**Application number/Title:** 42273 - Identification of novel rare genetic variants associated with COPD in the general population.

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**Keywords provided by the Applicant PI to describe the research project:**
COPD, individual susceptibility, lung function, rare genetic variants

**Application Lay Summary:**

Chronic obstructive pulmonary disease (COPD) is a chronic disease of the airways, which causes difficulties to breathe. Worldwide, over 250 million people suffer from COPD and it is expected that COPD will be the third leading cause of death in 2030. At this moment, we still don't know what causes the development of COPD.

What we do know is that both genetic and environmental factors play a role in the development of COPD. Several, so-called genome-wide association studies (GWAS) have been performed to find small differences or genetic variants in the DNA of people with COPD. However, the results of these studies can still only explain a small part of someone's risk to develop COPD. This might be caused by the fact that these studies only look into genetic variants that commonly occur in the population (at least in 5% of the population). Therefore, we looked into rare genetic variants that occur in less than 1% of the population. In our group of 36 subjects with COPD, we found 318 rare genetic variants that were present in at least 3 of our subjects. While these genetic variants are rare in the general population, they were not rare at all in our group of COPD patients. This indicates that these variants might be important in the development of COPD. In addition, we found several rare genetic variants in ciliary related genes that also might play a role in COPD.

Now, we want to test if these variants are also more present in COPD patients when we look into a big sample of the population. Therefore, we want to use the genotype data from the UK Biobank. The variants that are also different between COPD patients and controls in the UK Biobank might help to unravel the
individual susceptibility to develop COPD.