

Modification of Reoviridae

Market Sector: Therapeutics (human and veterinarian vaccines, oncolytic agents)

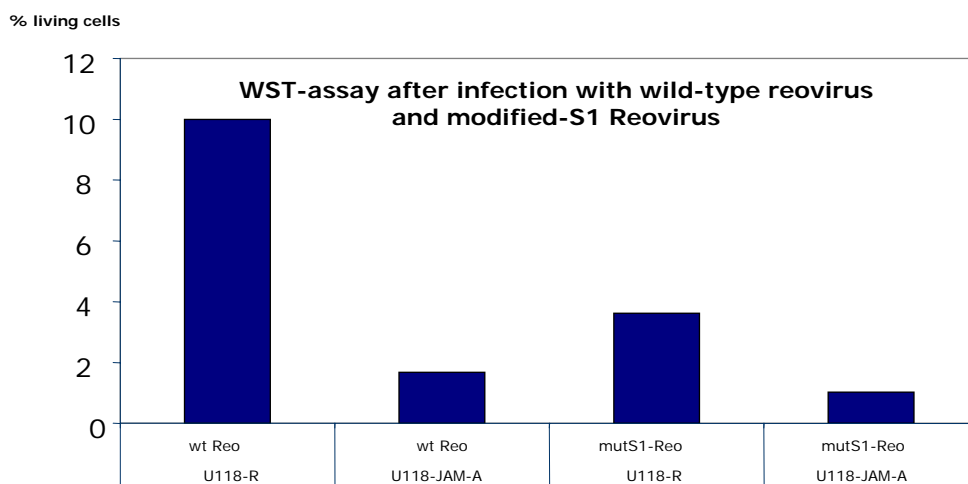


Fig.1 Cell survival of U118 cells expressing the reovirus receptor (JAM-A) or the targeted receptor (R), infected with either wt reovirus or the modified-S1 reovirus. Cell survival was assayed with the WST assay. The data show the modified, but not the wt virus, kills the U118 cells the express the receptor

The Reoviridae family includes viruses that affect the gastrointestinal system (such as Rotavirus), and that cause respiratory infections. Reoviridae have been found in association with various diseases, and as a consequence have considerable economic impact. Some cause diseases of domestic livestock, e.g. African horse sickness, blue-tongue disease, and others i.e. rotaviruses, are the etiologic agents of serious diarrheal illness, resulting worldwide in approx. 500.000 deaths annually.

Mammalian Orthoreoviruses have been isolated from the human respiratory and enteric tracts, but are not associated with serious human disease. The last 5 years one of these, reovirus T3D has been used as an oncolytic agent in experimental cancer therapy trials. So far at least 8 clinical trials have been initiated in the US, UK and Canada, to study the feasibility and safety of T3D of the approach.



Up to now, there was no robust system for reverse genetics in *Reoviridae*. We recently developed such a reverse genetics system, which to the best of our knowledge, is unique and novel. We have used it to create novel reovirus T3D variants that can utilize a new protein as receptor on cancer cells. This provides proof of concept for the efficiency of the technology. Our technology allows genetic modification of viruses of this family with relative ease.

Keywords

Infectious diseases, microbiology, oncology, vaccine, reovirus, rotavirus

Key Benefits

- Generating more efficient variants of reovirus T3D that can be used as oncolytic agents.

Our data demonstrate:

- 1) That we can generate genetically modified reoviruses; i.e. that the technology is operational;
- 2) That the position chosen to insert the stretch of amino acids facilitates retargeting of the virions;
- 3) That genetically retargeted reoviruses can be stably and efficiently propagated.

- Generating genetically modified variants of other *Reoviridae* (i.e. Orthoreovirus, Rotavirus, Orbivirus, and/or Coltivirus) for use as vaccine. Several members of the *Reoviridae* family can have considerable clinical (rotaviruses) or economical (blue-tongue) impact. The capacity to genetically modify the genomes of these viruses may make vaccine development independent of so-called reassortants.

Applications

- Generation of retargeted reoviruses, as well as a production system for propagation of such viruses.
- Generation of tumor cell-specific reoviruses that have an improved therapeutic index in oncolytic 'virotherapy' strategies.
- Generating 'marker vaccines' against infections with Orthoreoviruses, Rotaviruses, Orbiviruses, and/or Coltiviruses.
- Facilitate the development of new reassortants in *Reoviridae* for vaccine production.

- Facilitate studies on the replication of *Reoviridae*, which may lead to identification of new 'drugable' targets for development of antivirals.

Commercial Partner

- The partner has the capacity to produce clinical grade batches of viruses, and/or
- The partner provides support to carry out clinical studies, and/or
- The partner is involved in vaccine development against infections with *Reoviridae*

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