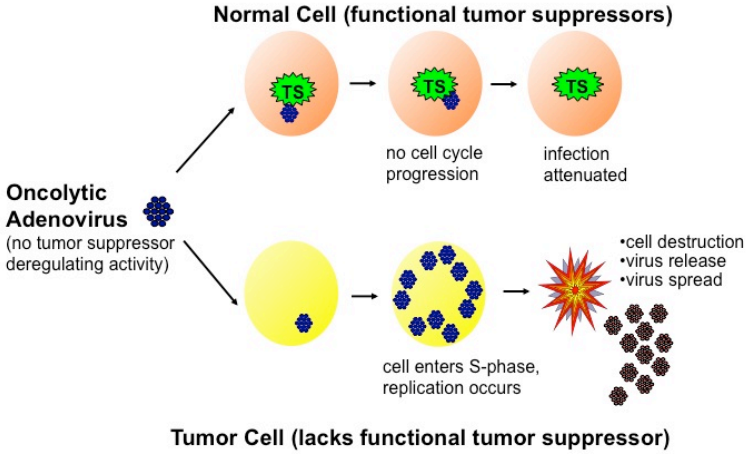
Rapid Generation of Customized Tumor-Selective Oncolytic Adenoviruses

INVENTION: The goal of oncolytic viral therapy is to specifically infect and kill tumor cells without causing damage to normal cells. Although adenovirus is one of the most commonly used gene transfer vectors in foundational and preclinical research, their potential as an effective therapy is limited by the use of only certain serotypes and the difficulties in manipulating the large 36 kb viral genome.

Researchers at Salk have developed a novel platform for the rapid assembly of oncolytic adenoviral vectors from libraries of component parts. The functions and diversity of the genomic parts is provided by previously reported mutations, directed evolution approaches based on structure, heterologous elements and disparate adenovirus serotypes, mutants, and species. The investigators used this assembly method to systematically engineer oncolytic adenoviruses that only replicate and therefore kill cells that have defects in either the p53 or Rb pathway respectively. These pathways are mutated in almost all human cancers, and these very same cellular controls are targeted and disabled by adenoviral-encoded proteins to allow for their replication, and therefore by taking advantage of this characteristic, Salk scientists were able to generate replication-selective oncolytic adenoviruses.



This new assembly platform holds great promise for advancing the development of new oncolytic viruses. The ability to efficiently optimize viruses for use in oncolytic viral therapies will facilitate the development of viruses that not only specifically target and kill cancer cells, but that can avoid liver toxicitiy, evade neutralizing antibodies, and reactivate beneficial host antitumor immune responses.

APPLICATIONS:

- Development of targeted oncolytic therapies
- Targeted cancer vaccines
- Cancer immunotherapy
- Precision medicine in cancer

ADVANTAGES:

- Rapid customizable platform for any immunotherapeutic molecule or target
- Provides for targeted immunotherapy
- Provides for a balanced approach between direct tumor killing and immunogenic cell death
- Overcomes many of the challenges currently faced by oncolytic viral development

STAGE OF DEVELOPMENT: Salk researchers have generated viruses that specifically target cancer cells defective for p53 or Rb. These viruses were able to infect, replicate, and kill cancer cells without deleterious effects on normal cells, and have also been tested in mouse models.

BACKGROUND: Cancer is a diverse group of diseases characterized by uncontrolled cell growth and is responsible for approximately 8 million deaths worldwide each year. Current therapies, including surgery, chemotherapy and radiotherapy, although effective, often have serious side effects and are frequently ineffective at eliminating all malignant cells. Oncolytic viral therapy holds great promise for a more targeted and effective treatment with minimal negative side effects.

INVENTORS: Dr. Clodagh O'Shea, Dr. Colin Powers, Dr. Shigeki Miyaki-Stoner

PATENT STATUS:

- U.S. Patents 9,217,160 and 9,187,733
- PCT application WO2014/153204 is pending

PUBLICATIONS: Ou, et al. 2012. A structural basis for the assembly and functions of a viral polymer that inactivates multiple tumor suppressors. Cell, 151:304-19.

CONTACT: Michelle A. Booden, Ph.D.; mbooden@salk.edu; (858) 453-4100 x1612

TECHNOLOGY ID: RD1201, RD1251, and RD1332