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COVID-19 and genetic individual susceptibility: Might double X-chromosome in females be protective against CoV-2 infection compared to single X-chromosome in males? The role of ACE1 / ACE2 genes, inflammation and immune response

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Abstract

In December 2019, a novel severe acute respiratory syndrome (SARS) from a new coronavirus (CoV-2) was recognized in the city of Wuhan, (China). Rapidly, it became epidemic in China and it has now a worldwide diffusion reaching pandemic proportions. High death rate characterizes CoV-2 disease (COVID-19) particularly striking elderly causing unrestrained cytokines-storm and consequent pulmonary shutdown. At the moment, no specific and dedicated treatments, neither approved vaccines are available, though very promising researches come from the side of anti-inflammatory and anti-malaria drugs. In addition, it seems that males are more susceptible to CoV-2 than females, with 65% more likely to die from the infection than females. Data from the World Health Organization (WHO) and Chinese scientists show that of all affected cases about 1.7% of women who contract the virus will die compared with 2.8% of men and data from Hong Kong hospitals state that 32% of male and 15% of female COVID-19 patients required intensive care or died. Conversely, in the long term the coronavirus fallout may be worse for women than men due to social and psychosocial reasons. Regardless the sex- or gender-gap data obtained from WHO and those recruited from scientific journals sometimes controversial, some central points should be considered. Firstly, CoV-2 has a strong interaction with human ACE2 receptor playing essential role in cell entry; interestingly the ACE2 gene lays on the X-chromosome rendering females potentially heterozygous and differently assorted versus men definitely hemizygotes. Secondly, the highest ACE2 expression rate in females, though controversial, might ascribe them the worst prognosis, in contrast with worldwide epidemiological data. Finally, the several genes involved in inflammation are located on the X-chromosome, which also contains high number of immune-related genes responsible for innate and adaptive immune responses to infection. Summarizing, X-heterozygous females might activate a mosaic advantage and higher sexual dimorphism than males to counteract CoV-2 infection progression, and unexpectedly, higher ACE2 levels, or ACE/ACE2 rebalancing, might ameliorate COVID-19 outcome being protective against CoV-2 fatality.

Biography:

Veronica Tisato has completed her PhD from Padua University, Italy. Post-doctoral experience in Ferrara University, she is professor of Human Anatomy. Interests: Translational research, Gender Medicine, Regenerative Medicine, Personalized and Precision Medicine. Focus on inflammation and biomarkers in cardiovascular and complex diseases, aging, neurodegenerative/cognitive impairment diseases. Editorial board member of International Journal of Molecular Sciences.

Speaker Publications:

1. "Changes in Adipose Tissue Distribution and Association between Uric Acid and Bone Health during Menopause Transition"
December 2019International Journal of Molecular Sciences 20(24):6321 DOI: 10.3390/ijms20246321

2. "Inflammation and Cardiovascular Cross Talk in Ischemic Vascular Diseases" March 2017Mediators of Inflammation 2017(12):1-2 , DOI: 10.1155/2017/3161968

3. "COVID-19 and Individual Genetic Susceptibility/Receptivity: Role of ACE1/ACE2 Genes, Immunity, Inflammation and Coagulation. Might the Double X-chromosome in Females Be Protective against SARS-CoV-2 Compared to the Single X-Chromosome in Males?
May 2020International Journal of Molecular Sciences 21(10):3474 DOI: 10.3390/ijms21103474

4. "Maternal Haplotypes in DHFR Promoter and MTHFR Gene in Tuning Childhood Acute Lymphoblastic Leukemia Onset-Latency: Genetic/Epigenetic Mother/Child Dyad Study (GEMCDS) " August 2019Genes 10(9):634
DOI: 10.3390/genes10090634.

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