Master Biologie Moléculaire et Cellulaire 'BMC',
Université de Paris - *UFR Sciences du Vivant*

Parcours : **Biologie et Développement Cellulaires 'BDC'**
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Fiche de Projet de Stage M2, Année 2021-2022

Unité INSERM : Institut *Imagine*, UMR-1163 **Intitulé Equipe :** *Imagine*-Institut Pasteur Unit of Heart Morphogenesis https://research.pasteur.fr/en/team/heart-morphogenesis/ **ED d'appartenance :** 562 (BioSPC-DGNRV) **Responsable de l'Equipe :** Sigolène Meilhac	**Responsable du Stage :** Sigolène Meilhac (DR2 INSERM, HDR), co-encadrement Tobias Holm Bønnelykke (PhD student) **Contacts** Adresse : Institut *Imagine*, 24 boulevard du Montparnasse, 75015 PARIS Email : sigolene.meilhac@pasteur.fr Tel : 01 42 75 44 82

Titre du projet : Novel pathways in the left-right asymmetric morphogenesis of the heart

Résumé du Projet de Stage

The acquisition of a specific shape is key for organ function. **Left-right asymmetric morphogenesis** partitions the heart into distinct halves, driving the systemic and pulmonary blood circulations. Whereas the molecular cascade breaking the bilateral symmetry in the early embryo has been well characterised, how it is sensed by organ-specific precursor cells to generate asymmetric organogenesis remains poorly understood. The rightward looping of the embryonic heart tube provides a striking example of asymmetric morphogenesis, during which the tubular primordium acquires a helical shape, essential to align cardiac chambers and establish the double blood flow [4]. Previous studies have focused on a binary (left or right) looping direction, as a readout of the symmetry-breaking event, but have not addressed the fine 3D shape of the heart helix, as a readout of asymmetric morphogenesis and as a precondition to heart function. In the recent years, the team of *Heart Morphogenesis* has developed a novel technological and conceptual framework to investigate asymmetric heart morphogenesis [1, 3, 5]. We have dissected the contribution of Nodal signaling to **heart looping** [1] and shown that it is not the only player of asymmetric heart morphogenesis. We have now performed a **transcriptomic screen** to identify novel genes asymmetrically expressed in the heart field. The master project aims at validating candidate genes, using advanced technologies in **quantitative imaging** of gene expression and shape in 3D, with a high spatio-temporal resolution. The project, which can be extended for a PhD, will thus contribute to identify novel pathways **patterning** the heart field and novel mechanisms of asymmetric organogenesis. Our work in the mouse is relevant to **congenital heart defects** in humans, which is explored with our collaborators of the Hospital Necker-Enfants Malades, where the Institut *Imagine* is located. The laboratory is also affiliated to the Department of Stem Cell and **Developmental Biology** of the Institut Pasteur.

Publications de l'équipe, relatives au projet de stage (max 5)

1-A. Desgrange et al., 2020 Developmental Cell 55(4):413-431, Transient Nodal signalling in left precursors coordinates opposed asymmetries shaping the heart loop

2-S. Bernheim and S. Meilhac, 2020 Philos Trans R Soc Lond B Biol Sci 375(1809):20190556, Mesoderm patterning by a dynamic gradient of retinoic acid signaling (Review)

3-A. Desgrange et al., 2019 Disease Models & Mechanisms, 12(7):dmm038356, , Standardised imaging pipeline for phenotyping mouse laterality defects and associated heart malformations, at multiple scales and multiple stages

4-A. Desgrange, J-F. Le Garrec, and S. Meilhac, 2018 Development 145(22):dev162776, Left-right asymmetry in heart development and disease : forming the right loop (Review)

5-J-F. Le Garrec et al., 2017 eLife, 6 :pii: e28951, A predictive model of asymmetric morphogenesis from 3D reconstructions of mouse heart looping dynamics.