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Propositions belonging to the thesis

**A Novel Preclinical Model for Chronic Thrombo-Embolitic Pulmonary Hypertension  
Development, Validation and Characterization**

Kelly Stam, Rotterdam, 24 September 2019

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1. The use of chronically instrumented animals allows serial assessment of cardiopulmonary function either during development of disease or evaluation of treatment, thereby increasing statistical power and limiting the number of animals required for a study  
(this thesis)
2. To induce CTEPH in young swine both repeated embolizations and the second hit endothelial dysfunction are required, as either intervention alone does not result in sustained CTEPH  
(this thesis)
3. Although the V/Q-mismatch plays an important role, the main cause of exercise intolerance in CTEPH is cardiac dysfunction  
(this thesis)
4. Secondary to pulmonary embolisms, worsening of PH results from pulmonary microvascular remodeling which is accompanied by alterations in the two major endothelial signaling pathways ET and NO  
(this thesis)
5. Although therapeutic Rho-kinase inhibition may not be beneficial for the pulmonary vascular tone and remodeling, it may prevent adverse cardiac remodeling  
(this thesis)
6. Like any other serious life-threatening rare diseases, PAH, CTEPH, and other severe forms of pulmonary hypertension should be diagnosed and treated at specialized centers  
(Hoepfer et al., Dtsch Arztebl Int. 2017)
7. Cardiopulmonary exercise testing is a critical tool in determining the degree of functional impairment and disease severity as well as in predicting prognosis and assessing interventional efficacy in PH  
(Weatherald et al., Annals ATS, 2017)
8. In a world of urgent translational challenges and limited resources, animal models should serve as paving stones rather than stumbling blocks on the road to new cures  
(Bolker, BioEssays, 2017)
9. The interplay between ET-1 and NO is crucial in the regulation of structure and function of the cardiovascular system, not only under physiological conditions but also, and especially, under pathological conditions.  
(Rossi et al., Int Rev Cytol, 2001)
10. Endothelial dysfunction is a key contributor to the initiation and progression of pulmonary hypertension  
(Budhiraja et al., Circulation, 2004; Huertas et al., Eur Respir J 2018)
11. Even if you fall on your face, you're still moving forward  
(Victor Kiam)