Focus of research group (I)

Name PI: Coen Ottenheijm
Department, UMC: Physiology (VUmc)
Size of research group: 10 (2 postdoc; 5 PhD; 3 tech.)

Current mission, vision and aims

Mission:
• Better understand the functioning of the diaphragm muscle, and the mechanisms underlying critical illness associated diaphragm dysfunction.

Vision:
• Prevention of diaphragm dysfunction by ‘diaphragm protective’ ventilation strategies, and
• Treatment of diaphragm dysfunction with compounds.

Aims:
• Study diaphragm function and structure during mechanical ventilation (with PEEP)
• Study the efficacy of troponin activators (col. with Industry)
• Study the role of mechanosensing proteins in diaphragm atrophy during mechanical ventilation-induced diaphragm unloading
Focus of research group (II)

Current expertise

• (Diaphragm) muscle contractility in animal models (rats/mice)
  \textbf{\textit{In vivo:}} Plethysmography
  Ultrasound
  MRI (Gustav Strijkers)

  \textbf{\textit{In vitro:}} Intact muscle strips (Newton)
  Permeabilized muscle fibers (milli-Newton)
  Myofibril (sarcomeres) (nano-Newton)

• (Diaphragm) muscle structure
  Low angle x-ray diffraction (Argonne National Laboratories)
  Electron microscopy
  Superresolution microscopy (STED; STORM; PALM with PALM \textit{compatible mouse models})

• Unique diaphragm biopsies of critically ill patients & rat/mouse models

Current funding

EU-H2020 (RISE)
NIH (R01)
ACS
Prinses Beatrix Muscle Foundation
Muscle Dystrophy Association UK
Foundation building Strength for Nemaline Myopathy (US)
Cytokinetics (Industry (US))
Future plans

Short term (1-2 year) plan
• Combined in vitro/in vivo assessment of diaphragm function in ICU patients;
• Mechanosensing proteins in the mechanically unloaded diaphragm: focus on titin.

Necessary infrastructure:
• Animal facility!
• In vivo/in vitro contractility assays (available)
• MRI (VUmc / AMC; under development)
• Microscopy platform (available)

Long term (>2 year) plan
• Diaphragm expertise center (clinical/pre-clinical) for patients on ventilation (not limited to critically ill)

Necessary infrastructure:
• Animal facility!
• Imaging (ultrasound/MRI/PET tracers for perfusion/metabolism)
• up-to-date microscopy platform
• Zebrafish facility (although they lack a diaphragm muscle…)

Collaboration in ACS
Leo Heunks (IC; VUmc)
Tim Marcus (Radiology: VUmc)
Janneke Horn / Marcus Schultz (IC; AMC)
Jeroen Hutten (Neonatology; AMC)
Gustav Strijkers / Aart Nederveen (Radiology; AMC)