Therapeutics & Vaccines

HELA-ADAPTED RHINOVIRUSES C (RV-C) AND ADAPTIVE GENOMIC MUTATIONS

WARF: P240269US01

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The Invention

UW-Madison researchers have developed HeLa cell-adapted Rhinovirus-C (RV-C) variants that induce a strong cytopathic effect and replicate vigorously in HeLa-E8 cells. The inventors had previously shown that two missense mutations in VP1 and 3A genes increase binding (via heparan sulfate) and replication, respectively, of adapted RV-C15 (C15a) in HeLa-E8 cells (WARF family P160050). A similar mutation made in 3A (E41->K) also improved replication of RV-C2 and RV-C41 whereas a mutation in VP1 was C15a-specific. The inventors then adapted both the wild-type and mutated (E41->K in 3A) RV-C2 and RV-C41 and wild-type RV-C11 isolate by serial passaging in HeLa-E8 and identified the adaptive mutations that were acquired by selection in vitro. The inventors performed 16-20 serial passages, purified the adapted variants, and sequenced their complete genomes. The inventors observed strong cytopathic effects and increased replication of all three adapted RV types in HeLa-E8 compared to wild-type isolates. Interestingly, C2a but not C11a or C41a had increased binding (one-log) to HeLa-E8 cells and increased replication (over one-log) in HeLa-H1 cells, which do not express CDHR3. Binding of C2a was inhibited by heparin suggesting that it binds to heparan sulfate similarly to C15a. This additional receptor binding specificity could be required for efficient virus spread because C2a but not C11a or C41a induced plaques in HeLa-E8 monolayers. Several adaptive mutations in structural genes VP1, VP2, and VP3 and non-structural genes 2B, 2C, 3A, and 3D were found in all three types. These findings demonstrate that RV-C types can adapt to efficient binding and replication in HeLa-E8 cells via specific mutations in similar structural and/or non-structural genes.

Additional Information

For More Information About the Inventors

- James Gern

Tech Fields

- Research Tools : Microbial technologies
- Research Tools : Other research tools
- Therapeutics & Vaccines : Vaccines

For current licensing status, please contact Jennifer Gottwald at jennifer@warf.org or 608-960-9854