CDHR3 Genetics and Rhinovirus C Respiratory Illnesses

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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.

General information
State: Accepted/In press
Organisations: University of Copenhagen, University of Wisconsin-Madison, University of Wisconsin, Copenhagen University Hospital, Brigham and Women's Hospital, University of Southern Denmark, University of Chicago
Publication date: 2017
Peer-reviewed: Yes

Publication information
Journal: American Journal of Respiratory and Critical Care Medicine
ISSN (Print): 1073-449X
Ratings:
BFI (2019): BFI-level 2
Web of Science (2019): Indexed yes
BFI (2018): BFI-level 2
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 2
Web of Science (2017): Impact factor 15.239
BFI (2017): Indexed yes
Scopus rating (2017): CiteScore 5.1 SJR 5.942 SNIP 2.998
Web of Science (2017): Impact factor 15.239
BFI (2016): BFI-level 2
Scopus rating (2016): CiteScore 5.33 SJR 6.137 SNIP 3.485
Web of Science (2016): Impact factor 13.204
BFI (2015): BFI-level 2
Scopus rating (2015): CiteScore 5.43 SJR 6.034 SNIP 3.514
BFI (2014): BFI-level 2
Scopus rating (2014): CiteScore 5.9 SJR 6.351 SNIP 3.792
Web of Science (2014): Impact factor 12.996
BFI (2013): BFI-level 2
Scopus rating (2013): CiteScore 6.5 SJR 5.56 SNIP 3.442
Web of Science (2013): Impact factor 11.986
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 2
Scopus rating (2012): CiteScore 6.82 SJR 6.038 SNIP 3.247
Web of Science (2012): Impact factor 11.041
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes