

## What is the ExposUM Doctoral Nexus ?

The Doctoral Nexus proposed by the ExposUM Institute are networks of 3 to 4 PhD students from different disciplines and affiliated to at least two different research units. Compared with a traditional PhD, taking part in a Doctoral Nexus will encourage the ability to work in a team and to design projects in a transdisciplinary way while deepening one's own field of expertise. A specific teaching programme will be offered and the doctoral students concerned will also have the opportunity to organise a seminar within the Nexus network. Theses are funded from the outset for 4 years, including the PhD student's salary and an environmental allowance.



### Project Summary Nexus

#### SECS (Society & Social Environment in the Face of Suicidal Behaviors)

Suicide, with 700,000 annual deaths, including 10,000 in France, represents a major challenge for global health. It generates enormous social and economic costs, particularly through healthcare consumption. The complexity of suicidal phenomena, influenced by individual, social, and environmental factors, requires a holistic approach. The current challenge lies in identifying reliable clinico-biological markers to enhance our predictive capabilities for individuals at risk and to develop effective and personalized therapeutic strategies.

Suicidal behavior appears as a means to escape unbearable psychological and social pain rather than life itself. Indeed, isolation and social exclusion, unfortunately, a very current issue, are sources of pain that precipitate suicidal acts. Through excessive healthcare consumption, individuals at suicide risk might attempt to alleviate this pain and reconnect with society.

Social bonds are essential for survival. When their integrity is threatened, psychological/social pain and an inflammatory response are induced similarly to physical pain and inflammation in the face of threats to physical integrity. Studying painful and inflammatory responses in situations of social adversity is therefore necessary for a better understanding of the pathophysiological mechanisms of suicidal behaviors.

Suicide prevention is an obvious health priority that, at the societal level, must be aligned with the upcoming legalization of assisted suicide, which could alter social representations of suicide. Our proposal is an integrated research program, anchored in ethics (ED Droit et science politique ED 461), statistical modeling (IDESP, UMR1318), and biomarkers (IGF, ED CBS2), offering a comprehensive approach to understand, prevent, and manage suicidal behaviors.

Axis 1 - Ethics and Social Representations:

The debate on assisted suicide raises complex ethical questions, juxtaposing pain relief and suicide prevention. A thorough reflection on suicide prevention, adapting to its changing social representations, will be addressed.

#### Axis 2 - Modeling and Prediction of Suicide Risk:

The use of healthcare consumption data provides a unique opportunity to model suicide risk. Using a statistical and artificial intelligence approach, the construction of predictive algorithms, notably through the use of neural networks, aims to better predict suicidal behaviors.

#### Axis 3 - Biomarkers of Suicidal Behaviors:

Exploring the psychological pain and specific immuno-inflammatory response of individuals at suicide risk exposed to social stress, the identification of biomarkers will strengthen the pathophysiological understanding of suicidal behaviors, paving the way for personalized treatment strategies.

By approaching suicidal phenomena from different perspectives, our project contributes to understanding the impact of the exposome on suicidal behaviors and initiates a reflection on the transformation of social environments, promoting the development of personalized and effective interventions. The project will naturally allow the three axes to interpenetrate, as each aspect questions the others: personalized medicine - pain - ethics - use of artificial intelligence.

## Thesis Topic:

### Social Neurosciences: Inflammatory and painful Responses to Social Stress in Suicidal Behaviors

Facing psychosocial stressors such as breakups, financial or professional difficulties is central to our human condition; however, some individuals attempt suicide in such contexts of social adversity, suggesting the existence of interindividual differences in vulnerability to social stress. Clinically, interpersonal social stressors induce social pain, which could be likened to psychological pain; the latter is associated with suicidal ideation and predictive of suicide attempt (SA) within a year among depressed individuals. Also, perceived psychological pain in daily life in individuals with a history of SA and the level of basal inflammation correlate with orbitofrontal cortex activation during an experimental social exclusion task (Cyberball game), promoting altered decision-making, which is a cognitive trait of suicide vulnerability. Biologically, childhood maltreatment, loneliness, and social exclusion, suicide risk factors, are associated with increased hypothalamo-pituitary-adrenal axis activity and inflammation. However, the emergence of psychological/social pain and its link to the inflammatory response remains to be established, especially in individuals at risk of suicide. Our team (and others) identified, through salivary cortisol measurement, that increased reactivity to social stress during an experimental social stress (Trial Social Stress Test) characterized a specific group of suicide risk subjects. However, studies on the inflammatory response to social stress in individuals with a history of SA are still lacking.

We hypothesize that suicide risk patients have a specific biological (inflammatory) and painful (psychological pain) response to situations of social exclusion or devaluation, promoting suicidal ideation or behaviors. **Our overall goal is to identify biomarkers for suicidal behavior in**

**interpersonal social stress situations through the study of inflammation and psychological pain in patients with a history of depression. Based on data already collected in clinical studies conducted by our team, we propose to:**

- Compare peripheral immune-inflammatory and painful responses to experimental social stress (TSST) in subjects with and without a history of SA.
- Test the predictive value of these markers (clinical and biological) on the risk of SA occurrence within a year.
- Study the influence of individuals' baseline inflammatory status on psychological/social pain following experimental social stress.
- Identify, both cross-sectionally and prospectively, the link between psychological pain, peripheral inflammatory markers (serum, cellular, gene expression of inflammation, and epigenetics), and suicidal ideation in local cohorts of depressed patients and a national cohort of bipolar disorder patients.
- Evaluate the modulating or mediating effect of inflammation between the presence of early (childhood maltreatment) or late (loneliness) adversity.
- Assess the impact of social support on psychological pain and inflammation in suicide risk patients.

To achieve these objectives, we will leverage data collected from clinical studies conducted by our team (using TSST (N=75) and Cyberball Game (N=155)), a cohort of depressed patients followed in our Department (N>800), or a cohort of bipolar disorder patients followed in the national FACE-BD network (N>3000).

The project aims to identify pathophysiological mechanisms involved in vulnerability to suicidal behavior related to exposure to interpersonal stressors, leading to the precise identification of particularly at-risk individuals, therapeutic target identification, and personalization of therapeutic strategies based on patient profiles.

## Application Procedure

The application must consist of the following elements:

A resume (CV)

A letter of motivation

A copy of the diploma allowing enrollment

Specific documents requested by the doctoral school Sciences Chimiques et Biologiques pour la Santé (CBS2) (<https://edcbs2.umontpellier.fr/>)

If you wish to apply for this position, please send an email as soon as possible to:

[philippe.courtet@umontpellier.fr](mailto:philippe.courtet@umontpellier.fr)



[e-olie@chu-montpellier.fr](mailto:e-olie@chu-montpellier.fr)

cc : [exposum-aap@umontpellier.fr](mailto:exposum-aap@umontpellier.fr) afin de les informer de votre intérêt.

**Before Sunday, April 21st, 8:00 PM CET**





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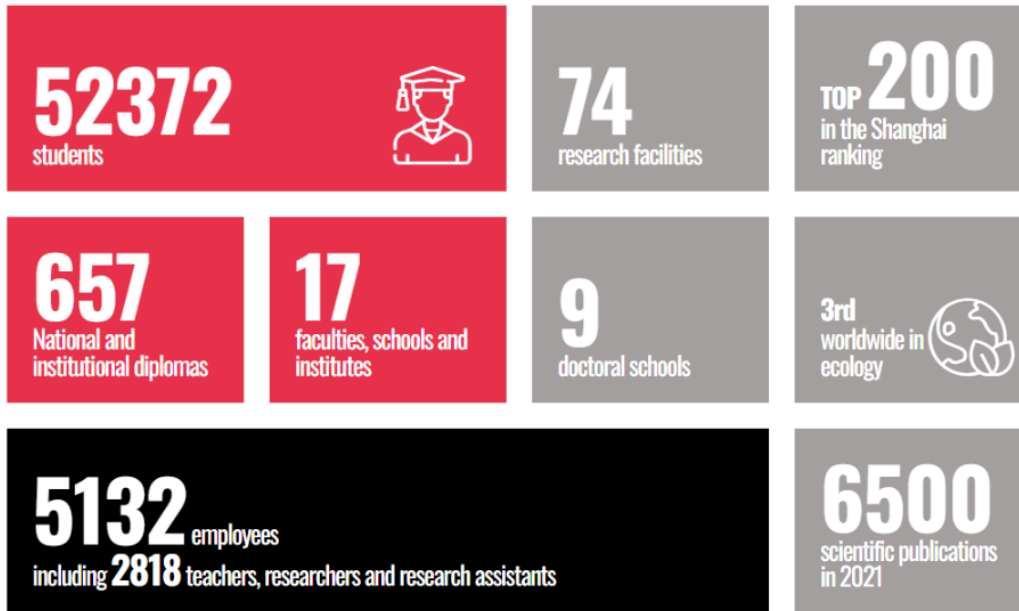


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# The University of Montpellier

## KEY FIGURES



## RESEARCH CENTERS

From space exploration and robotics to ecological engineering and chronic diseases, UM researchers are inventing tomorrow's solutions for mankind and the environment. Dynamic research, conducted in close collaboration with research organizations and benefiting from high-level technological platforms to meet the needs of 21st century society.

The UM is committed to promoting its cutting-edge research by forging close links with local industry, particularly in the biomedical and new technologies sectors.

**More Information:** <https://www.umontpellier.fr/en/recherche/unites-de-recherche>

## SCIENTIFIC APPEAL

Open to the world, the University of Montpellier contributes to the structuring of the European higher education area, and strengthens its international positioning and attractiveness, in close collaboration with its partners in the I-SITE Program of Excellence, through programs adapted to the major scientific challenges it faces.

**More Information:** <https://www.umontpellier.fr/en/international/attractivite-scientifique>



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