

# RESEARCH AREA II

# HIGHLIGHT

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## SOME BACKGROUND

COPD (Chronic Obstructive Pulmonary Disease) shows a steadily increasing incidence and is among the world's leading causes of death. Cigarette smoke and air pollution are the most important factors in the development of the disease. Despite the importance of COPD, our understanding of the molecular mechanisms involved is rather limited and there is a lack of promising therapeutic approaches to cure it.

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## WHY IS IT IMPORTANT?

As a chronic and progressive disease, there is no causative treatment that heals COPD. Therefore, many COPD patients worldwide are in urgent need of new treatment options. By making use of the concept of evolutionary medicine, findings in our *Drosophila* model should later be transferred to the human system in order to drive the development of novel therapeutic strategies for COPD.

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## TITLE OF THE WORK

*A Drosophila* model of cigarette smoke induced COPD identifies Nrf2 signaling as an expeditious target for intervention

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## WHAT DID SCIENTISTS DISCOVER?

Utilizing the fruit fly *Drosophila melanogaster* as a genetically tractable model, we characterized the molecular response of airway epithelial cells to chronic cigarette smoke. This treatment induced phenotypic changes resembling major hallmarks of COPD, such as reduced lifespan, reduced respiratory surface and increased metabolic rate. Based on transcriptomic analyses we found stress signaling pathways such as Nrf2, JAK/STAT and TGF- $\beta$  being strongly regulated upon cigarette smoke exposure. Genetic and pharmacological activation of the antioxidant pathway Nrf2 partially rescued the reduced lifespan upon cigarette smoke exposure and might serve as a potential way of intervention for therapeutic approaches in treatment of COPD.

## 05 WHO DID THE RESEARCH?

Ruben Prange  
Christine Fink  
Thomas Roeder

## 06 WHY DID THEY CHOOSE THE DESCRIBED METHODS?

The fruit fly *Drosophila melanogaster* turns out to be a simple but effective model to study cigarette smoke induced responses of the airway epithelium. Both genetic and pharmaceutical interventions are easily possible in this system and it is ideally suited to decipher molecular mechanisms and to test potential interventions. A major advantage of the *Drosophila* system is to easily link interventions with the most important fitness parameter, lifespan.

## 07 DETAILS FOR SCIENTISTS – PUBLICATION

A *Drosophila* model of cigarette smoke induced COPD identifies Nrf2 signaling as an expendent target for intervention  
*Aging* 2018; 10: 2122-2135  
Prange R\*, Thiedmann M\*, Bhandari A, Mishra N, Sinha A, Häsler R, Rosenstiel P, Uliczka K, Wagner C, Yldirim AÖ, Fink C, Roeder T

doi: 10.18632/aging.101536

