Hypothesis Article: COVID-19 unexplained mortality in the young adults: could it be due to ACE2 polymorphisms?

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Fang and his colleagues have suggested to investigate the genetic predisposition for an increased risk of SARS-CoV-2 infection and they've proposed an explanation that might be linked to its receptor ACE2 polymorphisms<sup>1</sup>. The author agrees with their suggestion and would like to discuss it in a more elaborative manner.

ACE2 polymorphisms and its induced mutations have been previously linked to enhanced susceptibility of heart diseases including coronary heart disease, myocardial infarction as have been revealed both clinically and experimentally<sup>2,3</sup>. Further, The ACE2 rs4646188 variant was suggested as a potential and optimal genetic susceptibility marker for essential hypertension, dyslipidemia and its related ischemic stroke<sup>4</sup>. Similarly, three ACE2 variants (rs4240157, rs4646155, and rs4830542) were found to be associated with essential hypertension and hypertension-related atrial fibrillation and left atrial remodeling<sup>5</sup> Further, genetic variants in the ACE2 gene have been suggested to be associated with left ventricular mass, septal wall thickness and left ventricular hypertrophy in hemizygous men<sup>6</sup>. Noteworthy, genetic variants in the ACE2 gene were significantly associated with diastolic blood pressure responses to cold stress in the Chinese female population<sup>7</sup>. The author would like to suggest that It might be probable that ACE2 polymorphisms in the lungs could be one of the causes linked to a higher morbidity and/or mortality rate encountered in some groups of COVID-19 patients rather than the drugs suggested by Fang and his colleagues which have been refuted<sup>8</sup>. Further, these polymorphisms might also be one of the answers why some young, apparently healthy adults have been deceased while some very old patients have been rescued. The author recommends examining COVID-19 consented autopsies to explore this hypothesis as it might help us to develop some genetic tests to warn those more susceptible individuals exempt vulnerable health care professionals from duty.

## Conflict of interests:

The author has no conflicts of interest to declare.

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