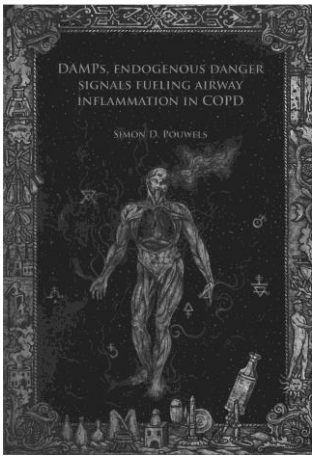
Simon Pouwels winner NVVI Van Bekkum Thesis Award 2017

Unraveling underlying mechanisms of COPD



Simon D. Pouwels PhD, lung researcher at the Department of Pathology and Medical Biology of the UMCG, is this year's NVVI Thesis Award winner. His research on DAMPs as endogenous danger signals fueling airway inflammation in COPD was highly appreciated by the jury, somewhat to Simon's surprise: "I'm not a hardcore immunologist, which makes winning this award even more special to me."

COPD is a serious and progressive lung disease characterized by both chronic bronchitis and emphysema. In the Netherlands alone, almost 7,000 people per year die from the consequences of COPD. The disease is caused by the chronic inhalation of toxic gases, such as cigarette smoke. Atmospheric pollution or, for instance, coal mine dust, may also trigger the disease. In addition, genetic predisposition contributes to the risk of developing COPD. To date, the underlying molecular and cellular mechanisms of COPD are largely unknown. "Historically, research has been focusing on asthma. Currently, there is no curative treatment for COPD. With my research I hope to contribute to unraveling the underlying mechanisms and, ultimately, to finding a cure", says Simon Pouwels.

Understanding molecular mechanisms

COPD is not just one disease, it is in fact a number of lung diseases with the same symptoms. In his thesis, Simon focuses on two main questions: "The first is to understand the molecular mechanisms of COPD, to really comprehend what happens in the lungs. The second question is why it affects around 20% of the smokers and not all." He soon figured that endogenous hazard signals called DAMPs were involved in COPD. "We hypothesized that exposure of the lungs of genetically susceptible individuals to toxic gases induces immunogenic cell death, followed by the release of Damage-Associated Molecular Patterns (DAMPs) that contribute to airway inflammation in COPD patients." He used *in vitro* cellular models with cells isolated from COPD patients and controls as well as *in vivo* mouse models to show that airway epithelial cells release DAMPs after exposure to cigarette smoke and that these DAMPs have pro-inflammatory functions. In addition, he showed that the release of specific DAMPs is increased in COPD patients.

DAMPs target for therapies

But why are some individuals more susceptible than others? Simon: "We have identified several new susceptibility genes for cigarette smoke-induced airway inflammation and DAMP release. Our results indicate that DAMPs play an important role in the pathophysiology of COPD, which really is a new conclusion." This means that DAMPs are a new possible target for future therapies of COPD patients. Future studies are needed to investigate which DAMPs or DAMP receptors exhibit the highest therapeutic potential in inhibition. Simon, who got his PhD in May, already started this research last January: "I currently focus on the RAGE receptor, one of the most important DAMP receptors. Firstly, I want to map out the importance of DAMPs and RAGE for COPD. Secondly I want to investigate the possibility to suppress RAGE signaling and thus suppress the inflammatory response. Our ultimate goal is to cure COPD."