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G6PD+SARS-CoV-2 Pathogenesis

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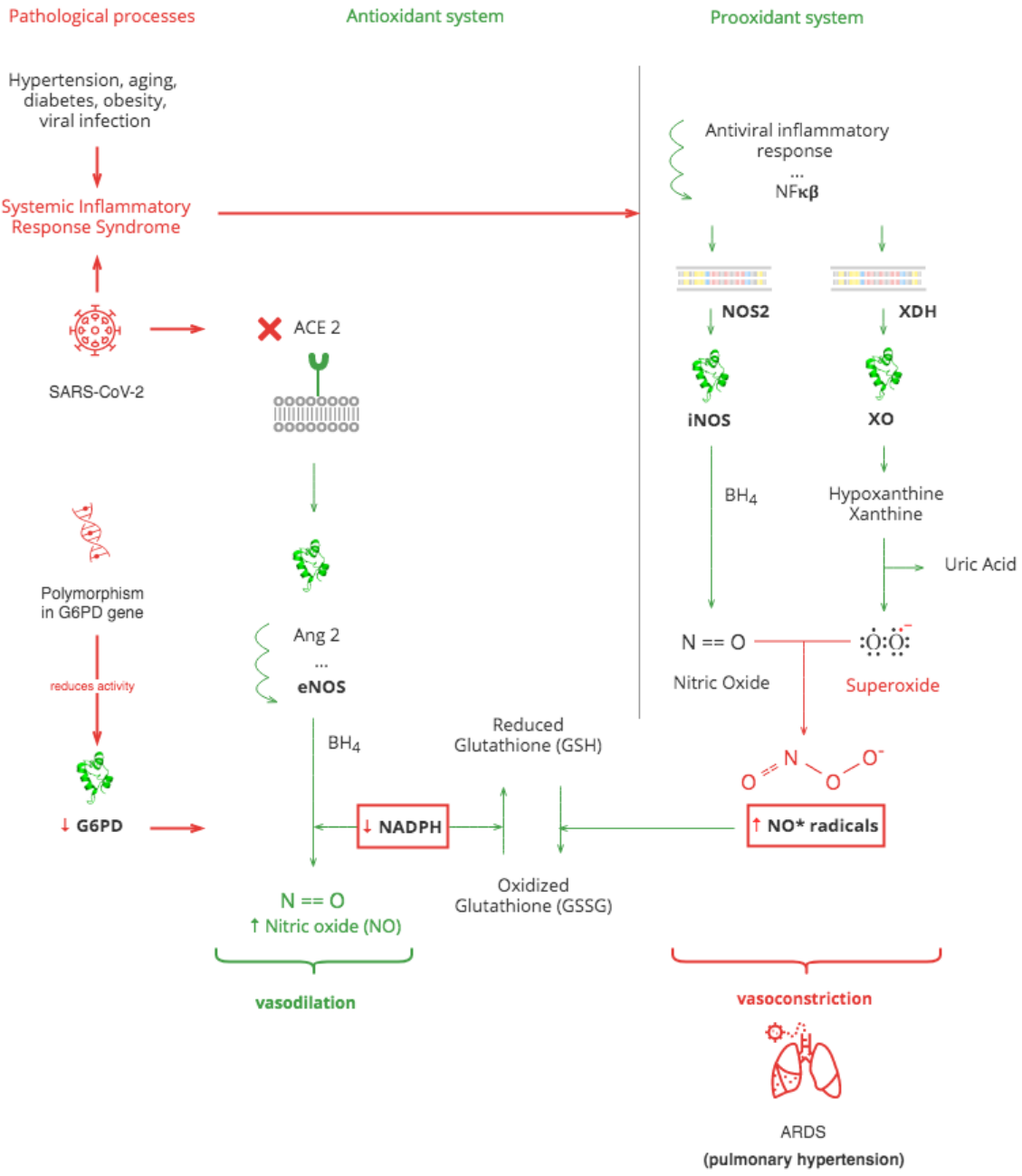
Graphical Abstract

COVID-19 aggravates already compromised NO production in cohort with G6PD deficiency. Management of NO level can prevent development of severe ARDS.



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Abstract

OBSERVATION: As was estimated by E. Nkhoma et al, 2009, glucose-6-phosphate dehydrogenase (G6PD) deficiency is present in 4.9% of global population and severe form occurs more often in Asian and Mediterranean populations.

Yi-Hsuan Wu et al., 2008, demonstrated experimentally that G6PD-deficient cells have an increased susceptibility to human coronavirus (HCoV) 229E.

HYPOTHESIS: Cohort with G6PD deficiency can be vulnerable to SARS-CoV-2.

METHODS: Domain expert provided starting points (*SARS-CoV-2, G6PD. ...*) to trigger chain reaction-like facts extraction and reasoning by machine operating on publications available in Pubmed and PMC (https://sci.ai/). Extracted facts and presynthesized steps were validated by expert to form (1) evidence-supporting dataset and final (2) normal, (3) pathological and (4) drug-induced pathways.

RESULTS:

COVID-19 stimulates a pro-inflammatory systemic organism's response (pro-oxidant) and inhibits an anti-inflammatory (anti-oxidant) system. As a result of dysbalance, Reactive Oxygen Species (ROS) overproduction maintains Systemic Inflammatory Response Syndrome (SIRS).

The role of G6PD is to produce NADPH which, in turn, participates in Glutathione (GSH) reduction and production of a Nitric Oxide (NO). These 2 anti-oxidant molecules are involved in neutralization of ROS and vasodilation during recovery phase.

Age-dependent decrease in G6PD activity is a contributing factor in development of diabetes and hypertension. Genetically G6PD-deficient individuals are predisposed to infections and metabolic diseases even at relatively young ages.

Nonsteroidal anti-inflammatory drugs (NSAIDs) are contraindicated for G6PD-deficient patients because of depleting intracellular glutathione levels and triggering ROS generation.

Worsening of COVID-19 patients' condition that were treated with NSAIDS confirms that anti-oxidant system of that patients is already compromised significantly.

As G6PD deficiency is a X-linked recessive inherited disease, it affects mostly men, probably, explaining gender differences of COVID-19 prevalence.

Current results complement previous research related to the role of NOS3 polymorphisms 10.6084/m9.figshare.12034962 in management of NO-deficient COVID-19 patients. Also suggests future research of susceptibility factors up and down the NO-production pathway.

Research data is available at 10.6084/m9.figshare.12084108

Points of consideration in management of G6PD+SARS-CoV-2 pathogenesis

Appropriate therapy should be prescribed by a doctor considering anamnesis. Points below are relevant as a part of pathogenetic treatment of a G6PD deficient cohort with insufficient NO production.

Potentially Beneficial Substances

Substance	Key function relevant to G6PD+SARS-CoV-2 pathogenesis
Lipoic Acid, Vit D, T_3, Insulin, normal range Glucose levels, Spironolactone	Upregulates G6PD
L-cystine, Glycin, Ascorbic acid, N-acetylcystein	Upregulates GSH
L-citrulline, Folic Acid	Potentiates eNOS

Potentially Harmful Substances

Substance	Key function relevant to G6PD+SARS-CoV-2 pathogenesis
Aldosterone, Glucagon, Dexamethasone, high Glucose, PIGF, Arachidonic acid, Salicylate, Polydatin	Downregulates G6PD
NSAIDs (APAP, especially), Alcohol, Smoke, Primaquine, Chloramphenicol, Sulfanilamide	Downregulates GSH

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References

1. 10.6084/m9.figshare.12034962