Synthetic Viruses Targeting Cancer

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SENS 3, Cambridge, UK

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Why is a new strategy necessary?

• Breast cancer remains a significant cause of illness and death

• The treatment options for breast cancer have remained virtually the same for the last 30 years, despite great advances in molecular biology

• The rate of new therapeutic development is too slow

• The economics of the current drug development model are unsustainable

• Current drug development strategies do not address the fact that each cancer is a unique disease

• Even the most modern cancer treatments work far downstream from the fundamental root of cancer, namely damage to DNA
The *Ideal* Cancer Drug

- Highly specific to an individual cancer
- Works at the level of DNA
- Effective, well-tolerated, with mild side effects
- Inexpensive and widely available
- Based on the best current biological understanding and technology
- Rapidly reconfigurable to target any resistant cell populations or for mixed cell populations
## Strategy Framework

<table>
<thead>
<tr>
<th>Desired outcome</th>
<th>Can be accomplished by</th>
</tr>
</thead>
<tbody>
<tr>
<td>Works at level of DNA</td>
<td>Gene-based agents such as viruses or, better, genetically engineered machines</td>
</tr>
<tr>
<td>Personalized and targeted</td>
<td>Incorporate molecular knowledge of individual cancer into the design; obviates need for wide clinical testing</td>
</tr>
<tr>
<td>Rapid development, reconfigurable</td>
<td>Modular components, semi- or fully-automated drug design and production</td>
</tr>
<tr>
<td>Best technology available</td>
<td>Open access to research data, development data, and clinical use results, allowing continuous innovation</td>
</tr>
<tr>
<td>Low cost</td>
<td>Free market competition leading to non-monopolistic pricing</td>
</tr>
</tbody>
</table>
Clinical presentation

Perform molecular diagnostics

Culture patient cells

Open Bio-Fabrication

Standardized Parts Library

Open Design Engine

DNA Synthesis

Production and QC

Shared knowledge base

Global R&D

Clinical experience

Best practices

Single-use drug (experimental GEM)

in vitro testing should show drug affects only cancer cells, otherwise failures analyzed and design process repeated

FDA approval

Clinical data

Clinical use

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WHAT ARE ONCOLYTIC VIRUSES?

Oncolytic ("onco" meaning cancer, "lytic" meaning "killing") viruses represent an innovative potential cancer therapy known as "virotherapy"—a therapy that seeks to harness the natural properties of viruses to aid in the fight against cancer.
News Releases & Announcements

$6.3M from Terry Fox Foundation to link researchers across Canada developing oncolytic virus therapies for cancer

OTTAWA, May 24, 2007 — Seven Canadian research teams, led by Dr. John Bell of Ottawa, will share a $6.3 million grant to collaboratively develop and test oncolytic viruses as cancer therapeutics. The grant was awarded by the Terry Fox Foundation through the National Cancer Institute of Canada after a competitive peer-review process.

“Canada is a leading country for oncolytic virus research. This grant will allow us to expand our efforts and work together to ensure that cancer patients benefit from our research as soon as possible,” said Dr. Bell, a Professor and Senior Scientist at the University of Ottawa, the Ottawa Health Research Institute and The Ottawa Hospital Regional Cancer Centre.

Oncolytic viruses infect and destroy cancer cells without harming normal cells. They work because many anti-cancer genes are also anti-viral genes, so when cells develop genetic mutations that lead to cancer, they often lose their viral defenses at the same time. While oncolytic viruses have been known to exist for decades, there has been a resurgence of interest in recent years as scientists have discovered new oncolytic viruses and engineered them to be better and safer. Studies in laboratory models have shown that these viruses are very effective against many cancers and early clinical studies in patients have been encouraging.
in vitro testing should show drug affects only cancer cells, otherwise failures analyzed and design process repeated
The breakthrough of our lifetime... the X PRIZE about each of us.

Revolution Through Competition.

First individual genome published online; shows humans less alike than thought
in vitro testing should show drug affects only cancer cells, otherwise failures analyzed and design process repeated
Synthetic Biology

“**Synthetic biology** is an emerging area of research that can broadly be described as the design and construction of novel artificial biological pathways, organisms or devices, or the redesign of existing natural biological systems.”

Effectively transforms DNA into a programming language
If you can write DNA, you're no longer limited to "is", but to what you could make.
- -5 years: 0.5 - 5kb, $10-$15/bp
- 0 years: 50 - 500kb $0.50-$1/bp
- +5 years: 5mb - 5gb <$0.0001/bp

Sponsored Links

**Blue Heron Bio GeneMaker**
Call now for promotional pricing!
The **DNA Synthesis** Specialists.
www.blueheronbio.com

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1 kb within 8 business days,
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**Gene Synthesis $1.10/bp**
For small, large & difficult genes.
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**Custom PNA Synthesis**
Peptide nucleic acid conjugates
PNA Chimera, PNA modifications
pnaoligos.com

**Rapid Gene Synthesis**
Superfast Turnaround Guaranteed!
Low Cost, Individualized Support
www.DNA20.com
Applications dependent on synthetic capabilities

single genes*

minimal life

base pairs

$10^2$  $10^3$  $10^4$  $10^5$  $10^6$  $10^7$

$10^2$  $10^3$  $10^4$  $10^5$  $10^6$  $10^7$

genetic circuits, viruses, GEMs

Engineered organisms

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Synthetic Oncolytic Viruses

- Designed using standardized genetic modules
- Similar to code libraries in computing

- Develop minimal oncolytic viral core

- Create libraries of functional components (targeting, gene knockdown, transgenes, selective promoters, control systems)

- Permits rapid development of individualized viruses based on well-characterized, standardized parts
### Transcriptional Regulators

#### Available repressible regulators (normally ON)

<table>
<thead>
<tr>
<th>Name</th>
<th>Description</th>
<th>Direction</th>
<th>Control</th>
<th>Output Low</th>
<th>Output High</th>
<th>Length</th>
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<tbody>
<tr>
<td>BBa_J14032</td>
<td>promoter P(Lac)IQ</td>
<td>Forward</td>
<td>aTc, tetracyline</td>
<td>37</td>
<td></td>
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<tr>
<td>BBa_R0040</td>
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<td></td>
<td>54</td>
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<tr>
<td>BBa_R0051</td>
<td>promoter (lambda cI regulated)</td>
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<td>lambda cI</td>
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</table>

#### Available inducible regulators (normally OFF)

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<th>Description</th>
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<tr>
<td>BBa_J12007</td>
<td>modified lambda Prm promoter (OR-3 obliterated)</td>
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<td>cl</td>
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<tr>
<td>BBa_R0062</td>
<td>promoter (luxR &amp; HSL regulated ... lux pR)</td>
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<td>luxR, HSL</td>
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<tr>
<td>BBa_R0079</td>
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<td>PAI</td>
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<tr>
<td>BBa_R0080</td>
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<td>Forward</td>
<td>araC</td>
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</table>

#### Available other regulators

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<tr>
<td>BBa_J0500</td>
<td>inducible pBAD/araC</td>
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<td>araC</td>
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<tr>
<td>BBa_J3453</td>
<td>Telp represses POPs/RIPS generator</td>
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<td>ATc</td>
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<td>BBa_J3022</td>
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<td>ATc</td>
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<td>araC</td>
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<tr>
<td>BBa_J3109</td>
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<td>araC</td>
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http://parts.mit.edu

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Open Source Biology

• Maximally drives innovation

• Very low development costs

• Permits wide oversight and review

• Inclusive and non-proprietary

• Results in diverse, empowered, technically competent community

• Speeds wide dissemination of ideas and technologies
The Jamboree
November 4-5, 2006
Massachusetts Institute of Technology,
Cambridge, MA, USA

This summer, 37 teams from around the world participated in a biology competition. The challenge: design and build biological systems and run them in living cells.

What they did in four months will astound you.

Find out more here...
in vitro testing should show drug affects only cancer cells, otherwise failures analyzed and design process repeated
Funding and political support
Summary

• Rapid development of state-of-the-art GEMs at minimal cost

• Each cancer is treated as it should logically be treated: as a unique instance of disease.

• All the components pre-exist and are becoming increasingly accepted and validated. The innovation here is assembling them

• Cost vs. performance, the strategy will be more effective yet cost less over time (as is the case with computing)

• The process can be used multiple times with the same speed and efficacy

• Minimal potential for harm (n = 1), problematic designs or parts never reused