Conditional reprogramming of pediatric airway epithelial cells

S. Wolf
G. F. Perez
L. Mukharesh
N. Isaza
D. Preciado
R. J. Freishtat
D. Pillai
M. C. Rose
G. Nino

Video Abstract

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Abstract

For the first time, scientists have figured out how to grow and extend the life of primary airway epithelial cells from newborns and young children. These cells line our nasal passages and lungs, protecting us from pathogens, and controlling our immune responses to allergens. Differences in these cells may help explain why certain infants develop wheezing and asthma later in life, but studying them has been challenging because they are difficult to obtain in babies and usually die in culture after dividing a few times. Now, researchers at Children's National Medical Center in Washington, D.C. and George Washington University have devised a way to reprogram pediatric airway epithelial cells so that they survive, creating a new model to study respiratory disorders that take hold early in life. The team collected airway epithelial cells from 23 donors, including newborns, infants and young children. They induced cell reprogramming in vitro with conditioned medium made from mitotically inactivated fibroblasts and a Rho kinase inhibitor. This special medium allowed the cells to expand much faster and to survive multiple subcultures for more than a month. If scientists removed the conditioned medium after the second passage, the cells stopped dividing. After multiple subcultures, the conditionally reprogrammed cells maintained their original phenotype, and differentiated into respiratory epithelium when grown in air-liquid interface cultures. This method of reprogramming also worked in cells taken from premature neonates and from the bronchial airways of young children. Next, the researchers tested whether conditionally reprogrammed cells from infants maintained airway epithelial immune responses. They exposed these cells to double-stranded RNA to mimic a virus, and saw that they turned on typical innate immune pathways and antiviral chemokine genes. The cells also secreted epithelial interferon, and upregulated a variety of interferon response and airway inflammation and remodeling genes. More work will be needed to identify any differences between reprogrammed airway epithelial cells and their in vivo counterparts. But the results suggest that they retain their properties in culture, and could be a powerful new tool for scientists investigating the mechanisms behind asthma and other respiratory diseases that get their start in early childhood.