



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

Parcours : **Biologie et Développement Cellulaires 'BDC'**

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Fiche de Projet de Stage de M2, 2026-2027

Unité INSERM ou CNRS ou Université : INSERM U1163-Institut Imagine	Responsable du Stage : Ménasché Gaël
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Titre du projet : Antisense oligonucleotides technology for inhibiting mast cell degranulation to treat allergic asthma

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

Allergies (i.e. **asthma**, atopic dermatitis, food allergy, urticaria and anaphylaxis) have increased steadily since several decades in developed countries now affecting one person in three and constitute a major health problem. This epidemic explosion is the result of an interplay between a genetic predisposition in the population and a growing imbalance between the immune system and the altered environment in a modern hygienic society. This drives a Th2 response involving various immune effector cells that promote the formation of specific IgE antibodies to otherwise harmless allergens. Allergic diseases are then driven by activation of **mast cells (MCs)** which are hematopoietic granulocytes residing in most tissues of the body. IgE-dependent activation of MCs occurs through the **high-affinity IgE receptor (FcεRI)**. Cross-linking of FcεRI by allergen-IgE complexes triggers a complex signaling cascade resulting in secretory granules release, which orchestrate inflammation.

Beside drug development of small molecules and monoclonal antibodies, **the antisense oligonucleotide (ASO)** strategy is a rapidly growing innovative therapeutic approach that aims to selectively modulate gene expression. ASOs are short chemically modified oligonucleotides that can base-pair RNA and activate the RNaseH1 leading to the selective cleavage of the targeted RNA. Although all approved ASOs are for treating rare diseases, antisense technology has advanced and are now evaluated to the benefit of a wide range of common diseases.

We propose a novel therapeutic strategy for allergic diseases using ASO technology to selectively silence MC-specific genes critical to their function. By leveraging local delivery methods (e.g., aerosolized ASOs for asthma), this approach enables precise inhibition of MC activation while minimizing systemic exposure. This strategy offers a truly innovative route to the development of MC-specific treatments for allergic diseases, addressing a major unmet need in the field of allergy therapy. The overall goal of the M2 project is to evaluate the efficacy of ASO therapy in a **house dust mite-induced allergic asthma model** that closely recapitulates the pathophysiology of human asthma. The impact of ASO treatment will be assessed under both prophylactic and therapeutic conditions using this model.

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

1. Pierre Duquesne, Céline Aoun, Mathieu Kurowska, Briec P. Perot, Kerui Zhang, Mounia Debili, Mirjana Weimershaus, François-Xavier Mauvais, Nicolas Cagnard, Nicolas Goudin, Bernardita Medel, Juan Eduardo Montero-Hernandez, Linda Diedhiou, Jian-Dong Huang, Alain Fischer, Geneviève de Saint Basile, Mickaël M. Ménager, Pablo Vargas, Fernando E. Sepulveda and [Gaël Ménasché](#). Kinesin-1 coordinates crosstalk between microtubule and actin cytoskeletons during dendritic cell migration. *Science Advances*. 2025 Oct 17;11(42):eadx7672. doi: 10.1126/sciadv.adx7672.
2. Longé C., Bratti M., Kurowska M, Vibhushan S., David P, Desmeure V., Huang JD, Fischer A, de Saint Basile G, Sepulveda FE, Blank U., [Ménasché G.](#) Rab44 regulates murine mast cell-driven anaphylaxis through kinesin-1-dependent secretory granule translocation. *J Allergy Clin Immunol*. 2022 Apr 22:S0091-6749(22)00544-9.
3. Belabed M, Mauvais FX, Maschalidis S, Kurowska M, Goudin N, Huang JD, Fischer A, de Saint Basile G, van Ender P, Sepulveda FE, [Ménasché G.](#) Kinesin-1 regulates antigen cross-presentation through the scission of tubulations from early endosomes in dendritic cells. *Nat Commun*. 2020 Apr 14;11(1):1817.
4. I. Munoz, L. Danelli, J. Claver, N. Goudin, M. Kurowska, J.D. Huang, A. Fischer, C. Gonzales-Espinosa, G. de Saint Basile, U. Blank and [G. Ménasché](#). Kinesin-1 controls mast cell degranulation and anaphylaxis through its PI3K-dependent recruitment to the granular Slp3/Rab27b effector complex. *J Cell Biol*. 2016; 215 (2) 203-216.
5. Montero-Hernández JE, Zhang K, Blank U, [Ménasché G.](#) LRO biogenesis and function: what can we learn from mast cells? *Front Cell Dev Biol*. 2025 Jun 25;13:1613677. doi: 10.3389/fcell.2025.1613677.
6. [Ménasché G](#), Longé C., Bratti M., Blank U. Cytoskeletal transport, reorganization and fusion regulation in mast cell-stimulus secretion coupling. *Front Cell Dev Biol*. 2021 Mar 16;9:652077.