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ACE2 is on the X chromosome: could this explain COVID-19 gender differences?

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This commentary refers to 'Circulating plasma concentrations of angiotensin-converting enzyme 2 in men and women with heart failure and effects of renin–angiotensin–aldosterone inhibitors', by I.E. Sama *et al.*, 2020;41:1810–1817.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the resulting disease termed coronavirus disease 2019 (COVID-19) shows a fatality rate greater in men compared with women.[1] To explain this, some hypotheses have been raised, from genes that regulate the immune system encoded on the X chromosome to smoking behaviour,[2] to expression levels[1] or variants for angiotensin-converting enzyme 2 (ACE2), the receptor for SARS-CoV-2.[3]

However, we would like to point out that the *ACE2* gene is located on the X chromosome (location: Xp22.2; nucleotides 15 494 402–15 602 148, GRCh38.hg38 version). To our knowledge, the importance of *ACE2* localization on the X chromosome has not been explored previously. Often, to have two copies ameliorates the deleterious effects of X-linked diseases and, as a consequence, most X-linked syndromes produce male diseases.

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