SAND2018-11781C

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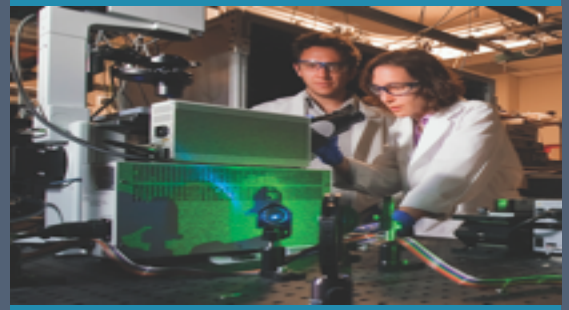
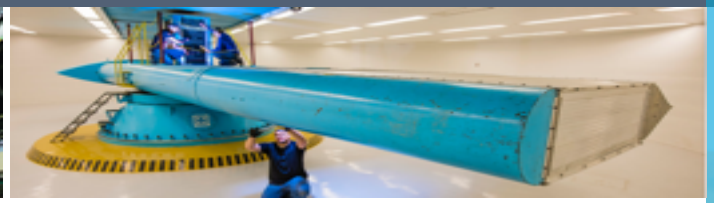
Indirectly-Directed Evolution





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2018 Nobel Prize for Directed Evolution

Synthetic Biology

- **Well-recognized threats via genetic engineering tools; e.g., CRISPR, delivery vectors**

- **Detection of genetic manipulations via horizontal gene transfer**
  - **Varies from easy to very difficult via forensic analyses**

What is indirectly-directed evolution?

Manipulate upstream vectors/gene pools to create biothreats in target species

- **Introduce (mixture of) partially engineered non-pathogenic viruses/microbes/insects etc. into ecosystem**
- **Primed to evolve into threat**
- **Difficult to assign attribution because actual target is a different species**
- **Evidence of (years-earlier) manipulation in initial species likely will be non-existent**

Identify Suitable Target and Pools of ‘Infectious’ of Transferring Organisms

Pools: Phage/viruses, microbes, worms, flies, birds, frogs, animals, . . .

Targets: Animals, humans, entire ecosystems (trophic cascades)

‘Surgical’ Genetic Engineering *vs.* Mutagens

- **CRISPR, nanoencapsulation technologies**
  - **Modify selected gene/genes likely to evolve into threats**
    - **e.g., resurrect dead pox close to smallpox**
  - **Create error-prone polymerases in carefully targeted organisms; apply selective pressures**

- **Simple chemical or radiation (e.g., UV) mutagens**

All approaches likely require large numbers, so utilize large pools within ecosystem and create selective advantages to boost mutagenesis, where possible.

Rural areas vulnerable.

Impacts: Positive

- Increased scientific understanding
  - Ecosystem connections/resiliency
  - Remediation
  - Horizontal gene transfers

- Agriculture and medical defenses
  - Drought, cold, floods, diseases

Impacts: Negative

- Devastating effects
  - Ecosystems
  - Crops (e.g., grapes, corn, wheat) or animals
  - Vital ecosystem targets (bees, bats, birds, etc.)

- Centuries to recover?

Defenses?

- **Case dependent**
  - **Causes of many diseases already known but little protection available despite awesome power of synthetic biology; e.g., Huanglongbing, Zika, Ebola, etc.**
  - **Vital ecosystem targets (bees, bats, birds, amphibians)**
  - **Rapid selective-breeding programs so compensating mutations arise**

Summary

- **Threat from indirectly-directed evolution**
  - **More subtle than directly attacking target**
  - **Potentially devastating to human and non-human targets**
  - **Difficult to detect: unidentified perpetrator because genetic manipulations camouflaged by ‘pool’ species and time**
  - **With well-chosen initial targets, attack need not require synthetic biology**
  - **Defenses difficult**