

Collaborative Approaches to Engineer Biology for Cancer Applications

An NCI and NIBIB Partnership

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Concept Overview

Promote innovative synthetic biology approaches to challenges across cancer research

- ❖ Engineer and cancer researcher partnerships
- ❖ Trans-NCI, National Institute of Biomedical Imaging and Bioengineering (NIBIB) collaboration

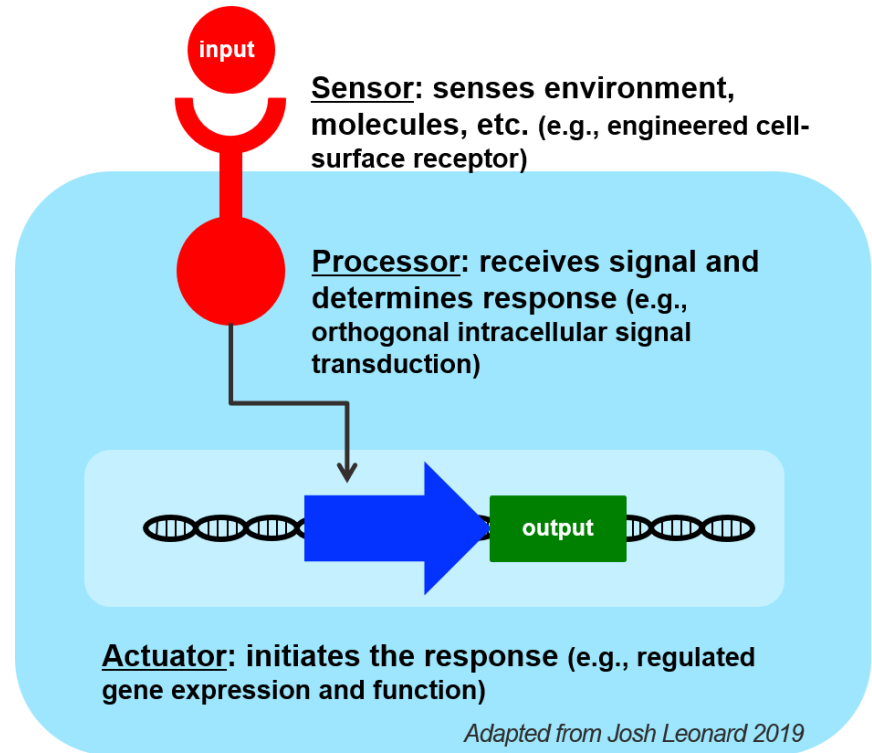
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 - James Lacey
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* Signed on to concept

Opportunities to Engineer Biology for Cancer

- Design, construction, and characterization of improved or novel biological systems using engineering design principles = Synthetic Biology
- Enabled by advances with cell/molecular engineering, computation
- Complement to systems biology
- Transformative potential across cancer biology, prevention, diagnosis, and treatment



Capitalizing on the Opportunity: NCI-NIBIB Collaboration

- NIBIB supporting engineers for technology development
- NCI driving cancer research needs



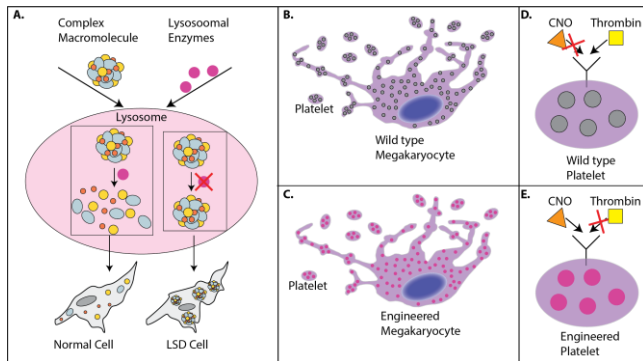
Research potential at this intersection

Build on NIBIB and other NIH investment

- NIH Synthetic Biology Consortium, annual meeting
 - Cancer challenges amenable to synthetic biology approaches
 - More bridges across communities needed
- ~25 funded NIBIB grants
 - Technology development, variety of biological systems (limited cancer)
 - Projects primed for cancer application

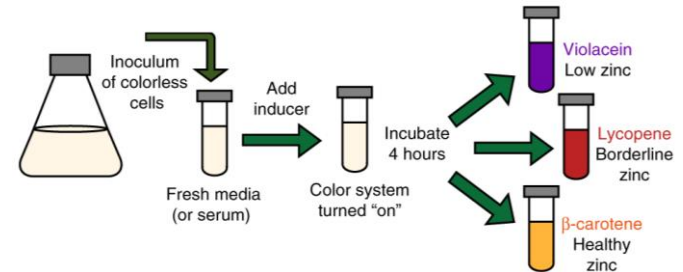
Cancer-ready Technology Examples 1

- *Engineering novel delivery systems with synthetic biology*
 - R21 NIBIB, Tara Deans, University of Utah
 - Engineered platelets release therapeutic content after receptor activation – lysosomal storage diseases
 - Now engineering platelets to target circulating tumor cells (DP2 NCI, Director's New Innovator Award)



Courtesy of Tara Deans

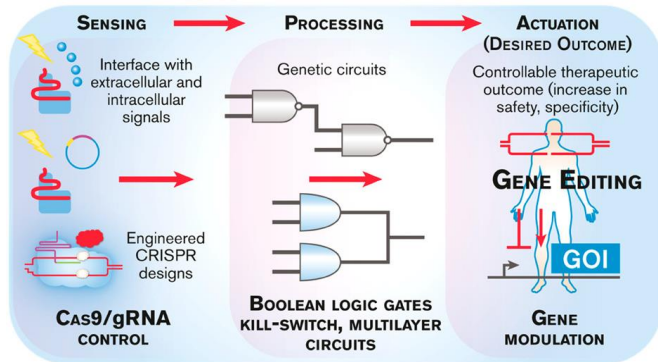
- *Synthetic biology-based detection of micronutrients with minimal equipment*
 - R01 NIBIB, Mark Styczynski, Georgia Tech
 - Engineered bacteria sense micronutrients and produce colored pigment based on the concentration – general nutrient deficiency



McNerney, M.P. *et al.* *Nat Commun* **10**, 5514 (2019)

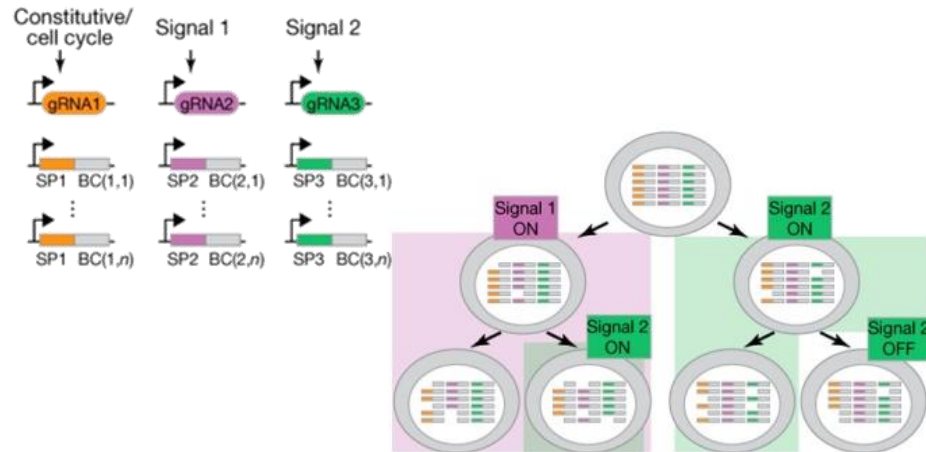
Cancer-ready Technology Examples 2

- *CRISPR logic circuits for safer and controllable gene therapies*
 - R01 NIBIB, Samira Kiani, University of Pittsburgh
 - Genetic safety switches to modulate gRNA or Cas9 to spatiotemporally control CRISPR – liver injury application



Pineda M. *et al.* *ACS Synth Biol* **6**, 1614 (2017)

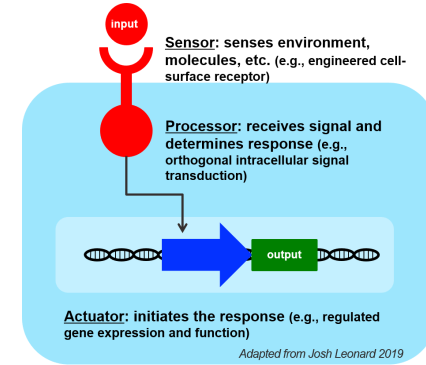
- *Recording and in situ readout of cell lineage and transcriptional history*
 - R01 NIMH (Director's Transformative Research Award), Long Cai and Michael Elowitz, Cal Tech
 - Genomically integrated memory circuits to track and record single cell lineage – brain development focus



Frieda, K.L. *et al.* *Nature* **541**, 107 (2017)

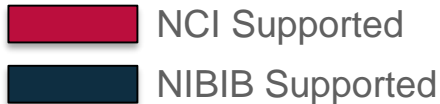
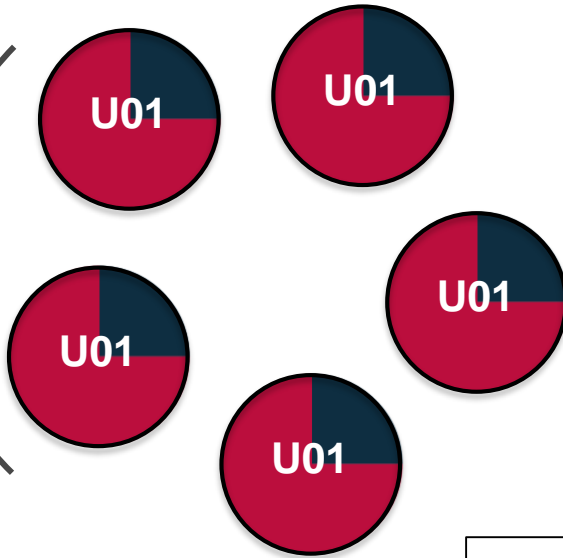
Overall Goal

- Stimulate collaborations between engineers and cancer researchers to expand use of synthetic biology to advance understanding and management of cancer
 - Bring more engineers and novel approaches and technologies to cancer research
 - Cancer research needs drive technology application
- Example research directions (*technology and cancer research advancement*)
 - in situ recording of exposures and genetic changes in pre-cancer and cancer
 - sensitive, minimally invasive biosensors to amplify signals and/or report levels of cancer-related biomarkers
 - targeted, controlled therapeutic delivery or therapeutic action using engineered mammalian cells or microbes



RFA Request

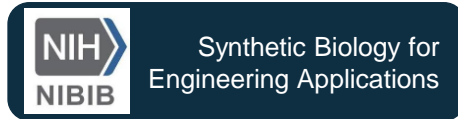
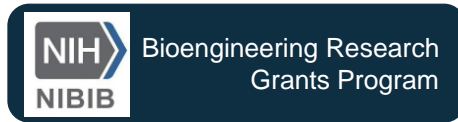
Synthetic Biology
Consortium & NCI
Networks/Consortia



- U01s: requirement for both cancer research/oncology and engineering expertise; multi-PI encouraged
- 4-6 awards (<\$500k direct)
- Connect to NIH Synthetic Biology Consortium & appropriate NCI Networks/Consortia, including meetings
- Engineering PIs in SynBio Technology Development Consortium
- RFA, FY21 set aside request
 - Support emerging, promising area
 - Limited NCI portfolio
 - NCI-convened special review
 - Partnership with NIBIB

Total budget request = \$4.2 M total costs year one
\$3.2 M from NCI and \$1.0 M from NIBIB
(~75% NCI funding and ~25% NIBIB co-funding)

Fit Among Technology Development Examples



Successful Application Features & Evaluation Metrics

Application Success

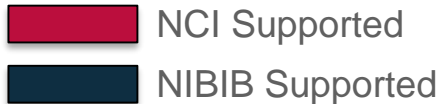
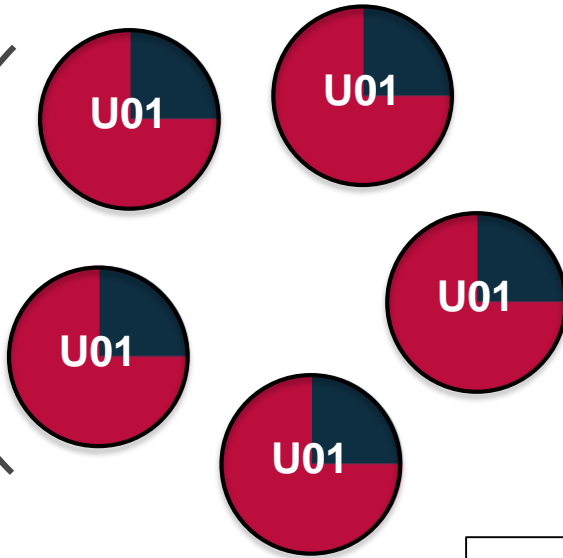
- Significance of cancer research question & potential of technology
- Expertise: engineering, cancer, mathematical modeling
- Technology feasibility
- Application in mammalian tissue or model system

Program Success

- New collaborations
- Publications, presentations, patents, grants in areas
- Research resources – models, protocols, controllable cellular components
- Trained fellows and early-career investigators

RFA Request Summary – Trans-NCI & NIBIB Collaboration

Synthetic Biology
Consortium & NCI
Networks/Consortia



Synthetic biology approaches addressing important cancer research questions

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