CDHR3 Genetics and Rhinovirus C Respiratory Illnesses

Background Experimental evidence suggests that CDHR3 is a receptor for rhinovirus-C (RV-C), and a missense variant in this gene (rs6967330) is associated with childhood asthma with severe exacerbations. Objective To determine whether rs6967330 influences RV-C infections and illnesses in early childhood. Methods We studied associations between rs6967330 and respiratory infections and illnesses in the COPSAC2010 and COAST birth cohorts, where respiratory infections were monitored prospectively for the first 3 years of life. Nasal samples were collected during acute infections in both cohorts and during asymptomatic periods in COAST and analyzed for RV-A, RV-B and RV-C, and other common respiratory viruses. Results The CDHR3 asthma risk-allele (rs6967330-A) was associated with increased risk of respiratory tract illnesses (IRR 1.14 [1.05-1.23], P=0.003). Particularly, this variant was associated with risk of respiratory episodes with detection of RV-C in COPSAC2010 (IRR 1.89 [1.14-3.05], P=0.01) and in COAST (IRR 1.37 [1.02-1.82], P=0.03) children, and in a combined meta-analysis (IRR 1.51 [1.13-2.02], P=0.006). In contrast, the variant was not associated with illnesses related to other viruses (IRR 1.07 [0.92-1.25], P=0.37). Consistent with these observations, the CDHR3 variant was associated with increased detection of RV-C but not of other viruses during scheduled visits at specific ages. Conclusion The CDHR3 asthma risk allele is associated specifically with RV-C illnesses in two birth cohorts. This clinical evidence supports earlier molecular evidence indicating that CDHR3 functions as an RV-C receptor, and raises the possibility of preventing RV-C infections by targeting CDHR3.