



# Clodagh O'Shea

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## The Problem

Cancer is a leading cause of death in the United States. Most cancer patients are treated with nonspecific poisons, but a holy grail of treatment is therapeutic agents that are as sophisticated as the disease itself, able to precisely target the cancer. To develop better cancer therapies, scientists must first decipher what goes wrong with cellular mechanisms that normally regulate cell growth and survival. But finding these targets to create truly game-changing treatments requires rethinking how we approach cancer research and cancer medicine.

## The Approach

Clodagh O'Shea exploits the common cold virus, adenovirus, as a powerful agent to both understand and treat cancer. Viruses are nature's nanomachines: their outer coats enable them to enter specific tissues in our body where they express a small number of proteins that hijack the cell's replication machinery to reproduce. The very same cellular replication machinery controls are targeted by the mutations that give rise to cancer.

One way O'Shea's team is exploiting this overlap is by creating synthetic viruses that act like guided missiles, infecting and replicating only in tumor cells. These helpful, hijacked

viruses burst apart cancer cells and release thousands of virus progeny that can seek out and destroy distant metastases. Such intelligent viral therapies have enormous potential in improving the treatment of patients suffering from cancer.

## The Innovations and Discoveries

- O'Shea identified how adenovirus uses a protein polymer to hijack a cell's molecular machinery, including large cellular machines involved in growth, replication and cancer suppression. She is testing new cancer therapies that mimic the strategies employed by the viruses.
- Her team discovered a mechanism used by adenovirus to sidestep the cell's suicide program. This could help explain how tumor suppressor genes are silenced in tumor cells, and could pave the way for a new type of targeted cancer therapy.
- O'Shea is working on new methods to visualize DNA and its surrounding proteins in a living cell to better understand what goes wrong in those interactions that can lead to disease.

For more information, please visit:

<http://www.salk.edu/faculty/oshea.html>

Cancer, Cellular Biology, Therapeutics, Virology