

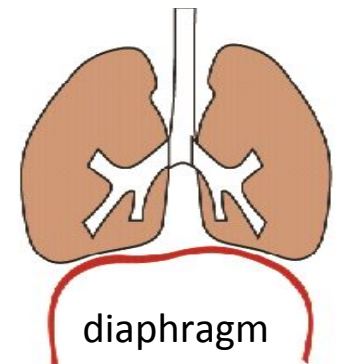
# Focus of research group (I)

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

## Current mission, vision and aims

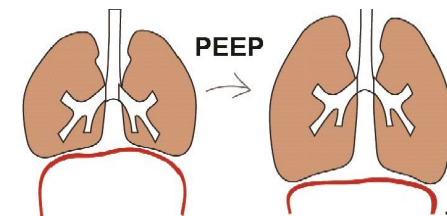
### Mission:

- 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



Heart Failure & Arrhythmias



Pulmonary Hypertension & Thrombosis



Atherosclerosis & Ischemic Syndromes



Diabetes & Metabolism



Microcirculation

# Focus of research group (II)

## Current expertise

- **(Diaphragm) muscle contractility in animal models (rats/mice)**  
in vivo: Plethysmography  
Ultrasound  
MRI (Gustav Strijkers)  
  
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 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))



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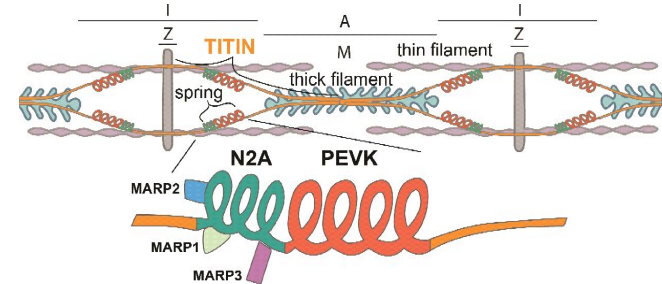
# Future plans

## 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)