Researchers spot molecular control switch for preterm lung disorders

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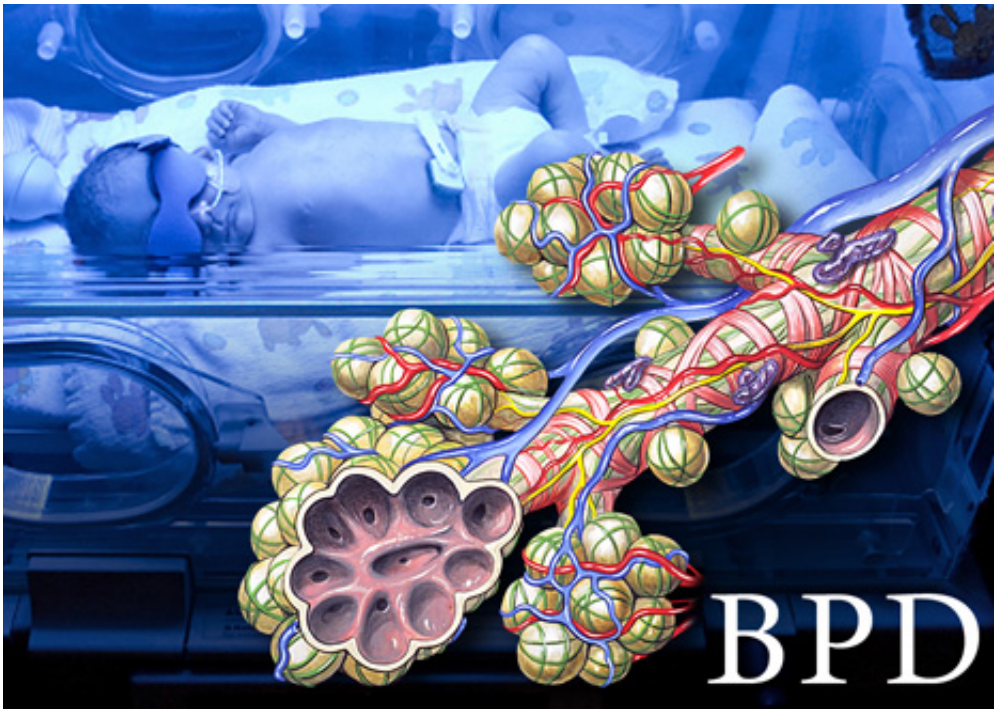

(Medical Xpress)—Researchers at Yale School of Medicine have made major discoveries that could lead to new treatments for lung disorders in premature babies. In a mouse study, the team located key molecules that switch on stress pathways in preterm lung disorders, and also found that when parts of these pathways were blocked with a pain drug, lung damage was prevented or reversed.

The findings are published online ahead of print in the March issue of *American Journal of Respiratory Cell and Molecular Biology*.

Bronchopulmonary dysplasia (BPD) is the most common chronic lung disease in premature infants and does not have any specific treatment. The disorder affects about 97% of infants with birth weights below 1,250 grams, and can lead to repeated respiratory tract infections, as well as to emphysema and chronic obstructive pulmonary disease in adulthood.

A research team led by Dr. Vineet Bhandari, associate professor of pediatric neonatology and obstetrics, gynecology & reproductive sciences at Yale School of Medicine, theorized that if the molecules that cause these disorders can be blocked early on, they could essentially prevent lifelong lung problems.

Bhandari and his team studied the lung tissue of newborn mice. The team noted that when this lung tissue was exposed to hyperoxia —excess oxygen in tissues and organs that activates all components of the stress pathways in the newborn lung— there was a marked increase of cyclooxygenase 2 (Cox2) in the lung's stress pathways. This action resulted in BPD in mice. Once the team used a drug that inhibits Cox2, they were able to reverse BPD in mice.

"This is the first time hyperoxia has been comprehensively shown to be responsible for activating the stress pathway in developing lungs," said Bhandari. "Hyperoxia can induce interferon gamma and disrupt lung development, leading to BPD in mice. Once we used the Cox2 inhibitor Celecoxib, we were able to reverse the effects in the mouse BPD models. The drug, originally indicated to treat pain, protected the lungs from cell death, and was able to prevent destruction of and damage to the developing lung exposed to hyperoxia or excess interferon gamma in room air."

Bandari added that the findings suggest that Cox2 and or CHOP—a molecule important in the stress pathway—are potential new drug targets that can be inhibited to treat or prevent human BPD.

Bhandari said the next step is to conduct pre-clinical studies.

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