Session III: Gene-Targeting Therapy Technologies for CNS Disorders

Junghae Suh
Associate Professor of Bioengineering
Rice University
April 2019
Synthetic Virology

INPUT → OUTPUT

**Provector**

**Lumivector**

**Activatable Peptide Display**

Nuclear uptake
Call for more engineers, computational biologists, biophysicists, etc. to work in gene therapy
Acknowledgments

- Caleb Bashor (Rice)
- Sherry Gao (Rice)
- Caleb Kemere (Rice)
- Jordan Miller (Rice)
- Amina Qutub (UT San Antonio)
- Amanda Randles (Duke)
- Jacob Robinson (Rice)
- Ka-Yiu San (Rice)
- Jeff Tabor (Rice)
- Danielle Tullman-Ercek (Northwestern)
**Directed Evolution**

- Gene library
- Expression of gene library
- Mutagenesis (variation)
- Screening (fitness differences)
- Gene amplification (heredity)
- Activity assay
- Isolation of desired variants
- Mutagenic PCR
- Gene
- Gene isolation

**Enzymes**
- Laundry detergents – lipases
- Pesticides – P450s
- Biofuels – cellulases
- Antibacterials - lysozyme

**Antibodies**
- Anthrax treatment - ABthrax
- Cancer drugs – Portrazza
- Macular degeneration – Lucentis
- Arthritis – Humira

**Develop better delivery vectors**

Viviana Gradinaru will discuss more

(Image adapted from Thomas Shaftee, U Cambridge)
(Slide courtesy of Danielle Tullman-Ercek)
Example: Optogenetic Transcriptional Control of Gene Expression

Control Systems Engineering
- Input, output, process, sensor, feedback $\rightarrow$ control

Multiplexed Control

Control transgene expression profiles in complex environments

(Olson et al., Nat Methods 2014)
(Slide courtesy of Jeff Tabor)
Cargo Choice | Systems Biology

Bioengineering | Computer Science | Statistics

• aka Computational Neuroscience
• Data science
• Extract non-obvious patterns from complex datasets
• Develop multi-pronged therapeutic approaches

Treat more complex diseases

(Geschwind and Konopka, Nature 2009)
Quantitative modeling of transport in complex environments

Heart Flow
FDA approved 2014

Patient-Derived Imaging Data → Data Segmentation → Patient-Specific 3D Geometries

Computational Modeling

Develop better administration strategies

(Slide courtesy of Amanda Randles)
Orchestrate Coherent Endeavor

**Structure**
decoupled, organized, and collaborative

**Connectors**
draw lines, be translators, & facilitate synthesis