

1 Post-doctoral Position

Title: Identification and characterization of mosquito factors interacting with the untranslated terminal regions (UTRs) of the RNA genome of Dengue and Zika viruses

Zika (ZIKV) and Dengue (DENV) are mosquito-borne viruses belonging to the Flaviviridae family. With an estimated 390 million new infections every year, dengue is considered by the World Health Organization to be the most critical mosquito-borne viral disease worldwide. No efficient treatments or vaccines are available against these viruses to date and strategies to contain infection rely mostly on prevention and vector control. Considering that DENV and ZIKV circulate in both vertebrate and invertebrate animal hosts, targeting specific steps of viral replication in the insect vector would be an efficient strategy to block viral transmission and spread. The development of new mosquito specific antiviral strategies against ZIKV and DENV requires a more thorough understanding of key steps of the viral lifecycle. RNA viruses often harbor, within their genomes, multifunctional non-coding structured RNA regions. The 5' and 3' untranslated regions (UTR) in DENV and ZIKV genomes are very conserved and have critical functions during viral replication. Although several roles of these regions have been proposed in mammalian hosts, their specific functions in the insect vector have never been investigated. A better understanding of the role of UTRs in the flaviviral replication cycle in mosquitoes would open new promising prospects for targeting key steps of their lifecycle. Our goal is to identify and characterize host proteins interacting with the 5' UTR and 3'UTR non-coding regions of DENV and ZIKV in the mosquito vector. We will use cutting-edge molecular biology and biophysical techniques to identify and characterize cellular host factors associated with viral UTRs both *in vitro* and *in vivo*. On the fundamental level, our study will shed light on the role of viral UTRs in the invertebrate host, which could be leveraged for the development of novel antiviral strategies focused on the insect vector to block transmission of these arboviruses.

Key words: Dengue and Zika viruses, *Aedes mosquitoes*, antiviral immunity, non-coding RNAs

Application:

The selected applicant will join a multinational team at the Research Unit M3i 'Insect Models of Innate Immunity' in the Institut de Biologie Moléculaire et Cellulaire on the central campus of the University of Strasbourg. This project will be co-advised by Dr. João Marques (group leader at CNRS UPR9022, Strasbourg, France) and Dr. Karim Majzoub (group leader at IGMM of CNRS, Montpellier France).

This is a multidisciplinary project and candidates should be skilled in molecular biology; prior experience in virology, immunology or biochemistry is a plus. Written and oral communication skills in English are required. This is a 30-month position funded by ANR. Starting date between March and August 2022 preferably.

Inquiries/applications should be made by e-mail including a motivation letter, CV and contact for two references to: João Marques (joao.marques@unistra.fr) and Karim Majzoub (karim.majzoub@igmm.cnrs.fr).

Lab website: <https://ibmc.cnrs.fr/laboratoire/m3i/equipes/reponses-antivirales-chez-le-moustique-aedes/>

Key publications:

1. Distinct Roles of Hemocytes at Different Stages of Infection by Dengue and Zika Viruses in *Aedes aegypti* Mosquitoes. Leite THJF, Ferreira ÁGA, Imler JL, **Marques JT**. Front Immunol. 2021 May 13;12:660873. doi: 10.3389/fimmu.2021.660873. PMID: 34093550
2. A single unidirectional piRNA cluster similar to the flamenco locus is the major source of EVE-derived transcription and small RNAs in *Aedes aegypti* mosquitoes. Aguiar ERGR, Almeida JPP, Queiroz LR, Oliveira LS, Olmo RP, Faria IJS, Imler JL, Gruber A, Matthews BJ, **Marques JT**. RNA. 2020 Jan 29. pii: rna.073965.119. doi: 10.1261/rna.073965.119. PMID: 31996404
3. Ooi YS*, **Majzoub K***, Flynn RA, Mata MA, Diep J, Li JK, van Buuren N, Rumachik N, Johnson AG, Puschnik AS, Marceau CD, Mlera L, Grabowski JM, Kirkegaard K, Bloom ME, Sarnow P, Bertozzi CR, Carette JE. An RNA-centric dissection of host complexes controlling flavivirus infection. Nat Microbiol. 2019 Dec;4(12):2369-2382. doi: 10.1038/s41564-019-0518-2. Epub 2019 Aug 5. PMID: 31384002
4. Control of dengue virus in the midgut of *Aedes aegypti* by ectopic expression of the dsRNA-binding protein Loqs2. Olmo RP, Ferreira AGA, Izidoro-Toledo TC, Aguiar ERGR, de Faria IJS, de Souza KPR, Osório KP, Kuhn L, Hammann P, de Andrade EG, Todjro YM, Rocha MN, Leite THJF, Amadou SCG, Armache JN, Paro S, de Oliveira CD, Carvalho FD, Moreira LA, Marois E, Imler JL, **Marques JT**. Nat Microbiol. 2018 3(12):1385-1393. doi: 10.1038/s41564-018-0268-6. PMID: 30374169
5. Sequence-independent characterization of viruses based on the pattern of viral small RNAs produced by the host. Aguiar ER, Olmo RP, Paro S, Ferreira FV, de Faria IJ, Todjro YM, Lobo FP, Kroon EG, Meignin C, Gatherer D, Imler JL, **Marques JT**. Nucleic Acids Res. 2015 Jul 27;43(13):6191-206. doi: 10.1093/nar/gkv587. PMID: 26040701