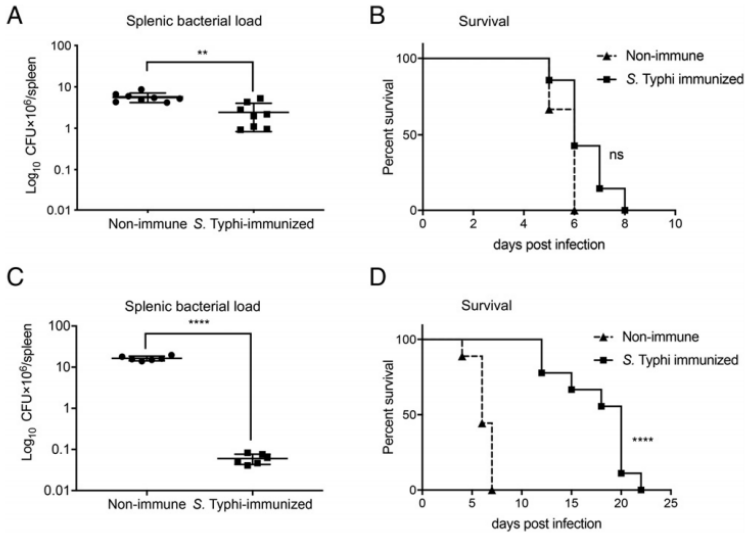
Accessibility of O-antigens shared between Salmonella serovars determines antibody-mediated cross-protection

Scientists at Department of Biotechnology's institute, the National Institute of Immunology (NII), New Delhi used a mouse model of infection to address whether infection or immunization with one *Salmonella* serovar can provide protection against other *Salmonella* serovars or not. Mice were immunized with live *Salmonella typhi* (this serovar does not cause disease in mice) and challenged with either *Salmonella enteritidis* or *S. typhimurium* (both these serovars produce disease in mice). Unimmunized mice infected with *S. enteritidis* or *S. typhimurium* had, as expected, bacteria present in high numbers in their spleens, and these mice died in a week. Mice immunized with *S. typhi* and challenged with *S. typhimurium* also died in a week even though there was reduction in splenic bacterial load in these mice. On the other hand, mice immunized with *S. typhi* and challenged with *S. enteritidis* survived till day 20 and these mice had greater reduction in splenic bacterial load. These results suggested that immunization with *S. typhi* provided greater resistance to mice against challenge with *S. enteritidis*.



To understand the reasons for this differential protection, team analyzed if the immune responses generated in mice upon immunization with *S. typhi* were reactive with antigens of *S. enteritidis* and *S. typhimurium.* T cells from mice immunized with *S. typhi* readily responded to antigens of *S. enteritidis* and *S. typhimurium*, and secreted two important cytokines, IL-2 and IFN-γ. On the

other hand, antibodies present in the sera of mice immunized with *S. typhi* bound live intact *S. enteritidis* but did not show detectable binding with live intact *S. typhimurium*. Further analysis revealed that the antibodies which bound *S. typhi* and *S. enteritidis* recognized carbohydrate antigens shared by these *Salmonella* serovars and these antigens were accessible on the surface of bacteria. On the other hand, even though there were antibodies present in the sera of *S. typhi* – immunized mice against carbohydrate antigens shared by *S. typhi* and *S. typhimurium*, these did not bind bacteria because the antigens were not accessible on the surface of bacteria.

These results suggested that antibodies against surface accessible carbohydrate determinants can provide significant immunity against *Salmonella* infection, and infection or immunization with one *Salmonella* serovar can impart antibody-mediated protection against another serovar provided the two share these surface accessible determinants. These findings have implications for understanding immunity against *Salmonellae*, and for designing effective vaccines against these pathogens.

Salmonella typhi, which causes systemic infection, typhoid, in humans, shares a high degree of homology with non-typhoidal *Salmonella* serovars such as *Salmonella enteritidis* and *S. typhimurium* that produce only localized gastroenteritis in humans.

Link: https://www.jimmunol.org/content/early/2020/06/14/jimmunol.1900624
Link: http://www.nii.res.in/

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