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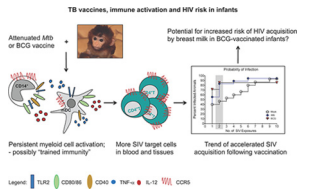
Articles of Significant Interest Selected from This Issue by the Editors

Balancing Trained Immunity with Persistent Immune Activation and the Risk of Simian Immunodeficiency Virus Infection in Infant Macaques Vaccinated with Attenuated *Mycobacterium tuberculosis* or *Mycobacterium bovis* BCG Vaccine

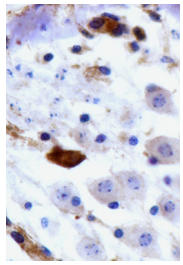
To reduce pediatric human immunodeficiency virus type 1 (HIV-1) and tuberculosis (TB) infections, Jensen et al. (e00360-16) tested a pediatric HIV-TB combination vaccine in infant rhesus macaques. Similarly to the *Mycobacterium bovis* BCG vaccine, attenuated *Mycobacterium tuberculosis* (A*Mtb*) vaccines enhanced functional responses of myeloid cell populations that persisted for several months. Concurrently, though, frequencies of activated $CD4^+$ T cells increased in blood and tissues. As a result, although statistically not significant, infant macaques vaccinated with A*Mtb* or BCG required fewer oral simian immunodeficiency virus (SIV) exposures to become infected than did unvaccinated controls. Thus, novel TB vaccines should be tested for their capacity to induce immune activation and any associated risks of enhanced HIV infection.



Enhanced SIV risk in infant primates vaccinated against TB.

Combined Use of Two Subunit Vaccine Targets (gB and pp65) Confers Augmented Protection against Congenital Cytomegalovirus Infection in an Animal Model

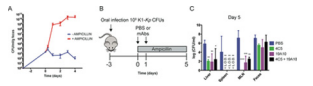
In the study performed by Schleiss and colleagues (e00300-16), a novel vectored vaccine based on recombinant lymphocytic choriomeningitis virus (LCMV) was evaluated for protection in a guinea pig cytomegalovirus model of congenital viral transmission. Both subunits (gB and pp65) were immunogenic, and the combination of both immunogens was superior to either subunit administered alone. This is the first demonstration that improved protection against congenital cytomegalovirus (CMV) is conferred by a combination of T-cell and antibody targets in a vaccine. Human LCMV vaccines based on these subunits were also highly immunogenic, and these vaccines are now in phase I studies in humans.



Cochlear infection in the guinea pig model of congenital CMV.

Monoclonal Antibodies against Gut Bacteria Can Prevent Dissemination from the Gut

Diago-Navarro et al. (e00456-16) present data on monoclonal antibodies (MAbs) 4C5 and 19A10, which bind to the K1 type polysaccharide capsule of mucoid *Klebsiella pneumoniae* strains. These strains are emerging in Asia and cause liver abscesses and disseminated infections with poor outcome. Live *in vivo* imaging in murine livers demonstrated that these antibodies promote phagocytosis of *Klebsiella* by Kupffer cells. Most importantly, protective efficacy was confirmed in a sepsis model and a novel pulmonary murine colonization model. The latter shows that mice colonized with *Klebsiella* in the gut and treated with MAbs can be protected against antibiotic-induced dissemination from the gut. These findings are encouraging because they suggest potential new therapeutic strategies, namely, that systemic treatment with monoclonal antibodies against gut-colonizing bacteria, including multidrug-resistant *Enterobacteriaceae*, can potentially be used to combat dissemination and invasive disease.



Systemic treatment with MAb prevents dissemination of K1 bacteria from the gut.

https://doi.org/10.1128/CVI.00535-16