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

Parcours : **Biologie et Développement Cellulaires 'BDC'**
https://master2bdc.ijm.fr/
Fiche de Projet de Stage de M2, 2024-2025

Unité INSERM ou CNRS ou Université : **Institut Pasteur/ U1224** **Intitulé Equipe :** **Stroma, Inflammation and Tissue Repair** **Dép IMMUNO et DEVELOPPEMENT** **ED d'appartenance : BIOSPC** **Responsable de l'Equipe : Lucie Peduto**	**Responsable du Stage : Lucie Peduto** **Contacts** Adresse : Institut Pasteur 25, rue du Docteur Roux 75015 Paris Email : lucie.peduto@pasteur.fr Tel : 0144 38 95 27

Titre du projet : Stromal regulation of mammary gland involution and postpartum breast cancer

Résumé du Projet de Stage (en 300 mots maximum, mots clés en gras)

Postpartum breast cancer, defined as a diagnosis within 5 years from childbirth shows a particular high risk for metastasis and poor prognosis. After termination of lactation, the mammary gland (MG) goes through a **physiological remodeling process called involution**, to allow the MG to return to steady-state. Post-lactational mammary gland regression includes massive cell death and removal of milk-producing epithelial cells in the first few days, accompanied by infiltration of immune cells such as macrophages, neutrophils, T cells and myeloid cells, followed by a remodeling phase including the vasculature, adipocytes and the ECM. The MG involution process shares several similarities to the **tumor microenvironment**, such as abundance of immunosuppressive cells, macrophages, activation of **PDGFRα+ stroma cells**, vascular abnormalities and tissue remodeling. Similar to carcinoma-associated-fibroblasts, stromal cells in the post-weaning MG promote breast tumor growth when injected in an orthotopic model, suggesting a key role in this process. As stromal cells are a heterogeneous population present in all tissues and essential for organ homeostasis, a major challenge is currently to identify specific stromal markers/pathways that can be safely and efficiently (co)-targeted in postpartum breast cancer. In this project, we will take advantage of **genetic mice models** to investigate, in vivo, **the role of stromal populations in mammary gland involution and postpartum breast cancer**, with a focus on the tumor microenvironment (tumor immunity and angiogenesis). To that aim, we will use different techniques, including **confocal microscopy, FACS and transcriptomics** (RNAseq or qPCR).

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

- Di Carlo SE, Raffenne J, Varet H, Ode A, Cabrerizo Granados D, Stein M, Legendre R, Tuckermann J, Bousquet C, Peduto L. 2023. Depletion of slow-cycling PDGFRa^{+}ADAM12^{+} mesenchymal cells promotes antitumor immunity by restricting macrophage efferocytosis. **Nature Immunology**, 24(11):1867-1878.
- Sylvestre M, Di Carlo SE, Peduto L. 2023. Stromal regulation of the intestinal barrier. **Mucosal Immunol**., 16(2):221-231.
- Jacob JM, Di Carlo SE, Stzepourginski I, Lepelletier A, Ndiaye PD, Varet H, Legendre R, Kornobis E, Benabid A, Nigro G, Peduto L. 2022. PDGFRα-induced stromal maturation is required to restrain postnatal intestinal epithelial stemness and promote defense mechanisms. **Cell Stem Cell**, 29(5): 856-868.