Bronchopulmonary dysplasia (BPD)—a form of chronic lung disease—is a leading complication of preterm birth affecting infants born before 32 weeks gestation. Exposure to high levels of oxygen (hyperoxia) plays a role in BPD pathogenesis, but the precise molecular mechanisms remain uncertain.

Jennifer Sucre, MD, and colleagues previously demonstrated a pattern of increased Wnt signaling in human BPD tissue and hyperoxia models of BPD. They have now used three different model systems—3-D human organoids, mouse lung slices and a mouse in vivo model—to define mediators of activated Wnt signaling after hyperoxia injury.

They discovered that increased expression of Wnt5A in lung connective tissue cells contributes to the impaired alveolarization (alveoli are the sites of gas exchange) and septal thickening observed in BPD.

The findings, reported in the *American Journal of Respiratory and Critical Care Medicine*, suggest that precise targeting of Wnt5A in the lungs of preterm infants may prevent or reverse BPD.