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Letter to the Editor

TRPC6 is altered in COVID-19 pneumonia

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ABSTRACT

In this Letter to the Editor supportive data were presented to a recent paper published in this journal reporting the involvement of TRP channels in COVID-19 pneumonia and its role for new therapies. Since gene expression of TRP channels was found in human lung tissues the protein was not being reported so far. TRP channels are supposed to be involved in the pulmonary inflammation and its symptoms such as fever, cough and others. Here, TRPC6 was investigated in tissues of normal human lungs and of SARS-Cov-2 infected lungs in a preliminary study. Tissue was obtained post mortem from anatomical body donations during dissections and during pathological dissections (13 normal, 4 COVID-19 pneumoniae) and processed for immunohistochemistry. In normal lungs TRPC6 was found in the ciliated epithelium, in the wall of larger lung vessels and in the alveolar septa. In COVID-19 pneumonia the distribution of TRPC6 was different. Inflammatory lesions, cellular infiltrates, hyaline membranes and fibrosis were labelled intensively as well as dilated capillaries. These observations are from four patients with COVID-19 pneumonia.The observations do not elucidate the molecular mechanisms but support the view that TRPC6 channels are involved in normal physiology of normal human lungs and in COVID-19 pneumonia. TRPC6 might aggravate SARS-2 induced inflammation and could be a target for inhibiting drugs.

Dear Editor,

A recent review of Jaffal and Abbas in this journal pointed out the involvement of TRP channels in the COVID-19 pneumonia and its symptoms as well as its role as targets for new therapies [1]. A genetic expression of TRP channels was found in human lung tissues but the protein has not been reported except its localisation in human alveolar macrophages [2,3]. TRP channels were recommended in general as targets in lung diseases before [4–6]. The TRP channels are most likely involved in the alveolar inflammation, fever, cough, edema, pain and other symptoms or complications of COVID-19. To validate this translational pathophysiological concept data of TRP channels from human tissues are necessary. Therefore, TRPC6 was investigated in normal human lungs and SARS-Cov-2 infected lungs in a preliminary study. Lung tissue was obtained post mortem from anatomical body donations during dissections and during pathological dissections (13 normal, 4 COVID-19 pneumoniae). The investigations were proofed by the Ethical Committee of the Saarland (numbers 163/20 and 130/21). The samples were processed for immunohistochemistry using a knock out validated anti-TRPC6 antibody (rabbit anti-human, anti-mouse, for details see Ref. [7]). In a recent report on human vessels TRPC6 could be demonstrated and yielded a similar staining pattern of the smooth muscles as the presented lung sections [7]. Appropriate controls using pre-immune rabbit serum and pre-incubation with the control peptide yielded the expected results. In normal lungs TRPC6 was found in the ciliated epithelium, in the wall of larger lung vessels and in the alveolar septa (Fig. 1). In COVID-19 pneumonia the distribution of TRPC6 is changed as compared to normal lungs (Fig. 2). The inflammatory lesions with edema, cellular infiltrates, hyaline membranes and fibrosis displayed an intensive staining for TRPC6. The dilated capillaries were also strongly labelled. In contrast, larger vessels and bronchioli were less intensively labelled as compared to similar structures in normal lungs. TRPC6 was also found within the typical hyaline membranes (Fig. 3). These observations are from four patients with COVID-19 pneumonia and therefore preliminary. In addition, the observations do not elucidate the underlying molecular mechanisms. However, TRPC6 channels seem to be involved in normal physiology of normal human lungs and in COVID-19 pneumonia. In other disease models of kidney or cancer drugs were already identified which target TRPC6 [8–11]. One can speculate that TRPC6 takes part in aggravation of SARS-2 induced inflammation and could therefore be a target for inhibiting compounds.

Ethical approval

The study was approved by the Ethical Committee of the Saarland (163/20, 130/21).

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Contributions

All authors planned and conducted the study. All authors read and approved the manuscript.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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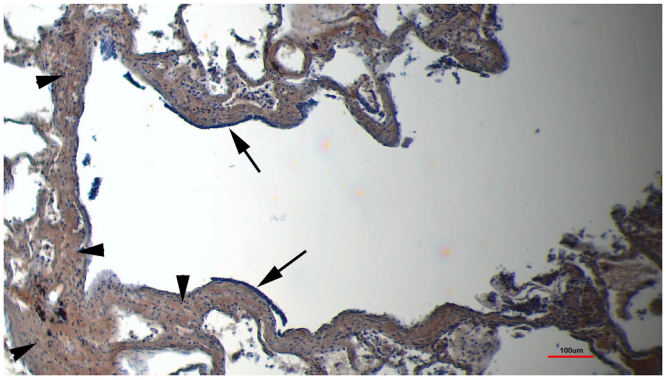

Fig. 1. A representative microphotograph from an immunohistochemical staining on a section of normal lung tissue using anti-TRPC6 is shown. The ciliated epithelium is labelled (brown color, arrows) as well as the thick layers of smooth muscles in the bronchiolar walls (arrowheads).

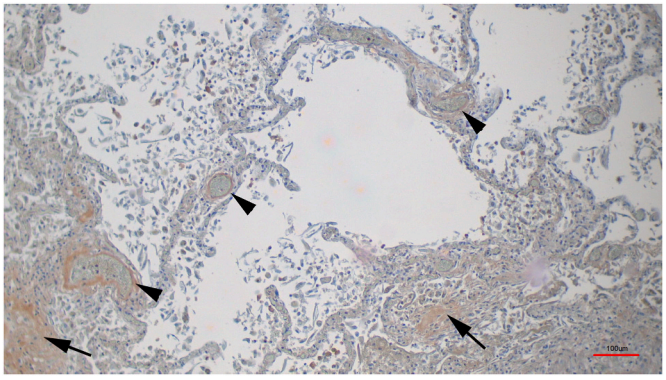

Fig. 2. A representative microphotograph from an immunohistochemical staining on a section of lung tissue of a patient with COVID-19 pneumonia using anti-TRPC6 is presented. The dilated capillaries are labelled (brown color, arrowhead) as well as fibrotic lesions (arrow).

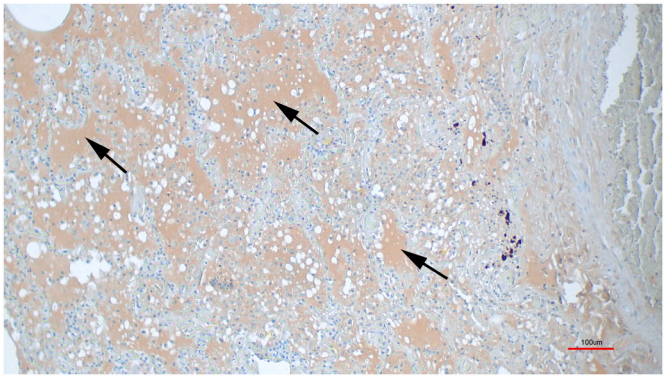

Fig. 3. A representative microphotograph from an immunohistochemical staining on a section of lung tissue of a patient with COVID-19 pneumonia using anti-TRPC6 is presented. Amorpheous, hyaline structures were labelled (brown color, arrows).

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Gina Leidinger
Institute of Anatomy and Cell Biology, Saarland University, Homburg, Saar, Germany

Fidelis Flockerzi, Johannes Hohneck, Rainer M. Bohle
Institute of Pathology, Saarland University Medical Center, Homburg, Saar, Germany

Armin Fieguth
Institute of Forensic Medicine, Hanover Medical School, Hannover, Germany

Thomas Tschernig*
Institute of Anatomy and Cell Biology, Saarland University, Homburg, Saar, Germany

* Corresponding author. Anatomy and Cell Biology, Kirrberger Straße, Bldg. 61, 66424, Homburg, Saar, Germany.
E-mail address: Thomas.Tschernig@uks.eu (T. Tschernig).