

Overview ongoing research Pulmonary Hypertension & Thrombosis Research Program ACS – February 2019

PI	UMC	Dept	Mission	Expertise
Frances de Man	AMC	Pulmonary Medicine	Right ventricular adaptation to increased pressure overload	RV functional measurements <ul style="list-style-type: none"> <li>- RV imaging (preclinical and clinical)</li> <li>- RV pressure volume analyses (preclinical and clinical)</li> </ul> Preclinical drug studies <ul style="list-style-type: none"> <li>- Pharmaceuticals</li> <li>- Gene therapy</li> </ul> Histology/protein/RNA analyses iPS cardiomyocytes/3D EHT (Aida Lucia-Valldeperas) Epidemiology / statistical methodology
Jurjan Aman	VUmc	Pulmonary Diseases / Physiology	<ul style="list-style-type: none"> <li>• Molecular mechanisms of pulmonary vascular leak</li> <li>• Link between vascular leak and vascular remodelling</li> <li>• Identify targets for pharmacological intervention</li> </ul>	<ul style="list-style-type: none"> <li>• Endothelial cell cultures</li> <li>• Endothelial barrier measurements (in vitro and in vivo)</li> <li>• Immunofluorescence imaging of cell-matrix adhesions</li> <li>• Pharmacological inhibitors</li> <li>• CRISPR/Cas9 genetic modulation in primary human cells</li> <li>• ChIP, Allelic Imbalance</li> </ul>
Michiel Coppens	AMC	Vascular Medicine/Hemophilia Treatment Centre	Clinical research that can directly impact patient care. <ul style="list-style-type: none"> <li>• Management and outcome of anticoagulant associated bleeding</li> <li>• Management of menorrhagia in women treated with oral anticoagulation.</li> </ul>	<ul style="list-style-type: none"> <li>• Reversal of DOACs / Bleeding registr(ies)</li> <li>• Menorrhagia (collaboration Middeldorp)</li> <li>• Oral DOAC resorption in Short Bowel Syndrome (collaboration Mathot/Serlie)                             <ul style="list-style-type: none"> <li>• Successful pilot, prospective cohort ongoing</li> </ul> </li> <li>• Gene therapy                             <ul style="list-style-type: none"> <li>• Steering committee AMT-060/Uniqure Phase I/II</li> </ul> </li> <li>• Phenotype in non-severe haem A/B (collaboration Fijnvandraat)                             <ul style="list-style-type: none"> <li>• Dynamo, Flow cohorts</li> </ul> </li> </ul>

			<ul style="list-style-type: none"> <li>• Oral resorption of DOACs in patients with short bowel syndrome</li> <li>• Gene therapy for haemophilia A/B</li> <li>• Bleeding phenotype in non-severe haemophilia</li> </ul>	<ul style="list-style-type: none"> <li>• National haemophilia collaborations <ul style="list-style-type: none"> <li>• HiN-6, TiN, Opticlot, DAVID, Pride</li> </ul> </li> </ul>
Saskia Middeldorp	AMC	Vascular Medicine	<ul style="list-style-type: none"> <li>• To remain a world's leading research group with high impact clinical research into the causes, prevention, diagnosis and optimal management of venous thromboembolism (VTE)</li> <li>• International, multi-center collaboration and combining pharma and investigator initiated research is essential</li> </ul>	<ul style="list-style-type: none"> <li>• Thrombophilia &amp; Women's issues in Thrombosis</li> <li>• PI of two international RCTs (Highlow, ALIFE2)</li> <li>• Cancer and VTE (collaboration Harry Buller, PW Kamphuisen, Nick van Es)</li> <li>• Optimal management of anticoagulation (collaboration Michiel Coppens)</li> <li>• Steering Committee of andexanet registry studies</li> <li>• Microbioma and VTE (collaboration Thijs van Mens) - biobanks</li> </ul>
Lilian Meijboom	AMC	Radiology and Nuclear Medicine, Pulmonology, Cardiology and Cardiothoracic surgery	<ul style="list-style-type: none"> <li>• To determine the clinical course of RV and lung vascular remodelling in CTEPH and CTED patients after PEA and BPA.</li> <li>• To improve our understanding of the mechanisms of late reverse and adverse remodelling of the lung vasculature and RV function.</li> </ul>	<ul style="list-style-type: none"> <li>• CTEPH expert centre: all treatment modalities available: PEA, BPA and PH medication</li> <li>• State of the art imaging:</li> <li>• ECG gated CTA pulmonalis</li> <li>• Novel cardiac MRI techniques: lung perfusion, tissue characterization mapping and strain quantification.</li> <li>• Only centre in Netherlands with invasive cardiopulmonary exercise test</li> </ul>

Leo Heunks	VUmc	ICU	To prevent and treat critical illness associated diaphragm dysfunction by understanding the mechanisms of disease	<ul style="list-style-type: none"> <li>• Diaphragm muscle function in ICU patients <ul style="list-style-type: none"> <li>• Transdiaphragmatic pressure</li> <li>• Electromyography (esophagus and surface)</li> <li>• Ultrasound (conventional)</li> <li>• MRI, high spatial / temporal resolution (Tim Marcus)</li> </ul> </li> <li>• International network <ul style="list-style-type: none"> <li>• Co-chair WEAN SAFE executive committee</li> <li>• Visiting professor Zhejiang University, School of Medicine, Hangzhou</li> <li>• Canada</li> </ul> </li> </ul>
Tim Marcus	VUmc	Radiology & Nuclear Medicine, Pulmonology	Use of cardiovascular MRI for <ul style="list-style-type: none"> <li>• follow-up of pulmonary hypertension (PH) patients,</li> <li>• improved understanding of pathophysiology in PH</li> </ul>	<ul style="list-style-type: none"> <li>• Cardiovascular MRI</li> <li>• Pulmonary hypertension</li> </ul>
Coen Ottenheijm	VUmc	Physiology	Better understand the functioning of the diaphragm muscle, and the mechanisms underlying critical illness associated diaphragm dysfunction	<ul style="list-style-type: none"> <li>• (Diaphragm) muscle contractility in animal models (rats/mice)</li> <li>• <u>in vivo</u>: Plethysmography</li> <li>• Ultrasound</li> <li>• MRI (Gustav Strijkers)</li> <li>• <u>In vitro</u>: Intact muscle strips (Newton)</li> <li>• Permeabilized muscle fibers (milli-Newton)</li> <li>• Myofibril (sarcomeres) (nano-Newton)</li> <li>• (Diaphragm) muscle structure</li> <li>• Low angle x-ray diffraction (Argonne National Laboratories)</li> <li>• Electron microscopy</li> </ul>

				<ul style="list-style-type: none"> <li>• Superresolution microscopy (STED; STORM; PALM with PALM compatible mouse models)</li> <li>• Unique diaphragm biopsies of critically ill patients &amp; rat/mouse models</li> </ul>
Anton Vonk Noordegraaf	AMC	Pulmonary Medicine, Clinical Genetics, Radiology and Nuclear Medicine, Physiology	<ul style="list-style-type: none"> <li>• Early detection of pulmonary hypertension in risk groups (gene variants, pulmonary embolism)</li> <li>• Improved strategies for diagnosis, classification and monitoring of PH</li> <li>• Identification of new treatment modalities and strategies for PAH and CTEPH</li> </ul>	<ul style="list-style-type: none"> <li>• National referral center for PH</li> <li>• Large cohort of patients with idiopathic and heritable PAH</li> <li>• Unique cohort of BMPR2 mutation carriers</li> <li>• State of the art imaging and biomarkers:</li> <li>• MRI &amp; PET imaging</li> <li>• Liquid Biopsy (ECFCs, platelet transcriptomics)</li> <li>• Tissue bank and patient derived primary lung vascular cells</li> <li>• Machine learning</li> </ul>