# Master Internship 2021-2022

## Coordination of Disseminated Cancer Cell Dormancy in the Bone Marrow by TGFB2 and BMP4 Signaling

**Abstract and objectives:** Most of breast cancer-related deaths are due to metastases that can arise months or years after treatment and primary tumor removal. The **bone marrow (BM)** is of major interest as **Disseminated Tumor Cells (DTCs)** detected in this site are commonly associated to poor prognosis as DTCs can survive and remain **dormant** before leading to relapse. In the BM, TGFb2 has been shown to be essential to induce breast cancer DTC dormancy, but crosstalk with other BM secreted factors is likely to be involved. Indeed, several signals are present in BM niches when DTCs home there. Among them, Bone Morphogenetic Proteins (BMPs) are a major soluble component of the BM microenvironment. The effect of BMPs on breast cancer cells is controversial and the role of BMP4 in breast cancer dormancy in the BM has not been assessed yet. The objective of this project is to decipher common molecular mechanisms (signaling pathways, epigenetic remodeling) and switch between the TGF/BMP pathways which controls dormancy features of DTCs.
**We aim to mechanistically understand differential and co-signaling of BMP4 and TGFb2 on the regulation of breast disseminated tumor cells in a human 3D co-culture model of the BM niche already developed in the lab to study hematological malignancies. You will participate in the development of this 3D niche to model solid cancer cell dormancy and awakening in the bone marrow, using a wide variety of assays.**

**Techniques**: 3D co-culture model of the bone marrow niche, Cell culture, Immunofluorescence, Confocal Microscopy, Flow Cytometry and Cell Sorting, qPCR, Western Blot.

**Mentoring:** Dr. Véronique Maguer-Satta (lab head, PI), Emma Risson (PhD student, MD student).
If interested, please contact veronique.maguer-satta@lyon.unicancer.fr and emma.risson@gmail.com.
We'll be happy to discuss any questions you have (mentoring, funding,.), the lab is used to welcome MD residents for M2 internships.

**Team: Equipe « BMP, Ecosystème, Cellules Souches & Dynamique du Cancer », CRCL, Lyon**

**Selection of recent publications:**

*This project is part of an ongoing collaboration with Prof. Aguirre-Ghiso's lab, Mount Sinai, NYC, USA.*

1. Bragado P, Estrada Y, Parikh F, Krause S, Capobianco C, Farina HG, Schewe DM, Aguirre-Ghiso JA: **TGF-β2 dictates disseminated tumour cell fate in target organs through TGF-β-RIII and p38α/β signalling**. *Nature Cell Biology* 2013, **15**:1351–1361. [doi: 10.1038/ncb2861]
2. Jeanpierre S, Arizkane K, Thongjuea S, Grockowiak E, Geistlich K, Barral L, Voeltzel T, Guillemin A, Gonin-Giraud S, Gandrillon O, et al.: **The quiescent fraction of chronic myeloid leukemic stem cells depends on BMPR1B, Stat3 and BMP4-niche signals to persist in patients in remission [Internet]**. *Haematologica* 2020, doi:10.3324/haematol.2019.232793. [doi: 10.3324/haematol.2019.232793] [PMID: 32001529]
3. Risson E, Nobre AR, Maguer-Satta V, Aguirre-Ghiso JA: **The current paradigm and challenges ahead for the dormancy of disseminated tumor cells**. *Nature Cancer* 2020, **1**:672–680.[doi: 10.1038/s43018-020-0088-5]
4. Nobre AR, Risson E, Singh DK, Martino JD, Cheung JF, Wang J, Johnson J, Russnes HG, Bravo-Cordero JJ, Birbrair A, et al.: **NG2+/Nestin+ mesenchymal stem cells dictate DTC dormancy in the bone marrow through TGFβ2**. *bioRxiv* 2020, doi:10.1101/2020.10.22.349514. [doi: 10.1101/2020.10.22.349514]