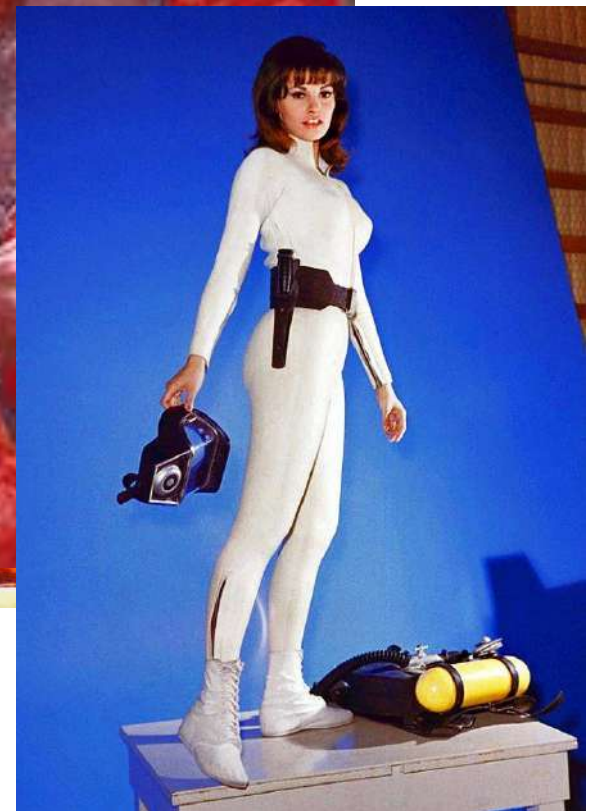
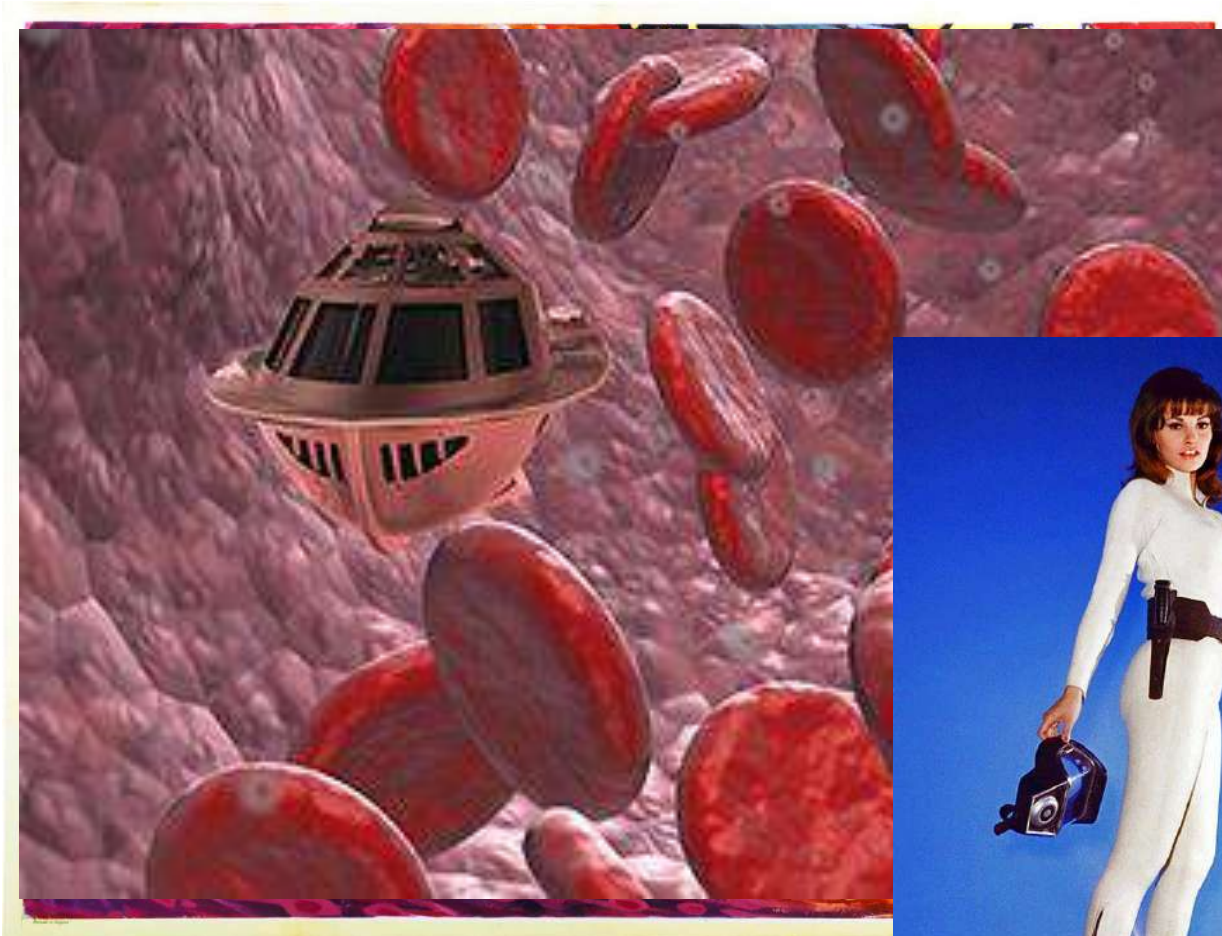


Oncolytic Viruses: Programmable Cancer Killing Machines

***John Bell
The Ottawa Hospital
University of Ottawa***

The Ottawa Regional Cancer Foundation
Terry Fox Foundation
Canadian Cancer Society Research Institute
Ontario Institute for Cancer Research]
Canadian Institute for Health Research
Prostate Cancer Canada
The Ottawa Hospital Foundation

1966



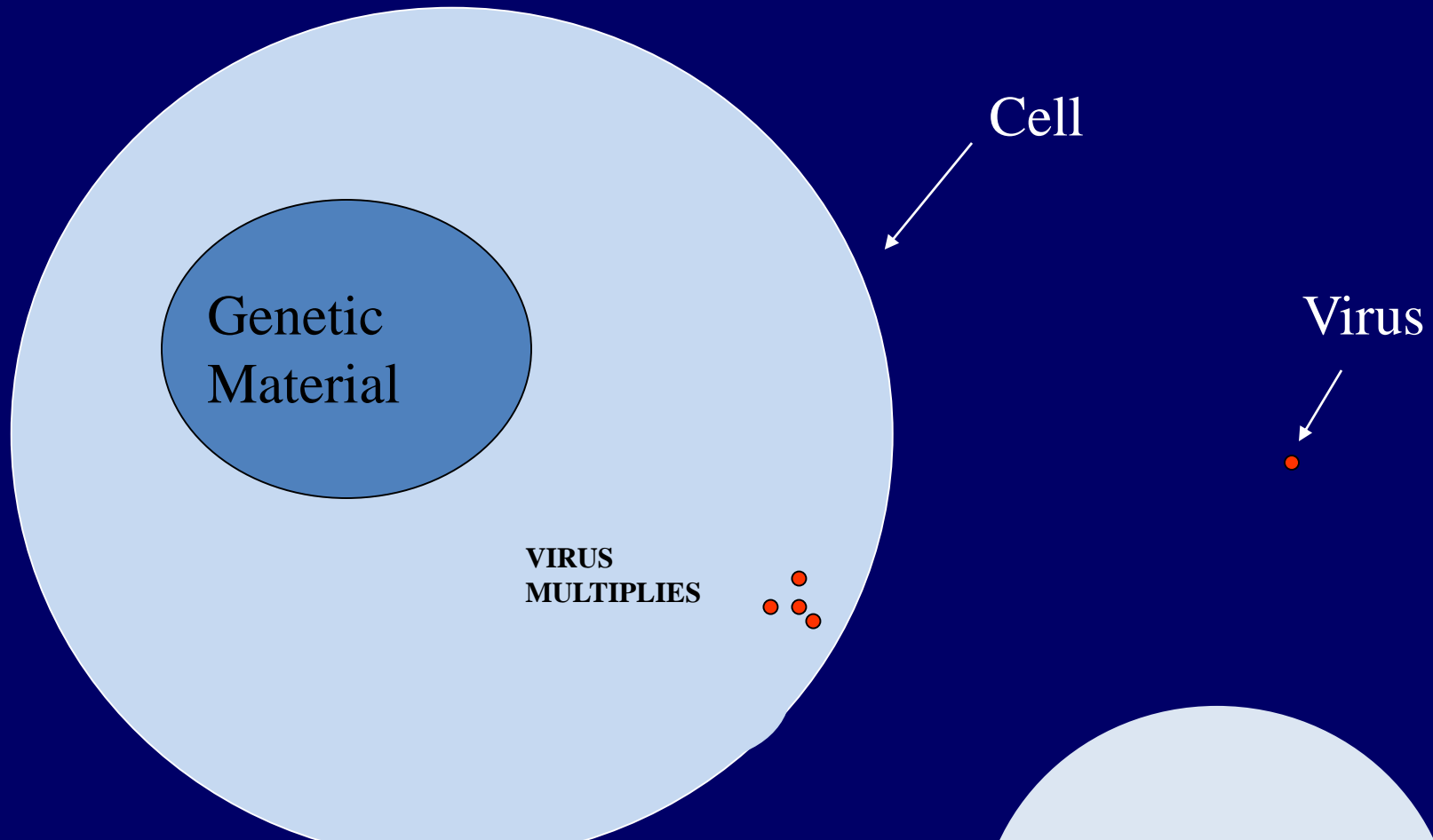
A close-up portrait of a woman with a shaved head, looking directly at the camera with a neutral expression. She has light skin and blue eyes. The background is a textured, greyish-brown wall. The word "CHEMOTHERAPY" is overlaid in large, black, sans-serif capital letters on the left side of the image.

CHEMOTHERAPY



CANCER TARGETED
THERAPIES

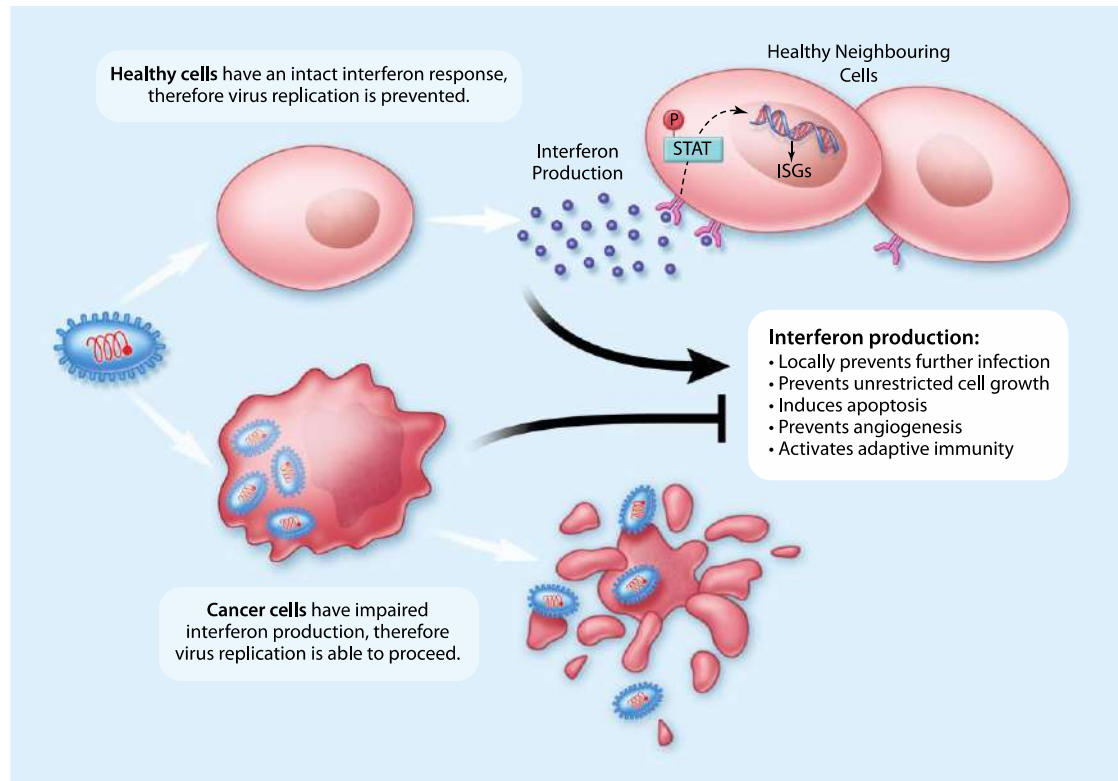
Our bodies are made of billions and billions of cells



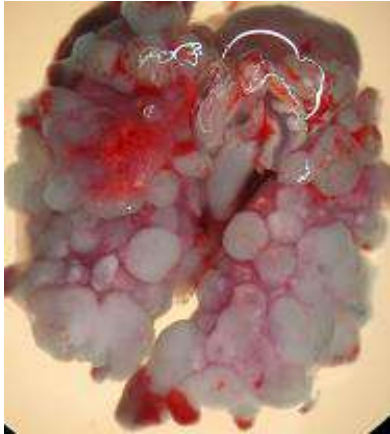
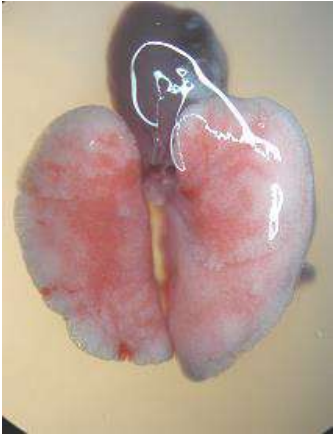
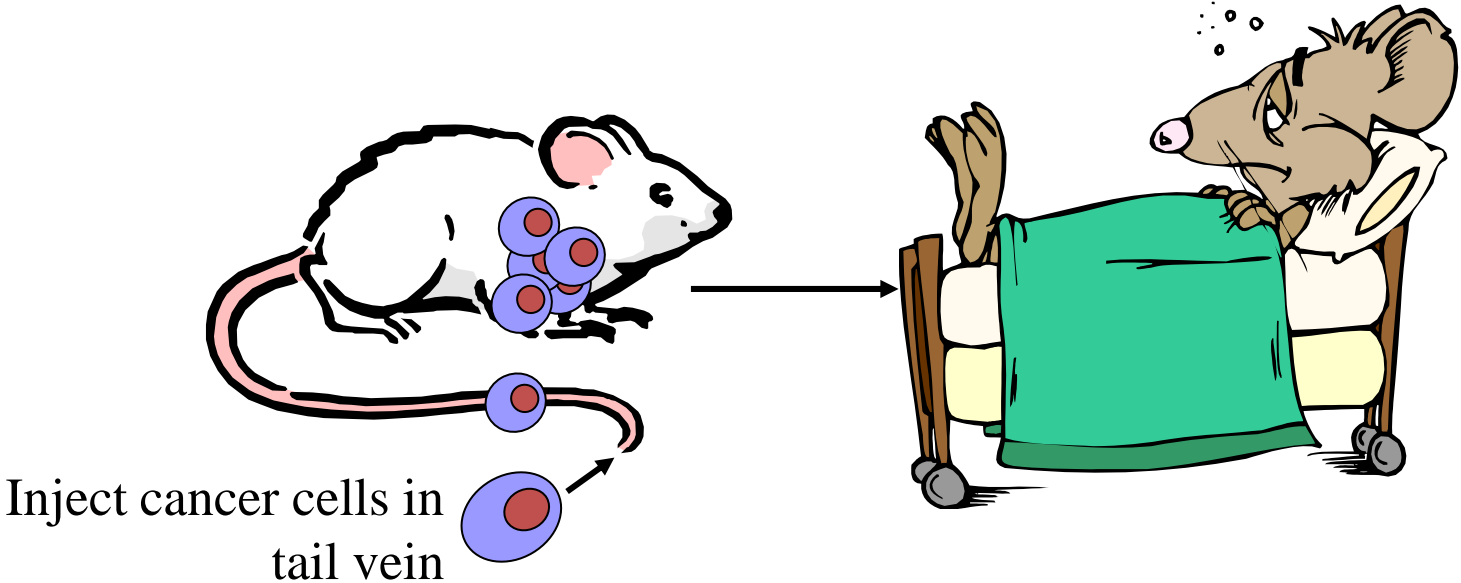
Viruses are parasites and can only reproduce inside of cells

We have Designed Viruses to be
Parasites of Cancer Cells!

Oncolytic Virus Paradigm



Model of Metastatic Cancer

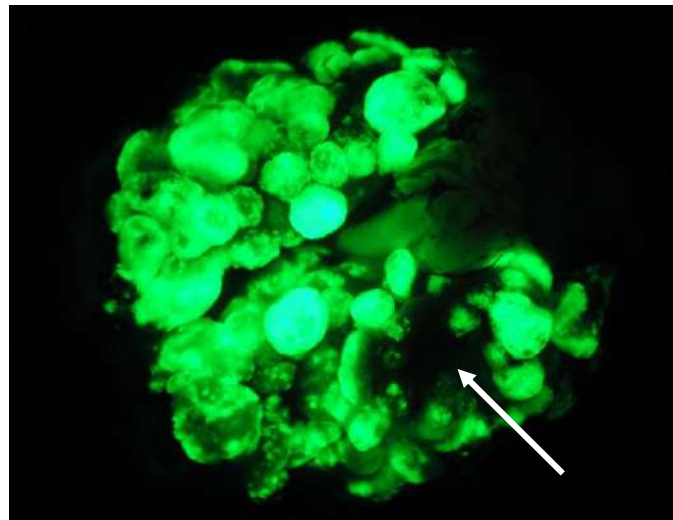


Treat with Virus
→
14 days later

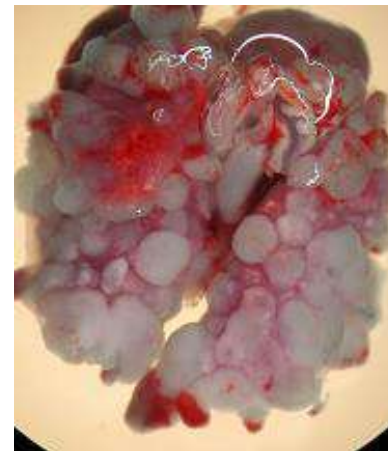
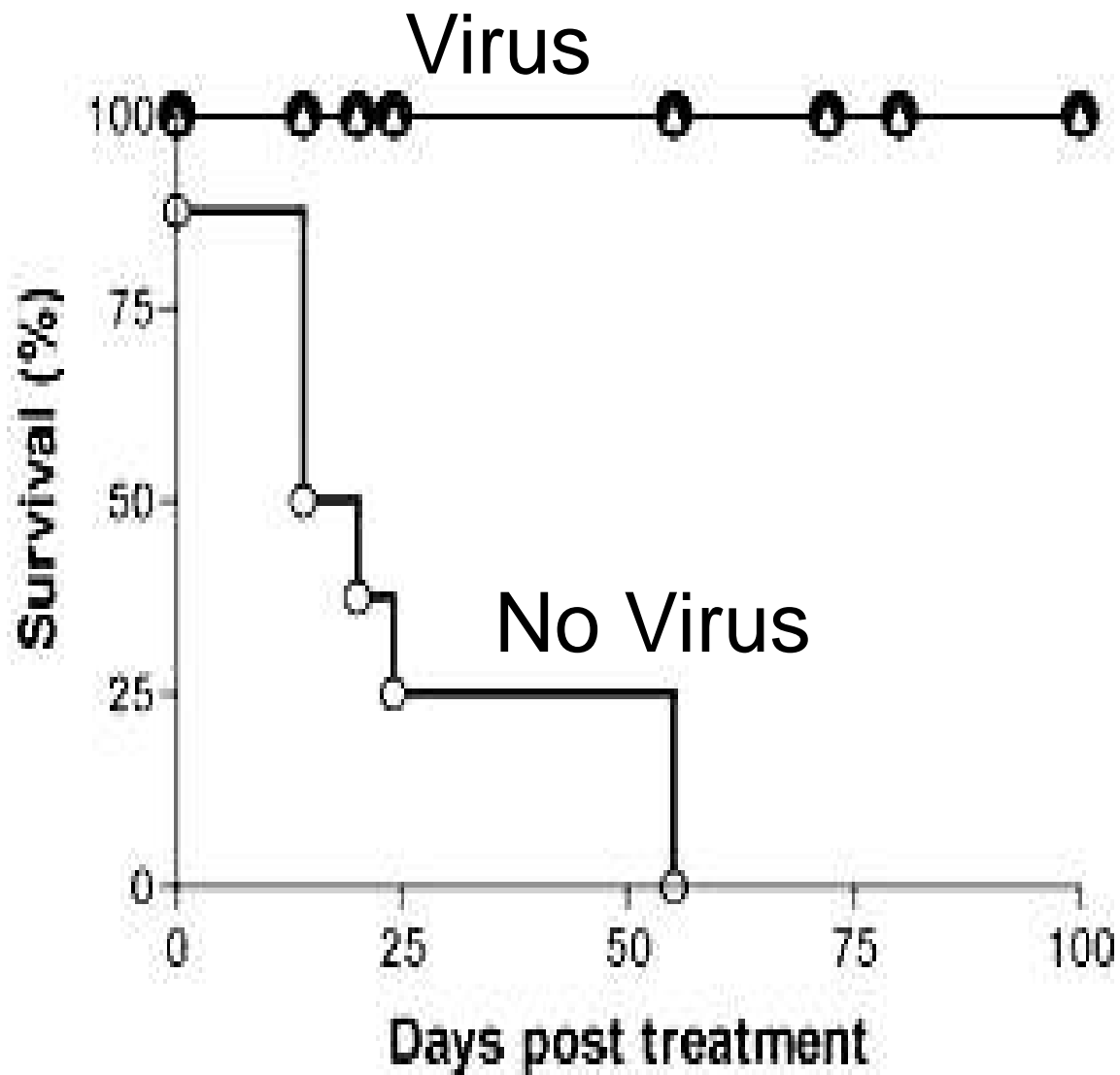
Virus - Lung Metastasis Model



2 weeks
following
intravenous
tumour cell
injection

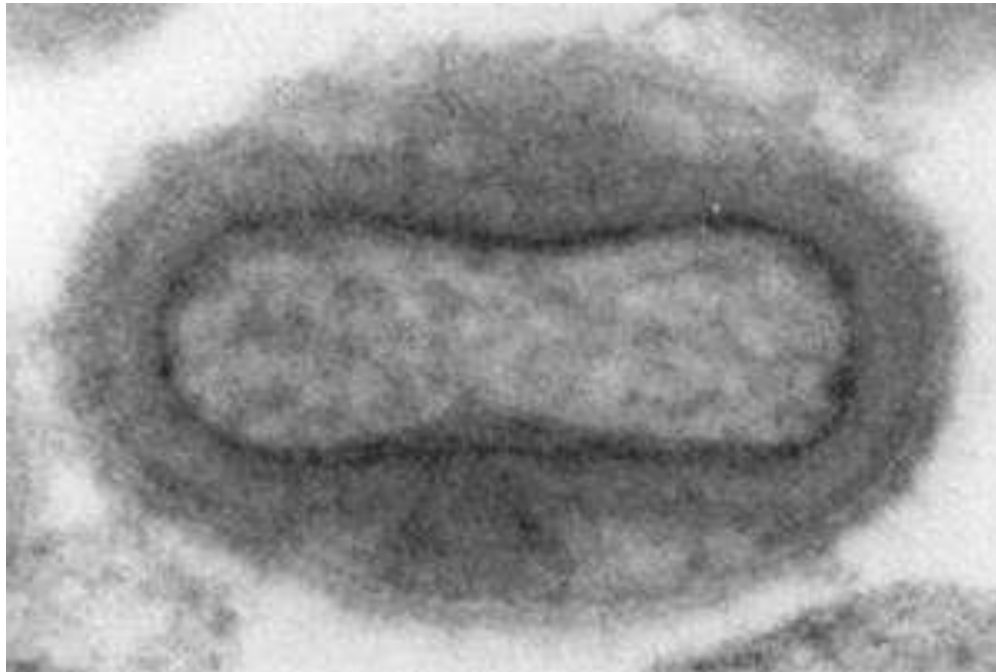


IV Administer
Virus (**GREEN**)
and wait 24 hours



Mouse Experiments can Lead to Therapies for Patients

Vaccinia: A Virus that Selectively Infects and Destroys Tumours: A Cancer Parasite!

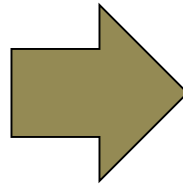


Vaccinia Virus: JX-594

Engineered to take advantage of the loss of anti-viral programs and the unregulated metabolism of tumour cells (TK deletions, mutant B18R protein)

Tumour Responses Following Oncolytic Virus:

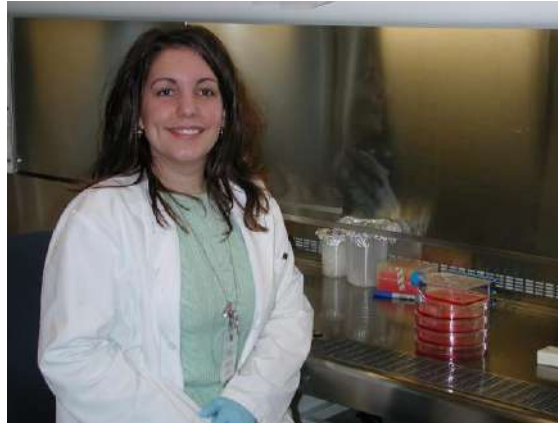
Examples of tumour responses on Phase 1 & Phase 2 trials



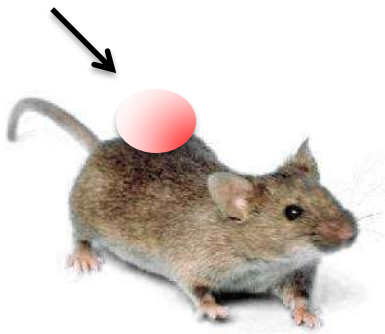
This happens in a minority of patients, elite responders!!....How can we make this happen more often?

***Oncolytic Viruses Engage the
Immune System***

Immunity and OV therapy



**Implant Colon
Tumour**



OV Tx



**"Cured" mouse
wait 7 months**

**Challenge with
Colon Cancer
cells**



**Mice reject
Colon Tumours!**

Phase I Clinical Trial Metastatic Melanoma: Evidence of Anti-tumour Immunity

32 year-old woman:

- Refractory, widespread met
- Complete tumor regressions:
 - Injected
 - Distant dermal, chest (surg)
- Disease-free 3.5+ years

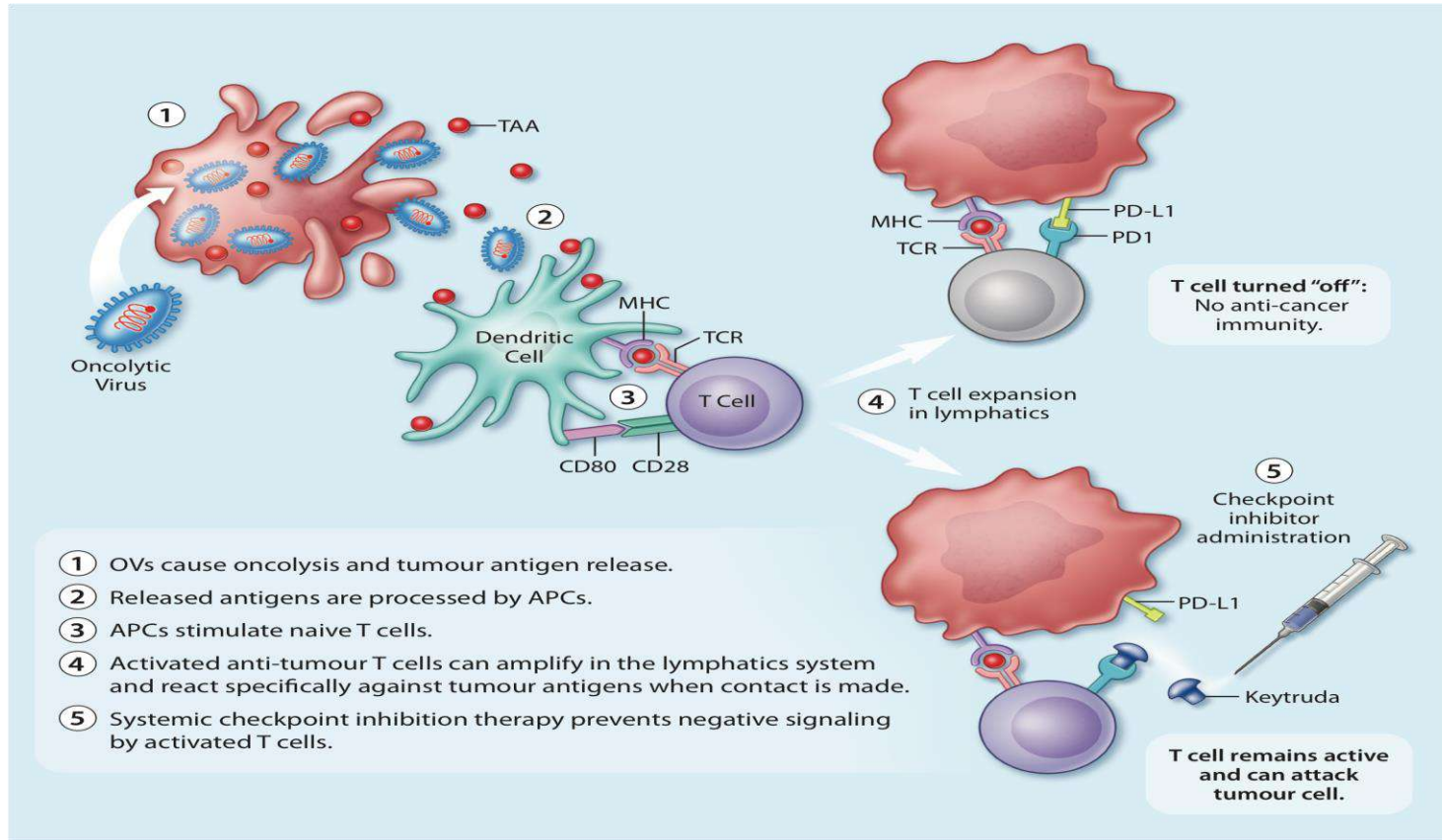
Pre-treatment



After Virus



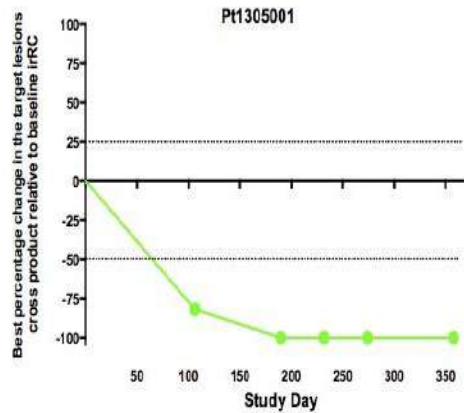
Oncolytic Viruses and Immune Checkpoint Inhibitors: Complementary Therapeutics



Combination of Virus Therapy with Immune Activating Agents is Likely to be Most Effective

Prior cancer treatments

1. BCG (PD)
2. Nivolumab (PD)



Pre-Treatment



Day 30



Day 90



Day 180







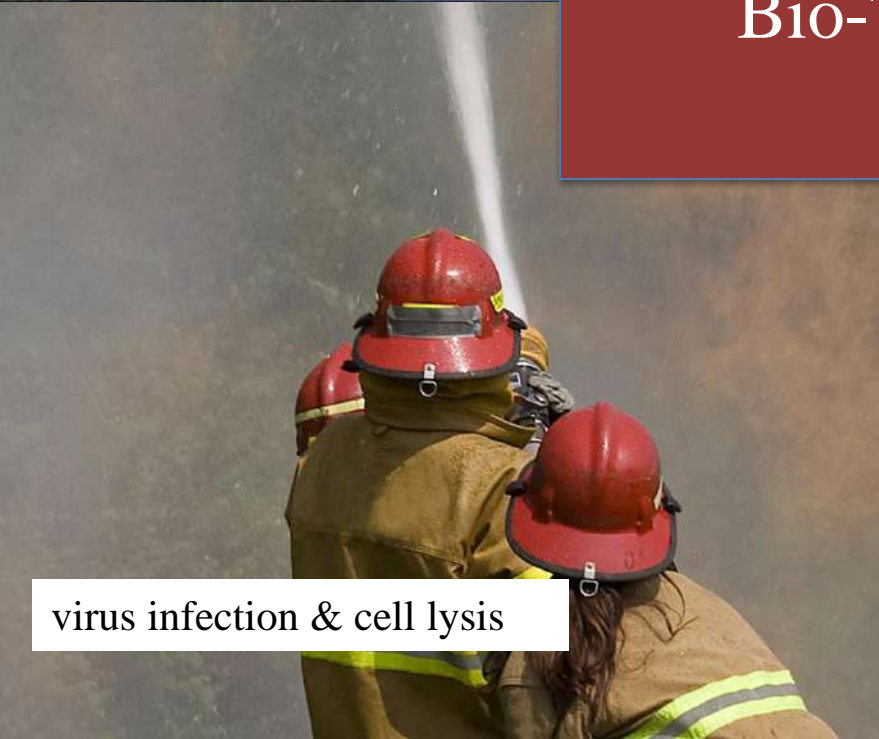
immune cells

NFFPC 2004



shutting off
tumor blood supply

Bio-Therapy



virus infection & cell lysis

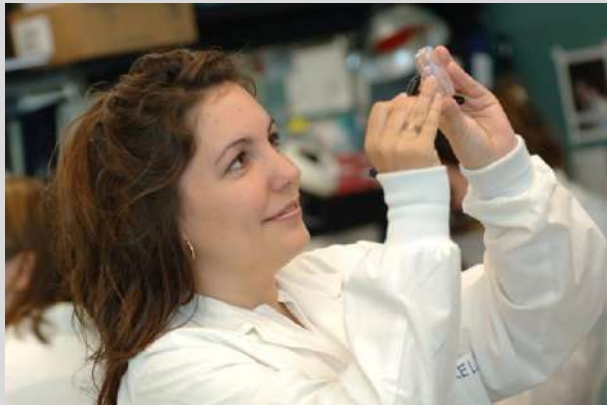
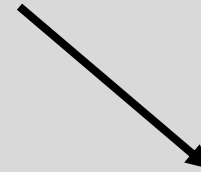
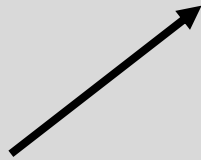


tumor-targeting
antibodies

Research Strategy at the Ottawa Hospital



MANUFACTURE



DISCOVERY



TESTING



