Helping pre-term babies avoid bronchopulmonary dysplasia by controlling immune responses

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Medical researchers are a big step closer to understanding the inflammatory responses in pre-term babies that can cause devastating

heart and lung conditions including bronchopulmonary dysplasia (BPD) and pulmonary hypertension (PH).

It is the immune system's job to defend the body from potentially harmful invaders. Because there is a myriad of such pathogens, stunningly versatile defense strategies have evolved, including one called type-2-polarized inflammation.

Type-2-polarized inflammation's regular job is to fight off parasites and to counterbalance type-1 and -3 responses. However, in babies with under-developed lungs, this inflammatory response is out of place and out of control, and can cause permanent damage to lung tissue, its supplying blood vessels and the heart.

Specific inflammatory responses

Now a team including Melbourne's Hudson Institute of Medical Research, Monash University and Monash Children's Hospital has identified the specific inflammatory responses that drive this process, and identified several risk factors that clinicians treating the mothers before birth and the babies thereafter—that is, obstetricians and neonatal pediatricians—can aim to avoid.

Professor Marcel Nold says the research, published this week in the journal *Science Translational Medicine*, is significant in various ways: "The discovery that type-2-polarized inflammation drives cardiopulmonary disease in these babies allows us to now work on ways to control it and avoid the damage it wreaks."

"We have also managed to identify that administering the hepatitis B vaccine shortly after birth—as is done in a number of neonatal intensive care units—can augment type-2-driven inflammation, but delaying this vaccine can avoid that problem," Prof Nold said.

"There is nothing wrong with the hepatitis B vaccine itself," he said. "But this is a good example of how better understanding of disease mechanisms, in this case regulation of the immune system early in the life of preterm babies, can improve the care we provide to our patients. Simply giving the vaccine later will likely do the trick for most babies."

Fellow researcher, Professor Claudia Nold, says this research has also provided insight into how some existing treatments work: "We have known that administration of magnesium sulfate and glucocorticoids to the mother before birth have protective properties in preterm infants, and our research now identifies a mechanism by which this protection works."

"Early life disease often leads to lifelong health problems. Our ultimate goal is to prevent preterm babies developing ongoing conditions, so understanding how the damage occurs is a huge step toward that goal," she said.

Early life cardiopulmonary disease

The team also believes there could be new treatment strategies to tackle early life cardiopulmonary disease. It has been known for some time that type-2-polarized inflammation also plays a critical role in diseases affecting older children and adults, for example in asthma and allergies, from which at least 2.7 million Australians suffer.

Medications targeting type-2 inflammation have been developed for these patients, and these treatments can now be considered as a means of controlling the type-2-polarized inflammation driving early life cardiopulmonary disease.

In fact, the team recently commenced a clinical trial in which they specifically target the inflammatory mechanisms they have identified as

culprits causing illness in preterm babies, to prevent damage to their lung and heart as well as their gut and brain, aiming to offer them and their families a brighter outlook on life.

More information: Jason C. Lao et al, Type 2 immune polarization is associated with cardiopulmonary disease in preterm infants, *Science Translational Medicine* (2022). DOI: 10.1126/scitranslmed.aaz8454

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