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 2026-2027

Unité INSERM, CNRS ou Université : Institut Curie - UMR144 - Biologie Cellulaire et Cancer **Intitulé Equipe :** Biologie cellulaire de la neurogenèse des mammifères **ED d'appartenance :** ED515 - Complexité du vivant **Responsable de l'Equipe :** Alexandre Baffet	**Responsable du Stage :** Alexandre Baffet Enzo Bresteau **Contacts** alexandre.baffet@curie.fr enzo.bresteau@curie.fr

Titre du projet : Live imaging of human brain organoids to investigate the role of extracellular matrix degradation during neuronal migration

Résumé du Projet de Stage

The **neocortex** is the part of the human brain responsible for higher cognitive functions such as memory, perception, and language. These functions rely on **neuronal circuits** that are formed during **fetal development**. To integrate into these circuits, **newborn neurons** must first **migrate** over very long distances through the **extracellular matrix** of the developing brain, a dense three-dimensional network of proteins and glycans. Because the pore size of this network is much smaller than the size of the migrating neurons, they need to develop strategies to overcome this **physical constraint**. One possible mechanism, which is the focus of this internship, is **the secretion of proteases** that remodel and **degrade the extracellular matrix**, locally increasing pore size and facilitating neuronal migration throughout the developing brain.

The goal of the internship will be to: (1) Characterize the composition and organization of the extracellular matrix in the human developing brain. (2) Define the role of matrix degradation during neuronal migration, identifying which proteases cleave which specific matrix proteins. (3) Determine how matrix degradation inhibition affects neuronal circuit organization. To investigate these questions, the internship will combine two complementary model systems. First, **human cortical brain organoids** differentiated from pluripotent stem cells will be used to recapitulate neuronal birth and migration in vitro. Second, the findings will be validated in **human fetal tissue** to remain as close as possible to physiological conditions. The project will involve a combination of cell culture, brain organoid generation, immunofluorescence, **long-term live imaging** using spinning disk microscopy, and image analysis. This project could lead to a PhD opportunity.

Publications de l'équipe, relatives au stage proposé

• ***Two translocation mechanisms drive neural stem cell dissemination into the human fetal cortex*.** Neuron. 2026. PMID: 41844158.

• ***A cell fate decision map reveals abundant direct neurogenesis bypassing intermediate progenitors in the human developing neocortex***. Nat Cell Biol. 2024;26:698–709. PMID: 38548890.

• ***Endosomal trafficking defects alter neural progenitor proliferation and cause microcephaly***. Nat Commun. 2022;13(1):16. PMID: 35013230.