23% of all deaths attributed to cancer

**Total Estimated New Cases:** 14,100,000

**Total Estimated Deaths:** 8,200,000

$263.8 billion annual cost associated with cancer in medical expenses and lost productivity.
LET’S TALK NUMBERS: CANCER STATISTICS
CURRENT CANCER THERAPIES

- Surgery
- Chemotherapy
- Radiation
- Targeted Therapy
To develop better cancer therapy:

**Specific** and **efficient**

**Personalized** for each tumor and patient genetics
CANCER: WHAT GOES WRONG

Genetic changes

Epigenetic changes

Promoter hyperactivation
RESULTS: PROMOTER ACTIVITY LEVELS

phTERT

pSurvivin

Cancer cell lines

hTERT expression (Vs. HF)

Survivin expression (Vs. HF)

Fibroblasts
liver
lung
Breast
Fibrosarcoma

Survivin expression (Vs. HF)

Fibroblasts
liver
lung
Breast
Fibrosarcoma

0
500
1000
1500
2000
2500
3000
3500
4000
4500
5000
5500
6000
6500
7000
7500
8000

ND
BOOMERANG CORE SYSTEM: CRISPR/CAS9

Pennisi E, Science, 2013
Let’s summarize...
CANCER CELL

SURVIVIN PROMOTER

VP64

dCAS9

hTERT PROMOTER

activation of the gene of interest

HEALTHY CELL

- NO permanent DNA mutation
- NO systemic affect
- Minimal foreign protein expression
1 Boomerang
3 Applications
DIAGNOSTICS

protein marker

cELL LABELING

healthy cells

cancer cells

KILLING CANCER

autocatalytic caspase 3
BOOMERANG: DESIGN HIGHLIGHTS

- “Master” template for modular cloning
- RGR design for gRNA - Ribozyme-gRNA-Ribozyme
- Synthetic activation promoter
BOOMERANG: FROM DESIGN TO REALITY

Validation of promoter hyperactivation

Transduction efficiency

Validation of BOOMERANG activation system
RESULTS: PROMOTER VALIDATION

Co-localized detection of fluorescent signals under specific promoters in cancer cells
RESULTS: PROMOTER VALIDATION

Co-localized detection of fluorescent signals under specific promoters in cancer cells
RESULTS: AAV TRANSDUCTION EFFICIENCY

Healthy fibroblasts

HT1080 fibrosarcoma

Control, CMV-GFP

Control, CMV-GFP

Similar transduction efficiency in normal and cancer cells under CMV promoter
RESULTS: BOOMERANG IN ACTION

Cancer-specific CRISPR-based gene activation by fully functional prototype
BOOMERANG: PERSONALIZED APPROACH

Tumor diversity → Biopsy

Patient → Recovery

Packaging and delivery → Boomerang construction

Promoter analysis
• ABBBA team is working on cancer diagnosis by engineering of a bacterial sensor (*Affibody*)
• We aimed to express an GPI-anchored *Affibody* on the plasma membrane of human cancer cells
• We cloned the *Affibody* into AAV vector, and transduced human cancer cells

Intracellular *Affibody* expression in human cancer cells
BOOMERANG: ACHIEVEMENTS

Registry parts (Biobricks) submitted and validated

Boomerang activation system functional prototype

Successful collaboration with ABBBA Stockholm

Complete design of Boomerang knockout system - see our Wiki
BOOMERANG: PRACTICES AND POLICIES

Collaboration and panels
✓ With experts from the fields of:
  basic and clinical cancer research and synthetic biology

Ethics and philosophy
✓ Discussion with bioethics experts

Education and Entrepreneurship
✓ School workshop
✓ Lecture to Entrepreneurs Programs
Social events
✓ Pub meet-up

Media
✓ Radio
✓ Social networks
✓ Nationwide coverage on news websites
✓ Video animation for broad audience
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Questions ?