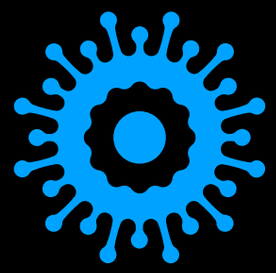

Corona Virus Infection

drbob

The following slides show the connection between the RAS (Renin/ Angiotensin) system, metabolism and the Corona virus.

All metabolism works on the absolute need to balance opposing forces in order to minimize excess free radical production.

The lethality of respiratory infections, as well as irritant chemical inhalation, is the free radical dependent development of ARDS (adult respiratory distress syndrome).

The coronavirus attaches to ACE2 proteins on the surface of cells, especially those of the lung and kidney.

The ACE2 protein creates a heptapeptide ANG1-7 that protects against the negative effects of angiotensin by turning on fat burning (autophagy) that recycles free radical-damaged cellular components.

Ang1-7, made by ACE2 acting on full sized membrane bound ANG, should compete with the virus and prevent the first step of a viral infection (entry).

ANG1-7 is a commercially available FDA approved pharmaceutical.

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THE RENIN-ANGIOTENSIN SYSTEM (RAS)

THE RENIN-ANGIOTENSIN SYSTEM (RAS) is an important regulator of arterial blood pressure (BP). Angiotensin II (ANG II) is the major effector molecule of the RAS, which exerts its biological effects mainly via the type 1 ANG II receptor (AT1R). Therefore, ANG II acts as a potent vasoconstrictor, regulates water intake and salt metabolism, and increases sympathetic outflow and blood pressure (Paul M, Poyan Mehr A, Kreutz R. Physiology of local renin-angiotensin systems. Physiol Rev 86: 747–803, 2006).

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Angiotensin (ANG)

Wikipedia: Angiotensin is a peptide hormone that causes vasoconstriction and an increase in blood pressure. It is part of the renin–angiotensin system, which regulates blood pressure. Angiotensin also stimulates the release of aldosterone from the adrenal cortex to promote sodium retention by the kidneys . (https://en.wikipedia.org/wiki/Angiotensin)

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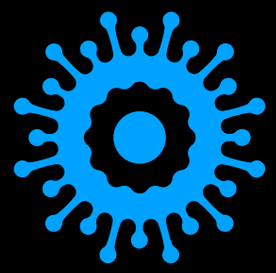
ANG 1–7

ANG 1–7 treatment also suppressed the production of reactive oxygen species via attenuation of NADPH oxidase activity and reduced inflammation in perirenal adipose tissue. Furthermore, ANG 1–7 treatment decreased lipid accumulation in db/db kidneys, accompanied by increased expressions of renal adipose triglyceride lipase (ATGL). Alterations in ATGL expression correlated with increased SIRT1 expression and deacetylation of FOXO1. The up-regulation of angiotensin-converting enzyme 2 levels in diabetic nephropathy was normalized by ANG 1–7.

ANG 1–7 treatment exerts renoprotective effects on diabetic nephropathy, associated with reduction of oxidative stress, inflammation, fibrosis, and lipotoxicity. ANG 1–7 can represent a promising therapy for diabetic nephropathy.

**Angiotensin 1-7 Am J Physiol Renal Physiol 306: F812–F821, 2014.
First published February 19, 2014; doi:10.1152/ajprenal.00655.2013.**



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Angiotensin-converting enzymes ACE1 and ACE2 - homologues with different key functions in the renin–angiotensin system .

ACE cleaves angiotensin I to generate angiotensin II

ACE2 inactivates angiotensin II and is a negative regulator of the system. ACE2 has also recently been identified as a potential SARS virus receptor The renin–angiotensin system has an important role in maintaining blood pressure homeostasis, as well as fluid and salt balance .
ACE2 is a homologue of ACE, and functions a negative regulator of the renin–angiotensin system . Although ACE2 is expressed in the lungs of humans and mice, nothing is known about its function in the lungs. However, mortality following SARS coronavirus infections approaches almost 10%

“Here we report that ACE2 and the angiotensin II type 2 receptor (AT2) protect mice from severe acute lung injury induced by acid aspiration or sepsis”.

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ACE2 inhibits breast cancer angiogenesis via suppressing the VEGFa/VEGFR2/ERK pathway

Zhang et al. Journal of Experimental & Clinical Cancer Research (2019) 38:173 https://doi.org/10.1186/s13046-019-1156-5

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Adam17

Excessive Glutamate Stimulation Impairs ACE2 Activity Through ADAM17-Mediated Shedding in Cultured Cortical Neurons

Neurons. Cell Mol Neurobiol 38, 1235-1243 (2018).

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Adam17

α-Lipoic Acid Reduces Neurogenic Hypertension by Blunting Oxidative Stress-Mediated Increase in ADAM17

We previously reported that type 2 angiotensin-converting enzyme (ACE2) compensatory activity is impaired by the disintegrin and metalloprotease 17 (ADAM17), and lack of ACE2 is associated with oxidative stress in neurogenic hypertension.

Taken together, these data suggest that LA might preserve ACE2 compensatory activity by breaking the feedforward cycle between ADAM17 and oxidative stress, resulting in a reduction of neurogenic hypertension.

de Queiroz, T. M., Xia, H., Filipeanu, C. M., Braga, V. A. & Lazartigues, E.Am J Physiol Heart Circ Physiol 309, H926-34 (2015).