Funded thesis offer

Title: DIMISH - Sequential diagnosis of inflammatory myopathies by infrared spectral histopathology

Keywords: myositis; infrared spectral imaging; artificial intelligence; sequential diagnosis

Summary of the doctoral project:

Idiopathic inflammatory myopathies (IIM) are rare autoimmune diseases that can be divided into several groups: dermatomyositis (DM), overlap syndromes largely represented by antisynthetase syndrome (ASS), immune-mediated necrotizing myopathies (IMNM), and inclusion body myositis (IBM). Each group is further divided into homogeneous subgroups of patients with characteristic phenotypes and prognoses, such as paraneoplastic forms.

In clinical practice, the diagnosis of IIM relies on pathognomonic clinical manifestations, the presence of specific antibodies, electromyography (EMG), histology of muscle biopsies, and immunostaining. However, an accurate early diagnosis of inflammatory myopathy can be difficult and time-consuming, especially for paraneoplastic forms. In some cases, the diagnosis may be nonspecific, and the final diagnosis remains suspected based on a combination of evidence. Moreover, there is no histological feature that can guide towards paraneoplastic forms, particularly in the presence of anti-TIF1γ antibodies, with over 50% of paraneoplastic cases being synchronous or occurring within 3 years before the discovery of cancer, or dermatomyositis with NXP2 antibodies, which are associated with cancer in over 20% of cases. However, these forms have different prognoses and therapeutic management.

Infrared spectral histology is a clinically promising tool that can differentiate the pathophysiological states of samples. It combines: i) spectral imaging of mid-infrared absorption, which probes the biochemical composition (proteins, lipids, amino acids, carbohydrates, etc.) of samples and can detect subtle structural and molecular changes from unlabeled samples, and ii) artificial intelligence that digests and exploits the large amount of information contained in these highly hyperspectral images. This technology has shown its potential for aiding the diagnosis of numerous pathologies (mostly cancers) from tissue sections. However, to our knowledge, no study has explored the potential contribution of this biophotonic tool for the characterization or diagnosis of IIM.

Therefore, the aim of this thesis is to develop infrared spectral histology and combine it with histological, clinical, and biological data to create a new tool for rapid and automated sequential diagnosis of different types, subtypes, and phenotypes of inflammatory myopathies. Using infrared spectral images acquired from thin sections of muscle biopsies obtained from different patient groups (without muscle disease, with IIM, or with other muscle pathologies mimicking IIM), various artificial intelligence algorithms will be trained to diagnose IIM at different levels of granularity: i) distinguishing different groups of IIM (DM, ASS, IMNM, IBM), ii) identifying different subgroups (often specific to different antibodies), iii) detecting paraneoplastic forms, which are particularly challenging to diagnose. Specifically, deep learning algorithms leveraging the properties of 1D to 3D convolutional neural networks (CNNs) will be implemented to exploit the richness of information contained in the spectral dimension and the two spatial dimensions of infrared images. These spectral data will be combined with clinical, biological, and histological data to train deep learning algorithms that take into account the variability.

This new multimodal tool based on biophotonic techniques and artificial intelligence will improve the diagnosis of myositis, enabling clinicians to make more informed treatment choices and enhance patient management.

Host laboratories:

This subject is a collaboration between the BioSpecT unit of the University of Reims Champagne Ardenne and the Rheumatology Department of the University Hospital of Reims.

The BioSpecT (Translational BioSpectroscopy) unit is a multidisciplinary group composed of clinicians, biologists, physicists, and bioinformaticians. Its mission is to develop vibrational spectroscopy approaches (Raman scattering and infrared absorption) for the characterization of biological samples, such as cells, tissues, and biofluids. These research efforts aim to identify new types of biomarkers, validated for clinical transfer (from bench to bedside approach), which could help clinicians predict the progression of a disease or its response to treatment as early as possible. These approaches rely on a combination of Raman or infrared techniques with multivariate chemometric data analysis, enabling the identification of reliable indicators of pathological biological processes in a completely objective, reproducible, and automated manner, without the need for labeling, reagents, or specific sample preparation. The identification of spectroscopic markers also involves characterizing biological models of the tumor microenvironment.
The Rheumatology Department of the University Hospital of Reims has extensive clinical experience in myositis, including their medical and biological characteristics, diagnosis, and management.

Nature of funding:
Université de Reims Champagne Ardenne and Région Grand Est

Candidate profile:
The proposed doctoral subject requires to collaborate with experts in different scientific domains (biophysics, chemometrics, medicine). The candidate will have a university education in artificial intelligence, signal and image processing, applied mathematics, bioinformatics or chemometrics. The candidate must justify of a strong interest in medical applications and of strong skills in Python.
The candidates must send their CV, motivation letter, letter of recommendation and academic transcript of their Master.

Contacts:

- Dr Cyril GOBINET, cyril.gobinet@univ-reims.fr
- Pr. Jean-Hughes SALMON, jhsalmon@chu-reims.fr
- Dr. Loïs BOLKO, lbolko@chu-reims.fr

Application procedure:
Visit https://adum.fr/as/ed/voirproposition.pl?langue=&site=edsfs&matricule_prop=50402 and click on the “Candidater” button.