Appel à projets ExposUM Stages de Master 2026

Matrice de candidature

Résumé du sujet de stage

Intitulé du sujet de stage	**Humanized Mouse Intestinal Organoids as a Model for Exposome Studies in EOCRC**
Trois mots-clé	Exposome – Intestinal organoids – Early-onset colorectal cancer (EOCRC)
Champ.s disciplinaire.s concerné.s	Cell and Molecular Biology; Cancer Biology; Environmental Toxicology; Organoid Biology

Porteur.se (encadrant.e principal.e ou co-encadrant.e)

NOM Prénom, mail	PASCUSSI Jean Marc
Corps, fonction	Chargé de Recherche
Statut si Permanent	CRHC
Statut si Contractuel Confirmer obligatoirement que le contrat de travail couvrira l'intégralité de la période de réalisation du projet	
Employeur	INSERM

Structure de recherche

Unité du porteur.se (acronyme et tutelles)	IGF, CNRS UMR5203, INSERM U1191, UM
Directeur.trice de l'Unité : NOM Prénom, mail	Sébastien GRANIER – sebastien.granier@igf.cnrs.fr
Gestionnaire administratif.ve : NOM Prénom, mail	Audrey FISSEAU – audrey.fisseau@igf.cnrs.fr

Visa du porteur.se de projet, valant engagement aux points énoncés dans le texte de l'AAP	Jean Marc PASCUSSI
Visa du.de la directeur.trice de l'unité porteuse	Sébastien GRANIER Directeur -IGF-

Projet global

Objectif principal du stage	The objective of this internship project is to validate humanized mouse intestinal organoids as a model to study environmental determinants of early-onset colorectal cancer (EOCRC).
Parcours de Master 2 visé(s) (optionnel)	
Cocher et expliciter l'adéquation avec les priorités stratégiques de l'institut ExposUM (cf. texte de l'appel)	X Approche One Health ☐ Santé Globale / Sud ☐ Lien Sciences Humaines et Sociales ☐ Nouveau partenariat ☐ Autre priorité This project adopts a One Health approach linking environmental exposure, biological responses and intestinal health. It asks whether incorporating human xenobiotic-sensing and metabolic pathways improves the prediction of responses to chronic environmental exposures and addresses key limitations of conventional models arising from interspecies differences in xenobiotic metabolism.

Description du stage

European populations are chronically exposed to a complex cocktail of environmental contaminants through diet, often at individually sub-regulatory levels, while their combined effects remain poorly characterized. Meanwhile, early onset colorectal cancer (EOCRC) incidence is increasing worldwide without clearly identified etiological factors (Hofseth et al. 2020), although chronic exposure to pesticides (Remigio et al. 2024; Maas et al. 2024) and metals, particularly cadmium (Al-Saleh et al. 2026), appear as solid contributors. Because interspecies differences limit the predictive value of conventional animal models, particularly for chronic low-dose chemical exposure, we will challenge a humanized model in which murine xenobiotic-sensing and metabolism genes, including Nr1i2 (PXR), Nr1i3 (CAR) and seven Cyp3a genes including CYP3A4 and CYP3A7, are replaced by their human counterparts. The PXR/CAR–CYP3A axis regulates xenobiotic metabolism and influences lipid/glucose homeostasis and colorectal cancer progression (Pascussi et al., 2008; Planque et al., 2016), providing a mechanistic link between exposure, metabolic dysfunction and tumor susceptibility. This internship is part of a broader project combining *in vitro* organoid-based approaches with long-term *in vivo* exposure studies in humanized mice. It will compare the direct effects of chemical contaminants and cadmium, in intestinal organoids from humanized PXR/CAR/CYP3A4-7 mice and C57BL/6 controls and thus provide the preliminary data and experimental framework for a future PhD project investigating the impact of chronic combined contaminant exposure on EOCRC susceptibility. Contaminants were selected based on their occurrence and potential low-dose effects in the European exposome (EAT2, ANSES; PRIMo V4, EFSA).

Déroulé du stage : diagramme de Gantt et commentaire

TASK	MONTHS 1	2	3	4	5	6
Bibliographic research (Exposome, organoids, doses...)						
Maintenance, caracterization and preparation of intestinal organoids settings						
Exposure of organoids to environemental polutants (alone or combined)						
Sample collection and processing (immunofluorescence stainings,RT-qPCR, ...)						
Data analys, data presentation and master report writing						

With the help of a postdoc fellow (G. Belthier), the master student will learn to maintain and characterize intestinal organoids from humanized and control mice. Once validated, organoids will be exposed to individual contaminants- including herbicides (glyphosate + AMPA), insecticides (acetamiprid, cypermethrin, lambda-cyhalothrin), fungicides (boscalid, tebuconazole, difenoconazole, pyraclostrobin, and imazalil) and cadmium - or mixtures at low doses (Admitted Daily Intake -ADI- and 1/10 ADI) to assess effects on morphology/growth, proliferation/apoptosis (Ki67, Annexin-V), stemness/differentiation (lgr5, krt20), DNA damage/genomic instability (γH2AX, micronucleus assay) and transformation (clonogenicity/anchorage-independent growth), using methods such as immunostaining, cytometry and RT-qPCR. The main risks relate to variability in organoid establishment and growth and potential weak or variable responses at low contaminant doses. These risks will be mitigated through close supervision, progressive validation of organoid cultures and readouts. Experimental phases will be partially overlapping where possible. In case of delay, priority will be given to contaminant screening and robust endpoints (morphology/growth, proliferation and apoptosis), while more time-consuming analyses (DNA damage and transformation assays) will focus on the most relevant conditions.

Equipe : intégration et encadrement prévus

The internship is part of a broader study comparing *in vitro* effects of contaminant exposure with long-term *in vivo* exposure (10 months) in humanized mice (C57BL/6 Nr1i3tm1(NR1I3)Arte Is(5CYP3A4-CYP3A7;Del5Cyp3a57-Cyp3a59)2Arte Nr1i2tm1(NR1I2)Arte, Taconics) and C57BL/6 controls providing a direct link between the two experimental approaches.

The trainee will be directly supervised by JM Pascussi (CR INSERM) with support from J. Pannequin ("Signaling, Plasticity and Cancer" team leader), G. Belthier (Postdoctoral Researcher, intestinal organoid specialist), and Lena Marie Schmitt (2nd-year PhD student, for IF/IHC, cytometry and RT-qPCR analyses). He/she will be fully integrated into the research team and share an office with the project supervisor and a PhD student, facilitating close scientific interactions and regular project follow-up. Scientific progress will be monitored informally on a daily basis and discussed weekly during team meetings.

Partenaires (le cas échéant) spécifiques au stage

Ajouter autant de lignes que nécessaire

Unité(s) ou structure(s) partenaire(s)	Expertise ou technique apportée par le partenaire
MRI RIO	Cytometry, miscrocopy
iExplore	Animal facility

Budget

Type de dépense	Montant	Commentaire
Gratification de stage	*3780 E*	4.50€/hour, 35 hours/week for 6 months
Frais d'environnement (dépenses de fonctionnement)	1220 E	*Consumables for intestinal organoid culture and treatment (including chemicals, culture media), and antibodies for IF, IHC, and flow cytometry analyses.*