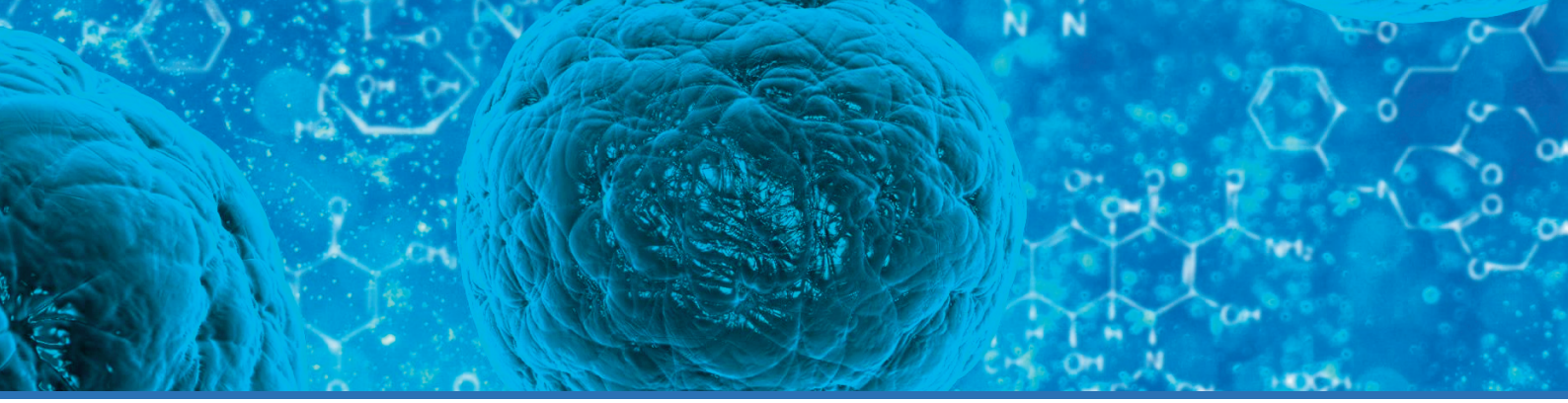

POSTDOCTORAL POSITION
in TEAM 2 of INSERM UMR 1064-CRTI (Nantes, FRANCE) for the RESHAPE EU H2020 Program

The project will aim to generate next-generation Treg products (more stable Treg, more potent Treg, etc) using genome editing and to apply cell therapy in patients with organ transplantation or autoimmune diseases. The project will focus on CD8+ Tregs that will be engineered by advanced technologies including CRISPR/Cas9. Despite that CD8+ Tregs were reported before CD4+ Tregs and although they have now been thoroughly characterized (Bézie et al., 2018), there has not been yet any clinical application with them. CD8+ Tregs have several features different from CD4+ Tregs and make them interesting potential therapeutic alternatives or complementary to CD4+ Tregs (Bézie et al., 2018). We have characterized CD8+ Tregs in rodents and humans as CD45RC-Foxp3+ suppressor cells representing about 1% of total CD8+ T cells that are non-cytotoxic and act through cytokines and cell contact dependent mechanisms, at least mediated by IL-34 and IFNgamma acting through pDCs (Bezie et al., 2018; Bezie et al., 2015; Guillonneau et al., 2007; Li et al., 2010; Picarda et al., 2017; Picarda et al., 2014). Human in vitro expanded polyclonal CD8+ Tregs inhibit human skin rejection in immune humanized NSG mice (Bezie et al., 2018). This project will be performed in the context of an European Union H2020 project with nine European partners (Charité-Berlin, Oxford University…) (an abstract of the objectives of RESHAPE is below). The candidate needs to have experience in flow cytometry, cell sorting, culture of cells. Expertise in molecular biology allowing to perform genetic modification of T cells and experience in animal work is desirable.

We seek a highly-motivated and autonomous postdoc. The postdoc position will cover 3 years of salary. The salary will depend on qualifications and previous training. Participations to national as well as international meetings will be covered.

The research activity will take place in a strong research environment within Team 2 of INSERM UMR 1064-Center for Research in Transplantation and Immunology (CRTI) (http://www.itun.nantes.inserm.fr/Team-2) led by Carole Guillonneau and Ignacio Anegon and under their direct supervision. INSERM is the public French National Institute for Health and Biomedical Research. INSERM UMR 1064-CRTI is the largest research center in France working in organ transplantation and autoimmunity. It comprises laboratories and animal facilities (4,000 m2) and is part of a transplantation institute together with the Transplantation Department of the Nantes University Hospital. Clinical and research areas as well as meeting and teaching rooms are housed in the same building, which is located within the Nantes University Hospital.

INSERM UMR 1064-CRTI (190 persons total) is organized in 5 research teams and houses several core facilities (small and large animal facilities, molecular biology, lentiviral vector production, high-speed cell sorting, microsurgery, protein and antibody purification, CRISPR/Cas9 generation and application and rat transgenesis). Topics span several areas of research related to Transplantation, including Molecular & Cell Biology, Immunology, Neuroscience, Infectious Diseases, Regenerative Medicine, Stem Cells, and Genomics.

INSERM UMR 1064-CRTI has strong interfaces with several University Hospital clinical departments and is part of a local research institute (SFR François Bonamy) bringing together several other INSERM laboratories and houses more than 850 faculty staff with several core facilities (e.g. confocal imaging, DNA microarrays, production of viral gene vectors).

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 825392.

The city of Nantes offers an attractive and dynamic cultural environment and is conveniently located within 2 hours train from Paris and 45 min drive or train of the Atlantic West Coast.

The position is open immediately. The application should be sent electronically to ianegon@nantes.inserm.fr and carole.guillonneau@univ-nantes.fr and should include:

- a cover letter with a short description of achievements, the reasons why the candidate applies to this program and a short statement on career planning;
- a CV with a complete list of publications;
- 2 letters of references.

RESHAPE project abstract (https://cordis.europa.eu/project/rcn/219121/factsheet/en)

Adoptive transfer of regulatory T cells (Treg) is a promising new therapeutic option to reshape undesired intra-tissue immune imbalance in immune-related disease entities. It supports long-term function of allografts and use of Advanced Therapy Medicinal Products (ATMP) by overcoming the challenge of unwanted immune reaction by the recipient of the ATMP. Therefore, adoptive Treg therapy is a potential game changer in health care, particularly in immune diseases, organ & hematopoietic stem cell (HSC) transplantation, and regenerative medicine, including gene therapy. Based on the Triple-T concept - Transdisciplinarity, Technology, Translation - the major goal of RESHAPE is to transform the treatment of patients suffering from undesired immunity/inflammation, who presently have limited curative treatment options, by applying novel Treg approaches that overcome the limitations of 1st generation Treg product developments. Members of the consortium, with academic & biotech backgrounds, are pioneers in the development of Treg therapy from basic science to very recent encouraging First-In-Human (FIH) clinical trials of the 1st generation Treg products. They have a long track record of collaboration, including in EC-funded projects. The first clinical trials were performed to combat organ transplant rejection and Graft-versus-Host-Disease. However, promising preclinical studies offer a broad application field of Treg therapy beyond allotransplantation. Based on our preclinical & clinical data, we have identified several opportunities for improving Treg therapy, such as enhanced antigen specificity & functional stability, and recipient conditioning, which will be addressed by RESHAPE. The next generation Treg products, developed by advanced technologies including CRISPR/Cas9, will be tested on platforms applying new methods for cell characteristics in both *in vivo* /*in vitro* models, and finally proven in FIH-clinical trials accompanied by biomarker and health economic studies.

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