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Editorial Office
Charité-Universitaetsmedizin Berlin
D-10117 Berlin, Germany
Tel.: +49 30 450 528162
Fax: +49 30 450 7528972
Carola Neubert, Editorial Secretary
(e-mail: carola.neubert@charite.de)
Production Editor: Kamalaasini Jothimohan (email: apha@wiley.com)

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COVER

On the picture is Copenhagen's Nyhavn

Conclusion
BPGM, constitutively expressed in the distal nephron, appears to sustain proximal nephron well-being, since a BPGM deficit in distal tubules rapidly leads to remote injury to proximal tubules. The mechanisms responsible for such inter-tubular crosstalk remain elusive.

B 02-30

Involvement of potassium channels in alveolar cells response to oxidative stress

R. Canella[1], M. Benedusi[1], A. Vallese[2], G. Valacchi[3,2]
[1] *University of Ferrara, Department of Neuroscience and Rehabilitation, Ferrara, Italy*
[2] *University of Ferrara, Department of Environmental Sciences and Prevention, Ferrara, Italy*
[3] *North Carolina State University, Department of Animal Science, Kannapolis, USA*
[4] *Kyung Hee University, Department of Food and Nutrition, Seoul, South Korea*

Introduction
The lung tissue is one of the main targets of oxidative stress due to external pollutants and respiratory activity. Biological and electrophysiological techniques were applied to study the action of ozone, one of the most noxious pollutants present in the troposphere, on K currents in A549 cells, which simulates the first barrier encountered by oxidants **(1)**.
Exposure of human lung epithelial cells to ozone alters cell membrane currents inducing its decrease with respect to the control, when the cell undergoes to a voltage-clamp protocol ranging from -90 to +70mV. The membrane potential of these cells is mainly maintained by the interplay of potassium and chloride currents. Our previous studies indicated an increase of chloride current by oxidative stress due to ORCC channels activation **(2)**.
In this study our aim wastounderstand the role of potassium current during oxidative stress and try to identify which potassium channel is mainly related to the effect of O_3, addressing our analyses first to BK channel an ubiquitarian K channel characterized by big conductance (up to 300pS) **(3)**.
Methods
The A549 cells were cultured in DMEM and kept in an incubator at 37° degrees temperature with 95% air and 5% CO2.
The cells were exposed to 0.1 ppm ozone for 30 minutes and were analyzed by patch clamp technique immediately after exposure.
Western blot analysis was applied to quantify the BK channel before and after ozone treatment.
Patch clamp technique in whole cell configuration was applied to measure membrane current.
Results
After measuring the total membrane current using an intracellular solution containing or not potassium ions, we obtained the contribution of potassium to the overall membrane current in control condition by a mathematical approach. In similar experimental conditions after ozone treatment, we observed a significant decrease of IK with respect to the control.
By Western blot analysis before and after ozone exposure we observed a decrease of the BK channel after ozone treatment that was recovered in about one hour. Adding Iberiotoxin (IbTx), a specific inhibitor of BK channel, to the bath we also verified the functionality of BK channels in control condition.
On the contrary, administrating of 4-Aminopyridine (an inhibitor of voltage dependent K channels but not BK channels) before and after ozone treatment the decrease of the total current is almost equal to that observed in control condition. This last finding is a strong indication that BK channel is the target of oxidative stress.

Conclusion
We suggest that ozone inhibits potassium current and that the main involved channel could be BK. We need further studies to clarify its role and its interplay with the other membrane channels under oxidative stress conditions. These findings can contribute to identify the biomolecular pathway induced by ozone allowing a possible pharmacological intervention against oxidative stress in alveolar tissue.

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B 02-31

The Na^+/H^+ exchanger NHE3 inhibitor tenapanor prevents intestinal obstructions in CFTR-deleted mice

X. Tan, A. Kini, D. Römermann, U. Seidler
Hannover Medical School, Department of Gastroenterology, Hannover, Germany

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Introduction
Mutations in the CFTR chloride channel result in meconium ileus in newborns and distal intestinal obstructive episodes (DIOS) in adults and in CFTR null (*cftr*$^{-/-}$) animal models. This study aims to explore the effect of tenapanor, a gut selective NHE3 inhibitor, on reducing the frequency of obstructive episodes in the *cftr*$^{-/-}$ mice, and study the underlying molecular mechanisms.
Methods
Age (9-13 weeks old) and sex matched *cftr*$^{+/+}$ and *cftr*$^{-/-}$(FVB/N-CFTRtm1CAM) mice were intragastrically gavaged with tenapanor (30mg/kg) or vehicle, twice daily for a period of 21 days. Body weight and stool water content was assessed daily while gastrointestinal transit time (GTT) was measured weekly once. Stool pH was assessed pre and 3 hours post gavage with tenapanor. The mice were either euthanized with a suspected intestinal obstruction, or after 21 days. The intestinal tissues were collected for further analysis including RT-PCR, histology and immunohistochemistry.
Results
While tenapanor did not result in an overall decrease in body weight, it resulted in a significant and consistent increase in stool water content in the *cftr*$^{-/-}$mice, compared to the vehicle group (vehicle- n ≥ 7/timepoint, tenapanor- n ≥11/timepoint; Day 21- vehicle: 58.757 ± 2.201 vs tenapanor: 72.514