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, 2026-2027

Unité INSERM ou CNRS ou Université : U1016 **Intitulé Equipe :** Destin, plasticité et reprogrammation cellulaire **ED d'appartenance :** BioSPC **Responsable de l'Equipe :** Antoine Zalc	**Responsable du Stage :** Antoine Zalc **Contacts** Adresse : 24 Rue du Faubourg St Jacques, 75014, Paris Email : antoine.zalc@inserm.fr Tel : 06.37.06.04.94

Titre du projet : Epigenetic control of neural crest development and plasticity

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

Craniofacial disorders represent a third of birth defects worldwide and originate from alterations in **cranial neural crest cells (CNCC)** development. CNCC arise in the anterior embryo, migrate to populate ventral locations, and differentiate into various craniofacial derivatives. Pre-migratory CNCC are patterned along the antero-posterior (AP) axis, expressing Otx2 (anterior) or Gbx2 (posterior), but this **positional identity** is erased upon migration. The **functional relevance of CNCC initial AP patterning remains unknown**.

To study the function of CNCC AP patterning, we developed à 3D *in vitro* CNCC differentiation system recapitulating AP identity establishment and erasure. We showed modulating diverse signaling pathways alters the proportion of $OTX2^+$ and $GBX2^+$ cells but never disrupts their boundary, revealing **intrinsic developmental robustness**. SUMOylation is described as a safeguard of cell identity and patients with altered SUMOylation present craniofacial defects. We showed SUMOylation inhibition disrupts CNCC AP patterning, reduces migration, and impairs differentiation, both in vitro and in vivo. However, when and how SUMOylation acts to provide robustness to CNCC development is unknown.

In this project, the student will address these open questions by combining stage-restricted in vitro SUMOylation inhibition and gene expression analysis (qRT-PCR), mouse embryo immunofluorescence, flow cytometry-based cell sorting, profiling of SUMO chromatin binding (ChIP-seq) and chromatin accessibility changes (ATAC-seq) to determine when and how SUMOylation acts to stabilize CNCC identity and ensure their proper development. The project sits at the interface of developmental biology, epigenetics and disease — offering training in state-of-the-art genomic approaches alongside classical embryology techniques. Our findings have direct implications for patients carrying SUMO1 mutations and presenting with craniofacial syndromes, and open new perspectives on how epigenetic mechanisms control cell plasticity in cancer.

Techniques to be used: Cell culture, FACS, qRT-PCR, ChIP-seq, ATAC-seq, immunofluorescence

2025 Fortunato S., Deschemin J.C., **Zalc A.** Cranial Neural Crest Cells Three-Dimensional In Vitro Differentiation Protocol for Multiplexed Assay. J. Vis. Exp. JoVE e67695 (2025) doi:10.3791/67695.

2023 Smeriglio P, **Zalc A.** Cranial Neural Crest Cells Contribution to Craniofacial Bone Development and Regeneration. Curr Osteoporos Rep. 2023 Jul 8. doi: 10.1007/s11914-023-00804-8.

2021 **Zalc A.**, Sinha R., Gulati G.S., Wesche D.J., Daszczuk P., Swigut T., Weissman I.L., Wysocka J. Reactivation of the pluripotency program precedes formation of the cranial neural crest. Science, 2021;371(6529):eabb4776.