

# **SARS-COV-2 Adults and Children: Two Phenotypically Different Viruses**

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## **Abstract**

The SARS-Cov-2 virions produced in human children, adults and elder people display slight differences in their makeup.

## SARS-COV-2 IN ADULTS AND CHILDREN: TWO PHENOTYPICALLY DIFFERENT VIRUSES

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The SARS-Cov-2 virions produced in human children, adults and elder people display slight differences in their makeup. Indeed, SARS-Cov-2 particles are made not just of viral structural proteins and RNA (Chen et al., 2020), but also of a foreign component: the lipid membrane stolen from the human endoplasmic reticulum-Golgi intermediate compartment (ERGIC) (Tozzi, 2020). It is no coincidence that coronaviruses display markers for the endoplasmic reticulum and Golgi (Brian and Baric, 2005). During intracellular assembly, coronaviruses anchor their structural proteins to the physical support of the hosts' ERGIC membranes. Subsequently, SARS-Cov-2 particles, including viral proteins, viral RNA and host ERGIC membranes, are released by exocytosis (Risco et al. 2002; Krijnse-Locker et al., 1994).

It is noteworthy that biochemical, morphological, and functional modifications of endoplasmic reticulum (REL) and Golgi membranes take place during ageing. Several clues point towards a difference in human ERGIC membranes at different ages. Liu et al (2018) found that Serum Golgi protein 73 (GP73), a promising marker for liver fibrosis in adults, decreases with age in healthy controls. Morphological studies on aging in rat brain revealed a disorganization on the normally well-laminated pattern of REL and Golgi vesicles (Brizzee et al., 1975). Janikiewicz et al. (2018) argued that mitochondria-associated membranes' biology, composition, and action play roles in longevity, through modifications in lipid biosynthesis and trafficking, calcium homeostasis, reactive oxygen species production, and autophagy. Calvo-Rodríguez et al. (2016) suggested that neuronal aging is associated to increased ER-mitochondrial cross talking and subcellular Ca<sup>2+</sup> remodeling. Acute murine  $\gamma$ -herpesvirus 68 infection, that causes apoptosis of type II lung epithelial cells in aging mice, up-regulates endoplasmic reticulum stress markers (Torres-González et al., 2012). Brown and Naidoo (2012) and Chadwick and Lajoie (2019) described the role of ER stress response pathways in aging and age-related diseases, occurring via pathways such as unfolded protein responses.

Once established that human ERGIC membranes modify with time passing, we are allowed to state that the SARS-Cov-2 particles produced in the tissues of children are phenotypically different from the SARS-Cov-2 particles produced in the tissues of adults and elder people. Whether SARS-Cov-2 strikes children, adults or elder people, the released virions will display different arrangement and composition of ERGIC membranes. These premises might unexpectedly help to investigate one of the most bothersome questions raised during these frantic months of pandemics: why do children are less affected by SARS-Cov-2 and display less severe COVID-19 symptoms? In turn, why are elder people more severely affected? The ERGIC structures discrepancy in different SARS-Cov-2 virions might contribute to variations in symptoms severity, viral load, infectivity in pediatric and elder populations. Also, this paves the way to build artificially attenuated virions.

Furthermore, it is noteworthy that intracellular structures like the Golgi complex and endoplasmic reticulum may cause autoimmune reactions and production of specific monoclonal antibodies during distinct events of cellular apoptosis and necrosis (Ma et al., 2019; Grossmann et al, 1989; Nozawa et al., 2002; Hong et al., 2004; Borradaile et al., 2006; Weber et al., 2010). We suggest to look for Golgi and endoplasmic reticulum antibodies in the serum and bronchoalveolar liquid of patients affected by COVID-19.

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