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An advance for a newborn vaccine approach

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(PhysOrg.com) -- Infectious disease is a huge cause of death globally, and is a particular threat to newborns whose immune systems respond poorly to most vaccines. A new approach developed at Children's Hospital Boston, using an adjuvant (an agent to stimulate the immune system) along with the vaccine, shows promise in a study of blood from Gambian infants. Results will appear in the open-access journal *PLoS ONE* on April 13.

The ability to immunize newborns would close their window of vulnerability to serious infections during the first months of life, such as respiratory syncytial virus, pneumococcus and rotavirus. It would provide a way to protect newborns both in resource-poor countries, where a baby may have limited opportunities to be vaccinated, and in wealthier nations like the U.S. where typical immunization schedules (at 2, 4 and 6 months of age) leave infants under 6 months vulnerable.

The research, led by Sarah Burl, PhD and Katie Flanagan, PhD, of the Medical Research Council (MRC; U.K.) laboratories in The Gambia, and Ofer Levy, MD, PhD, of Children's Division of Infectious Diseases, builds on a decade of work in Levy's lab studying stimulators of Toll-like receptors (TLRs), a family of receptors on immune cells, as potential vaccine adjuvants. In 2006, the lab showed that stimulating one TLR -- TLR8 -- triggered a robust immune response in a key group of white blood cells called antigen-presenting cells.

In the new multinational study, funded by the MRC, the Bill & Melinda Gates Foundation and the National Institutes of Health, investigators

stimulated blood samples from 120 Gambian infants with a panel of different TLR stimulators (agonists), and measured production of cytokines from white blood cells – all elements of the immune response that are difficult to elicit in newborns. The infants ranged from newborn to 12 months of age, allowing the researchers to examine age-specific effects and see if the adjuvants remained effective over time.

Many of the TLR agonists, including TLR4 and TLR5 agonists, elicited some form of immune response, but a thiazoloquinoline compound, stimulating TLR7 and 8, elicited the greatest production of the cytokine TNF-alpha, a key component of the immune response, during the first month of life, and was the only compound to elicit production of the cytokine interferon gamma in newborns. TLR8 agonists continued to induce the greatest production of TNFα and IFNγ throughout the first year of life.

"Currently, until an infant gets the full vaccination series, he or she is not fully protected," Levy explains. "The adjuvant could be combined with any vaccine, and if things work very well, it could provide single-shot protection at birth."

"Our findings in The Gambia highlight the importance of international collaboration and further underscore the potential of TLR8 adjuvants as a broadly applicable platform to enhance vaccine responses," Levy says. "This could possibly reduce the number of immunizations needed and the antigen dose required -- both of which would be major wins for global health."

More information: dx.plos.org/10.1371/journal.pone.0018185

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