3iA Côte d'Azur
Interdisciplinary Institute for Artificial Intelligence

# Ph.D. research topic

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- Title of the proposed topic: **Identification of biological patterns of abdominal aortic aneurysm outcomes using unsupervised machine learning**
- Research axis of the 3IA: AI for integrative computational medicine (axis 2)
- **Supervisor (name, affiliation, email):**

Juliette RAFFORT-LAREYRE (CHU NICE/ UNIVERSITE COTE D'AZUR)
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- Potential co-supervisor (name, affiliation):

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- The laboratory and/or research group:

Inserm U1065, C3M, Team 9

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**Apply by sending an email directly to the supervisor.**
**The application will include :**

- Letter of recommendation of the supervisor indicated above
- Curriculum vitæ.
- Motivation Letter.
- Academic transcripts of a master's degree(s) or equivalent.
- At least, one letter of recommendation.
- Internship report, if possible.

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- Description of the topic:

- Title: **Identification of biological patterns of abdominal aortic aneurysm outcomes using unsupervised machine learning**

Cardiovascular diseases are the leading cause of premature death in developed countries (1). Among them, abdominal aortic aneurysm (AAA) has become a significant health public challenge worldwide, with extremely high rates of mortality in case of rupture (2-5). The only curative treatment relies on surgery and clinicians are confronted to a critical lack of tools to evaluate the outcomes of patients. As a result, some patients are treated while they would never have ruptured and others with an AAA below the threshold for treatment do develop a fatal rupture.
Several circulating biomarkers reflecting these main pathophysiological features of AAA have been proposed (6-8). However, studies performed so far have shown that all strategies based on one-single biomarker have not proven enough sensitivity or specificity to screen for the disease, monitor its progression, choose the optimal therapeutic option, or evaluate the results of treatment. Clinicians are confronted to a **critical lack of biomarker**. There is an

urgent need to break with classical searching strategies and to switch from a single marker targeted approach into a non-hypothesis-driven approach using a combination of biomarkers. As no biomarker is yet currently used in clinical practice, imaging plays a central role in patients care. Several imaging techniques are available and computed tomography angiography (CTA) is the most commonly used (2, 9). Our team previously develop an automatic imaging software that allows to provide detailed anatomic characteristics of the AAA morphology from CTA of patients (10).

The step from identifying biomarkers and optimizing imaging analysis to predict patients' outcomes is challenging and the question that arises is: **can we predict AAA outcomes and help in the clinical decision-making using Artificial Intelligence (AI)?** There is a growing interest of the use of machine learning (ML) for cardiovascular disease prediction (11) and only a few studies developed Deep Learning (DL) algorithms to predict the outcomes of patients with AAA (12). The studies published so far only focused on one single risk prediction, mainly in-hospital or 30-day mortality (12). **None of them took up the challenge to use innovative techniques in biology and imaging to identify new patterns and to combine them using ML to develop efficient predictive models**.

The aim of the project is to **identify biological patterns of AAA outcomes and to develop predictive scores using ML** to enable precision medicine and propose a personalized therapeutic approach.

This project is based upon a pre-existing clinical cohort of patients with AAA for which all biological samples including aneurysmal aortic tissue and blood (serum, plasma) have already been collected. A database has already been built including the clinical characteristics of patients, the anatomical characteristics of AAA based on CTA imaging and the outcomes of patients.

New biomarkers of AAA outcomes will be identified at the transcriptomic and proteomic level using a targeted approach and high-throughput multi-omics approaches. RNAs sequencing and mass spectrometry-based proteomic approach (LC-MS/MS) will be performed in aneurysmal aortic tissues. The histological characteristics of the AAA (presence of inflammatory cells and calcifications) will be characterized using immunohistochemistry. Based on preliminary data from the lab, micro-RNAs profiling will also be performed using qPCR.

Several outcomes will be investigated including the AAA growth and progression, the occurrence of rupture and the mortality. For patients who underwent surgical repair, the risk of post-operative complications will be assessed. Patterns and profiles will be compared between patients according to the risk of each outcomes. Identified RNAs and proteins will be clustered using differential analysis and several unsupervised ML method will be tested to identify a biological signature of AAA outcomes. A panel of the most relevant biomarkers will then be selected and predictive scores combining clinical, biological and imaging characteristics will be developed using ML.

**References:**

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