CDHR3 Genetics and Rhinovirus C Respiratory Illnesses - DTU Orbit (25/11/2018)

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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.

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