova, M. van Wijhe, A. Garcia de Vinuesa, J. Caradec, H. de Boer, MJ Goumans, M. Eeckhoff, A. Morales Piga, J. Bachiller, P. Koolwijk, A. Bullock, J. Hoflack, Peter ten Dijke. Development of Macrocycle kinase inhibitors for ALK2 using Fibrodysplasia ossificans progressiva-derived endothelial cells. *JBMR Plus,* (2019). 3(11): e10230. https://doi.org/10.1002/jbm4.10230

- Gonzalo Sanchez-Duffhues, Amaya Garcia de Vinuesa, Esmeralda Blaney-Davidson, Arjan van Caam, Kirsten Lodder, Yolande Ramos, Margreet Kloppenburg, Ingrid Meulenbelt, Peter van der Kraan, Marie Jose Goumans, Peter ten Dijke. Cripto favours chondrocyte hypertrophy via TGF-β SMAD1/5 signaling during development of Osteoarthritis. J Pathology (2021) 255(3):330-42 . https://doi.org/10.1002/path.5774

- Francesc Ventura, Eleanor Williams, Makoto Ikeya, Alex N. Bullock, Peter ten Dijke, Marie-José Goumans, Gonzalo Sanchez-Duffhues. Challenges and opportunities for drug repositioning in Fibrodysplasia ossificans progressiva. *Biomedicines* (2021) 9(2): 213. https://doi.org/10.3390/biomedicines9020213

MORE INFORMATION

Please, send your CV with your academic grades and a short motivation letter to:

- Dr. Gonzalo Sanchez-Duffhues, Group leader "Tissue-specific BMP signaling".

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