Abstract

Hypoxic pulmonary vasoconstriction (HPV) is a local physiological mechanism in lungs that optimalises blood oxygenation during alveolar hypoxia. Arterioles in the affected region increase flow resistance which redirects blood to better ventilated parts of the lung. During global hypoxia – e.g. in high altitude or in chronic pulmonary illnessess – this mechanism doesn't work, as the blood cannot be redirected elsewhere. The pressure in pulmonary artery rises which leads to right heart hypertrophy and ultimately to cor pulmonale.

This mechanism has been studied for decades, but specific signalling pathways still lack full description and therapeutical solutions are not available. This thesis offers description of selected properties of pulmonary circulation and patophysiological context of pulmonary hypertension, introduces the reader to HPV localization and signalization, and discusses its most important steps from decreased oxygen availability to vessel constriction.

The practical part of this work explores Succinate dehydrogenase (SDH) – complex coupling Kreb's cycle to electron transport chain – as a primary detection site of hypoxia in pulmonary artery smooth muscle cells. We decided to test this hypothesis in isolated rat lungs by measuring if malonate (SDH inhibitor) causes vasoconstriction as hypoxia does. Also if (potentially) elevated pulmonary resistance won't further react to hypoxia. This elevation wasn't seen, so the hypothesis of SDH as a hypoxic sensor for HPV was conclusively disproved.

Keywords

Hypoxic pulmonary vasoconstriction, succinate dehydrogenase, hypoxia, reactive oxygen species