How immunity to RSV develops in childhood but deteriorates in adults

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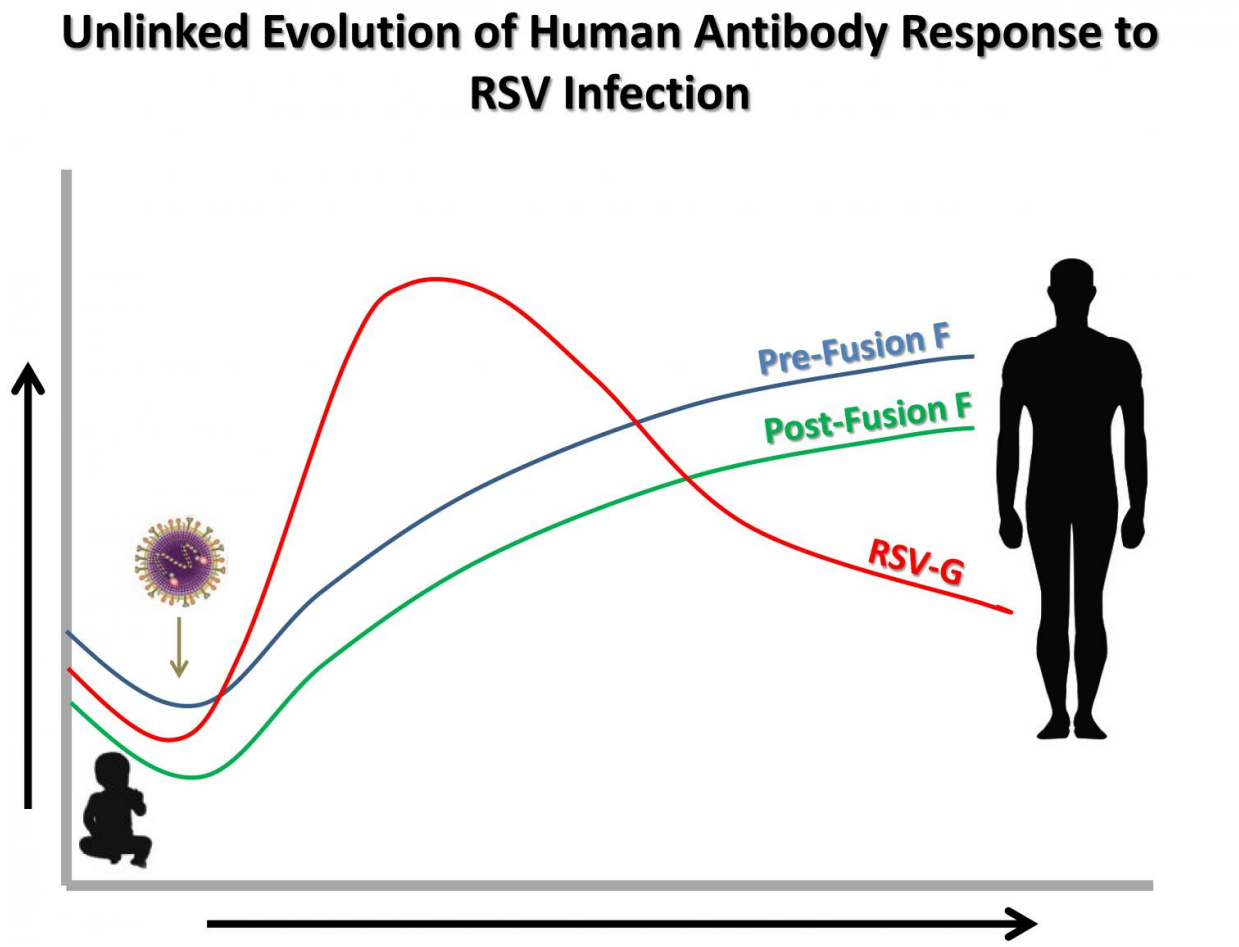

Unlinked evolution of human antibody response to RSV infection. Credit: Ketaki Singh, USP

The leading infectious cause of severe respiratory disease in infants, respiratory syncytial virus (RSV), is also a major cause of respiratory illness in the elderly. Approved vaccines do not yet exist, and despite the development of partial immunity following infection during childhood, individuals remain susceptible to RSV reinfection life-long. A comprehensive characterization of the antibody-response to RSV published on April 21st in *PLOS Pathogens* advances our understanding of the human immune response against RSV and has implications for vaccine design.

RSV is nearly ubiquitous, and most children are born with some protective immunity conveyed by maternal antibodies. As the maternal antibodies wane over time, infants become susceptible, and are often infected for the first time between nine months and two years of age.

Studies over the past three decades have explored the antibody responses before and after RSV infection in different age groups. We know that human antibodies that can mediate the destruction (or neutralization) of the virus target the two major proteins on the virus surface, namely the attachment protein G and the fusion protein F. However, which antibody combination conveys the best immune protection, and why RSV infections recur throughout life remain open questions.

To address them, Surender Khurana and colleagues from the US Food and Drug Administration in Silver Spring, USA, first performed a comprehensive and unbiased analysis of the human antibody response to the RSV F and G proteins in infants before and after RSV infection. They then characterized the changes in the response over time by analyzing antibodies from children, adolescents, and adults.

The blood of young infants, the researchers found, contains maternal antibodies that recognize several parts of both the F and G proteins. In older infants that had been infected with RSV, they saw a dramatic

expansion in both quantity and diversity of the antibodies that recognized the G protein. Surprisingly, infection prompted only a modest increase in the antibody repertoire against the F protein. Looking at changes over time, the researchers found that the antibodies against the F protein continued to expand with age whereas those against the G protein weakened.

Because the G protein sequence varies between RSV strains, whereas the F protein is highly conserved among strains, some vaccines under development use only the more tractable F protein as a vaccine antigen. The results here—strong expansion of anti-G responses in infants following infection as well as strong anti-F responses but weakened anti-G responses in adults—suggest that such a vaccine design might be problematic. On the other hand, the fact that the strong anti-G responses seen in children target a relatively conserved region in the G protein suggest that variability in other parts of the G protein does not necessarily compromise G's utility as a vaccine antigen.

Taken together, the researchers say, their results suggest "an unlinked evolution of the antibody responses to F and G proteins in humans", and propose that "the significant drop in anti-G antibody levels in adults may be a factor in sustained susceptibility to RSV infections throughout life". Consequently, they state that their findings "imply the need to include G proteins in future RSV vaccines in order to boost the anti-G responses".

More information: *PLOS Pathogens*, DOI: 10.1371/journal.ppat.1005554