Immune discovery should help develop improved vaccines for infants and newborns

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Scientists have just identified a class of 'danger signals' that are highly efficient at triggering an immune response in infants and newborns. They believe their discovery may have the potential to reduce both the age of vaccine administration and the need for multiple booster injections in infants and newborns, whose immune systems operate

differently to those of adults.

The scientists, from the School of Medicine, Trinity College Dublin, at the National Children's Research Centre (NCRC) in Ireland, have just published their findings in the prestigious *Journal of Immunology*.

Infection remains the most common cause of mortality in early life. Vaccination is by far the most effective intervention at preventing infectious disease, but newborn babies do not respond optimally to most vaccines due to their immature immune system. For this reason immunisations are scheduled over the first 13 months of life to coincide with the maturation of the infant immune system. This leaves a window of time where newborns and young infants are susceptible to vaccine -preventable infections, especially for vaccines such as the MMR that are only administered when a child is one year old.

Vaccines have two key components, one of which is an adjuvant. These adjuvants act as danger signals that instruct the immune system to mount a response to the infection, which in the case of a vaccine is usually an attenuated (reduced in virulence), inactive form, or a fragment of the bacteria or virus. The adjuvant is critical not only for triggering the immune system into action, but also for directing the type of response best suited to fight a particular infection.

Lead author of the study, Research Fellow in Trinity's School of Medicine, Dr. Kiva Brennan, said: "Many adjuvants used in vaccines today were developed in adults. However, babies and children are not simply little adults, and because of this, a child's immune system responds differently to that of an adult." As a result, key to improving vaccine efficacy is the design of adjuvants that specifically target and kick the newborn immune response into action.

Scientists know that the formation of the microbiome is a critical step in

a baby's development, where 'good bacteria' in the gut and on the skin establish and start functioning, and it is thought that newborns do not mount strong immune responses to allow for such colonisation by these commensal or 'good bacteria'. Viruses, however, have no beneficial function in newborns, which is why the scientists suspected that newborns may retain a more robust immune response to viruses. By exploring this theory, they found that a class of adjuvants that activate specialised sensors, which are critical in the response, drove a very strong immune response in newborns.

Commenting on the significance of the research, senior author, Assistant Professor in Immunology at Trinity, Dr. Sarah Doyle, said: "These sensors are normally activated in response to viral infection and direct the immune system to clear viral infections. Harnessing these efficient anti-viral immune responses will help in the design of targeted adjuvants for paediatric vaccines by directly activating immune responses that are fully functional in infants and newborns."

"Improving paediatric vaccine efficacy has the potential to reduce both the age of administration and the need for multiple booster injections, likely increasing compliance and protecting more of the paediatric population with fewer doctors' visits."

More information: Kiva Brennan et al, Type 1 IFN Induction by Cytosolic Nucleic Acid Is Intact in Neonatal Mononuclear Cells, Contrasting Starkly with Neonatal Hyporesponsiveness to TLR Ligation Due to Independence from Endosome-Mediated IRF3 Activation, *The Journal of Immunology* (2018). DOI: 10.4049/jimmunol.1700956

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