MyoRobot IBD

The impact of ulcerative colitis on structure and function of skeletal muscle

Inflammatory Bowel Disease represents a chronic inflammation in the colon affecting approx. 170,000 people in Germany. While symptoms range from stomach pain to bloody diarrhea, its cause is still unknown. We are particularly interested in the general weakness described by patients, which is expressed in a loss of strength in extremities and hampered movement speed. As for the cause of the disease, a rationale behind these effects remains speculative and a comprehensive study that systematically investigates the impact of inflammation in ulcerative colitis on the biomechanics properties of muscle is missing to potentially develop strategies to ameliorate disease progression or ease symptoms. Therefore, we conduct a pilot study on a colitis mouse model with our partners at the Med1.

In this setting, your work is reflected by investigating active and passive muscle biomechanics to potentially answers to the following objectives:

1) Functional aspects: Does UC (actue or chronic) alter the passive / active biomechanics performance in single muscle fibres?
   - 1.1 Maximum force generation affected?
   - 1.2 Calcium sensitivity affected?
   - 1.3 Passive restoration force or axial elasticity?
   - 1.4 Speed of contraction?

   How do they relate

2) Structural aspects. Does UC (actue or chronic) change the myofibrillar alignment / the homogenity or regularity of sarcomeres? (do they branch, or fork up?)
   - 2.1 Cosine Angle Sum (CAS) changes?
   - 2.2 Vernier Density (VD) increases?

Together with our research team, you will work with two to three unique metrologies of our institute: The *MechaMorph*, the *MyoRobot,* and the *TrimScope*. While "functional" aspects are mainly investigated by our research team with the *MyoRobot* technology by researching maximum force generation and calcium sensitivity. You will complement these experiments by performing structure-function investigations with the *MechaMorph* and the *TrimScope* (this does not mean you will be excluded from *MyoRobot* experiments). The *MechaMorph* basically reflects a small-scale system with similar functionality as the *MyoRobot*, despite that it can be placed under a microscope (*TrimScope*). This is essential, since you will carry out passive elasticity recordings in so called resting-length tension curves to analyze passive axial stiffness, and the influence of stretch on sarcomere integrity (via Cosine Angle Sum and Vernier Density). The latter are determined label-free (auto-fluorescence of myosin) by recording image stacks with our 2-photon microscope (*TrimScope*) before and after each resting length-tension assessment. Eventually, it will also be your task to analyze these results, evaluate them and put them in context with the "functional" data obtained from *MyoRobot* experiments.

MyoRobot
Can cover 1.1 to 1.4

MechaMorph
Image stack for 2.1 & 2.2 (prior)

RLT to assess 1.3

Image stack for 2.1 & 2.2 (post)

SHG
Cover 2.1 & 2.2 with whole cleared muscle (EDL)

If you feel interested and/or challenged, please contact Dr. Michael Haug (michael.haug@fau.de) or Mena Michael (mena.michael@fau.de).

Literature and Links:

- Nardone et al. “Inflammatory Bowel Diseases and Sarcopenia: The Role of Inflammation and Gut Microbiota in the Development of Muscle Failure”; Frontiers in Immunology; DOI: 10.3389/fimmu.2021.694217
- Zaltman et al. “Lower extremity mobility limitation and impaired muscle function in women with ulcerative colitis”; Journal of Chron’s and Colitis; DOI: 10.1016/j.crohns.2013.11.006