TRIO$_2$ (Translational Research In Oncodermatology and Orphan skin diseases)

INSERM U1312 - BRIC

Postdoctoral position on pigmentary abnormalities in xeroderma pigmentosum at the Bordeaux Institute of Oncology

30 months Post-Doc offer at Bordeaux/France

Field: Pigmentation, Skin, rare disease
Contract: 30 months
Application deadline: 30/08/2023
Recruitment: 01/11/2023
Localization: Bordeaux University, France

Laboratory: TRIO2 INSERM team (https://www.bricbordeaux.com/en/bric-team/recherche-translationnelle-en-cancerologie-cutanee-et-maladies-cutanees-rares/)

This team work on oncodermatology in tight collaboration with dermatoloy department at the Bordeaux University Hospital.

Project description:

Xeroderma pigmentosum (XP) is a rare autosomal recessive disorder owing to the defects in one of the factors implicated in the nucleotide excision repair (NER) system. XP is characterized by sun sensitivity, uneven solar damage such as freckle-like pigmentation, sunlight-induced ocular involvement, and great susceptibility to skin cancers. XP is classified into eight complementation groups XP-A to -G and XP-V. The complementation group C (XP-C, OMIM: 278720) is the most common form of XP in the United States and Europe. XP-C is caused by a defect in the XPC protein, which is involved in the genome-wide damage recognition step of NER.

One of the manifestations of the XP disorder, as the term implies, is pigmentary abnormalities, which have been neglected and have not been studied in detail until now due to the lack of an appropriate model. Our main goal in the proposed research project, which is a logical follow-up of our preliminary results, is to identify the mechanism(s) by which XPC expression affects skin pigmentation. The clinical data indicates that hyper- and hypo-pigmented spots in XP-C patients appear in the same field of irradiation. How both hyper- and hypo-pigmented patches are colocalized in this disease justifies a detailed investigation to identify the underlying mechanisms. To perform this mechanistic study, we developed several pertinent models

XPC-deficient Xenopus embryos. Of interest, our preliminary studies suggested that some common UV-induced lentiginous dyschromias share the same pathological features and may harbor common pathomechanisms with DNA repair disorders. Therefore, investigation of pigmentary abnormalities in XPC deficient cells using several pertinent models (2D and 3D human skin cultures, Xenopus embryos and mouse model), would be helpful for designing more effective therapeutic strategies not only for XP patients but also for other UV-related pigmentary disorders.

Recent publications of the team:

Moisan et al. PNAS, PMID: 33558238 ; Hosseini et al, Oncogenesis, PMID: 31551419; Mahfouf et al. J Invest Dermatol, PMID: 30878676, Hosseini et al, Cell Rep, PMID: 29925003.

Zebian et al. Mutat Res Rev Mutat Res. PMID: 35690409; Fayyd et al, Front Genet, PMID: 33329698; Kasraian et al. Pigment Cell Melanoma Res, PMID : 29938913

Knowledge / skills:

The main used techniques are CRISPR-Cas9-mediated XPC ablation in human cell, multiplex immunohistochemistry, omics approaches (e.g. Single-cell RNA sequencing by GeoMX Digital Spatial Profiler, spatial transcriptomic and proteomic analyses), RNA sequencing, and technics for studying the machinery of melanogenesis in 2D and 3D models.

Interested applicants should have a PhD degree in Biology or Biochemistry field as well as a background in molecular cell biology techniques. Ideally, these will include experience with mouse models, mammalian cell culture and above mentioned techniques.

How to apply:

Interested applicants should provide a *curriculum vitae*, a cover letter including a brief description of prior research experience and 2 supporting letters, to Hamid-Reza REZVANI (hamid-reza.rezvani@u-bordeaux.fr).