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Could the smoking gun in the fight against Covid-19 be the (rh) ACE2?

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Two interesting publications in the European Respiratory Journal recently by Russo et al.¹ and Leung et al.² discuss the possible role of nicotine in this pandemic and the “furious pursuit for better therapeutics”.

Not surprisingly, the angiotensin-converting enzyme-2 (ACE2) is known to be the likely host receptor for the coronavirus 2019-nCoV/SARS-CoV-2 (Covid-19). Further, at a basic level, cellular mechanisms of nicotinic receptor activity promote SARS-CoV-2 entry and proliferation in epithelial cells through co-expression of ACE2. Hence, this is the theory postulated by Olds and Kabbani³ for how nicotine consumption represents a special risk factor in Covid-19.

On the other hand, and very surprisingly, Changeux et al.⁴ hypothesize that the nicotinic receptor also plays a key role in the pathophysiology and might represent a target for the prevention and control of Covid-19 infection. Again, on a basic level, the hypothesis is that SARS-CoV-2 virus is a nicotinic agent which competes with nicotine for the receptor. The backbone of this hypothesis proposes that under controlled settings, nicotinic agents (such as nicotine patches) could provide an efficient treatment for an acute infection such as Covid-19.

So, tenuously, is the argument centred around the need for data about alternative nicotine delivery systems and their risk/benefit ratio in relation to Covid-19?³ Possibly, but are there perhaps other ways…?

Soluble ACE2 might impact viral spread, since binding to soluble receptor has been shown to block SARS-CoV-2 entry. Batlle et al.⁶ argue that if given in its soluble form as an appropriate recombinant ACE2 protein, this may represent a new tool to combat the spread of Covid-19.

Similarly, Guo et al.⁷ opined that exogenous supplement of recombinant human (rh)ACE2 might be a brilliant idea in the treatment of Covid-19. Here the soluble ACE2 may act as the bait to neutralize the spike protein on the surface of the SARS-CoV-2, thus inhibiting entry. Further, Guo et al. referenced a recent study that demonstrated fusion protein of rhACE2 (with an Fc fragment) showing high affinity binding to the receptor-binding domain of SARS-CoV-2. This, again, provides a
basis for further drug development as fusion protein technology has been very successfully deployed in various therapeutic areas such as rheumatology and haemophilia.

References