

Job Title	Marie-Curie fellowship application: Topic: Ca <sup>2+</sup> signaling in autoimmune diseases.
Main Research Field	<ul style="list-style-type: none"> <li>Life Sciences (LIF)</li> </ul>
Sub Research Field	Medical Science Biology
Key words	Calcium Signaling – Autoimmunity- B lymphocyte - Immunology
Job Description	<p>Ca<sup>2+</sup> signaling modulators as therapeutic tools for autoimmune diseases</p> <p><i>Our group is focusing on calcium signaling in B-cells in health and diseases such as autoimmune disorders and cancers. Our research ultimately aims to propose novel therapies for B-cell diseases targeting proteins involved in Ca<sup>2+</sup> Signaling. To reach these objectives we need to explore the role of calcium signaling in B-lymphocyte cell fate and development. We explore the role of BCR dependent and independent calcium signaling pathways in anergy, exhaustion and also in B cell differentiation.</i></p> <p><i>We developed research programs based on in vitro and in vivo studies that demonstrate a role of Ca<sup>2+</sup> influx deregulations in Systemic Erythematous Lupus development and that lead us to the identification of STIM1 as a therapeutic target for this disease. The laboratory strongly interacts with the Brest University Hospital, that allows us to develop strong interactions between practice and clinical departments (Rheumatology, Immunology, Hematology, Nephrology) providing human models of autoimmunity. Our technical platforms (Flow cytometry, Calcium signaling modulators screening and epigenomics analysis) are definitely strengthening our research and innovation projects.</i></p> <p><i>We are looking for a young and experienced scientist (3-4 years after PhD), willing to apply for a Marie Curie Individual Fellowship (IF H2020 program*) around a very innovative project. The Marie-Curie fellow will have to propose a subject on Ca<sup>2+</sup> signaling disorders in autoimmune diseases (Sjögren's syndrome, Systemic Lupus Erythematous and Rheumatoid Arthritis...). The project will use relevant and innovative approaches to decipher calcium dependent mechanisms in normal B cell fate and development and explore their deregulations in autoimmunity.</i></p> <p><i>This call targets young and promising scientist wishing to diversify their individual competence in terms of skill acquisition through advanced training, international and intersectoral mobility. We expect an open-minded fellow looking for opportunities to acquire and transfer new knowledge in the context of scientific network sharing and development. We are looking for a highly-motivated candidate who intends ultimately to setup his own research activity within our research group. The candidate will have the</i></p>

	<p><i>chance to apply for long-term opportunities.</i></p> <p><i>Fellow needs in his CV, to have demonstrated personal initiative and dynamism in research with some publications in significant journals.</i></p> <p><i>References :</i></p> <ul style="list-style-type: none"> <li>• <i>Calcium signaling: From normal B cell development to tolerance breakdown and autoimmunity. Hémon P., Renaudineau Y., Debant M., Le Goux N., Mukherjee S., Brooks W. and <b>Mignen O.</b> Clin Rev Allergy Immunol. 2017 Oct;53(2):141-165.</i></li> <li>• <i>Ion channels and transporters in lymphocyte function and immunity. Feske S, Skolnik EY, Prakriya M. Nat Rev Immunol. 2012 Jun 15;12(7):532-47</i></li> <li>• <i>Regulation of lymphocyte function by ORAI and STIM proteins in infection and autoimmunity. Shaw PJ, <b>Feske S.</b> J Physiol. 2012 Sep 1;590(17):4157-67.</i></li> </ul>
Supervisor(s)	<p><b>Olivier Mignen</b> (<a href="mailto:olivier.mignen@univ-brest.fr">olivier.mignen@univ-brest.fr</a>) is a senior scientist at the University of Brest (France) where he is leading the research theme « Calcium signaling in normal and pathologic B cells » inside the National Institute for Health and Medical Research (INSERM) Unit U1227. He spent a total of 7 years as postdoctoral fellow and assistant professor in the laboratory of Pr. Trevor Shuttleworth (Rochester University Medical Center; NY, USA) where he was involved in the identification and characterization of store independent Ca<sup>2+</sup> channels (IARC). He obtained a permanent position as a Research Assistant Professor at University Paris XI (Paris, France) in 2000 until 2004 before getting in 2009 an INSERM “Chaire d’excellence” position in the University of Brest where he created his research group focusing on the deregulation of calcium entries in different pathologies such as Cystic Fibrosis, pancreatitis. Taking advantage of his 15 years working on STIM and ORAI proteins, Olivier Mignen is now focusing his research on calcium entries deregulations in cancer and autoimmune disorders. He is deeply involved in Calcium Signaling networks such as the canceropole grand Ouest “ion channel and cancer Network” or the European COST action on ion channels as therapeutic targets for modulating the immune responses (1406 IONCHAN-IMMUNRESPON). O Mignen just won the 2017 MATWIN award as the best academic project of therapeutic development for cancer.</p> <p>- IARC: a novel Arachidonate-regulated, noncapacitative Ca<sup>2+</sup> entry. <b>O. Mignen</b> and T. Shuttleworth. (2000) <u>Journal of Biological Chemistry</u> - 275 (13), 9114-9119.</p> <p>- STIM1 regulates Ca<sup>2+</sup> entry via arachidonate-regulated Ca<sup>2+</sup>-selective (ARC) channels without store-depletion or translocation to the plasma membrane. <b>O Mignen</b>, J.L. Thompson, and T.J. Shuttleworth (2007) <u>Journal of Physiology</u> (London); 579(Pt 3):</p>

	<p>703-15</p> <p>- Constitutive calcium entry: updated views and insights. <b>Mignen O.</b> Constantin B., Potier-Cartereau M., Penna A., Gautier M., Guéguinou M., Renaudineau R., Shoji K., Félix R., Bayet E., Buscaglia P., Debant D., Chantôme A., Vandier C. <i>Eur Biophys J.</i> (2017), Jul;46(5):395-413</p> <p><a href="https://www.researchgate.net/profile/Olivier_Mignen">https://www.researchgate.net/profile/Olivier_Mignen</a></p>
<p>Department/Research:</p>	<p>Unit: INSERM U1227: "B Lymphocyte and Auto-immunity" <a href="http://www.univ-brest.fr/immunologie">http://www.univ-brest.fr/immunologie</a></p> <p>The laboratory's research main theme is "Study of normal and pathological B-cell to propose immunotherapy for B-cell diseases such as auto-immune diseases (Sjögren's syndrome, Systemic Lupus Erythematosus and Rheumatoid Arthritis) and cancer (Chronic lymphocytic Leukemia). Basic and clinical approaches to explore the role of B-lymphocyte in autoimmunity and cancer are developed. We are deciphering Ca<sup>2+</sup> signaling deregulations in B cells with a therapeutic final objective. We are exploring the role of BCR dependent and independent calcium signaling pathways in B cell fate and development and their implications in autoimmunity. We set up in vitro and in vivo studies to end up with innovative project proposing Ca<sup>2+</sup> signaling modulators as therapeutic tools for autoimmune diseases. O Mignen is in charge of a screening platform (3 labs) dedicated to the identification of Ca<sup>2+</sup> signaling modulators for therapies.</p> <p>Our international recognition and strong expertise in the field of autoimmunity, calcium signaling and cancer allowed us to set up extensive networks and strong collaborations. For example, the laboratory has been a member of the Labex "Immunotherapy, Graft, Oncology" (IGO) since its labeling in 2012. It co-hosts the "Ion Channels" and "Epigenetics" networks of the Cancéropôle Grand Ouest and is heavily involved in the European Consortium "Innovative Medicine Initiative" (IMI) "Molecular Reclassification to Find Clinically Useful Biomarkers for Systemic Autoimmune Diseases (PRECISESADS) and the European consortium HARMONization and integrative analysis of regional, national and international Cohorts on primary Sjögren's Syndrome (pSS) towards improved stratification, treatment and health policy making (HarmonicSS). Our research is part of the European COST action 1406 IONCHAN-IMMUNRESPON. We want now to use these networks to push forward the field of Ca<sup>2+</sup> signaling and autoimmune diseases.</p>
<p>Suggestion for interdisciplinary / intersectoral secondments</p>	<p>Bioinformatics and data mining. Optic and biophysics</p>

Skills Requirements  
(optional) :

*Skill and expertise Specific Requirements:*

*Immunology - calcium signaling*

*Imaging techniques – Molecular Biology – In vivo experimental approaches – Fluorescence Microscopy – cytometry*

*Skills and experience in training and knowledge transfer are required.*

*We expect complementary expertise of those we already have in the unit. (such as in vivo imaging)*

*We also are expecting from the fellow to have already personally applied for grants or awards, to have actively participate to several national and international conferences and showed his high motivation for mobility.*

*Required Languages: Spoken and written English*

*Senior post doc with at least 2-3 years post-doctoral experience.*

*Publications: at least 1 per year since the PhD in 1<sup>st</sup> author and at least 2 papers in journals with IF>8*