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Part of Thermo Fisher Scientific

DNA 2.0

 geneIOUS



GenScript
Transforming Biology Research



IDT
INTEGRATED DNA TECHNOLOGIES

SULSA
Scottish Universities Life Sciences Alliance

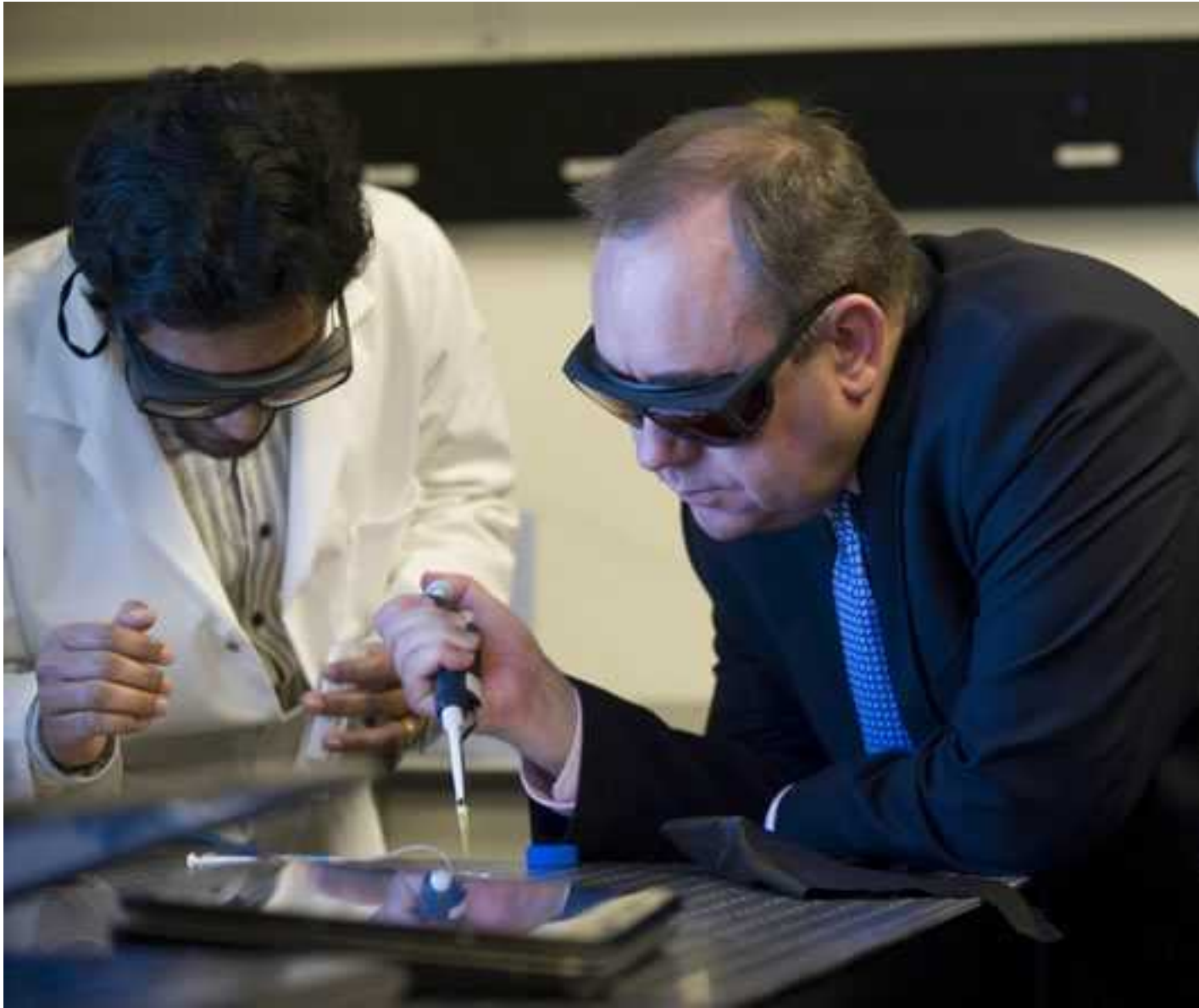
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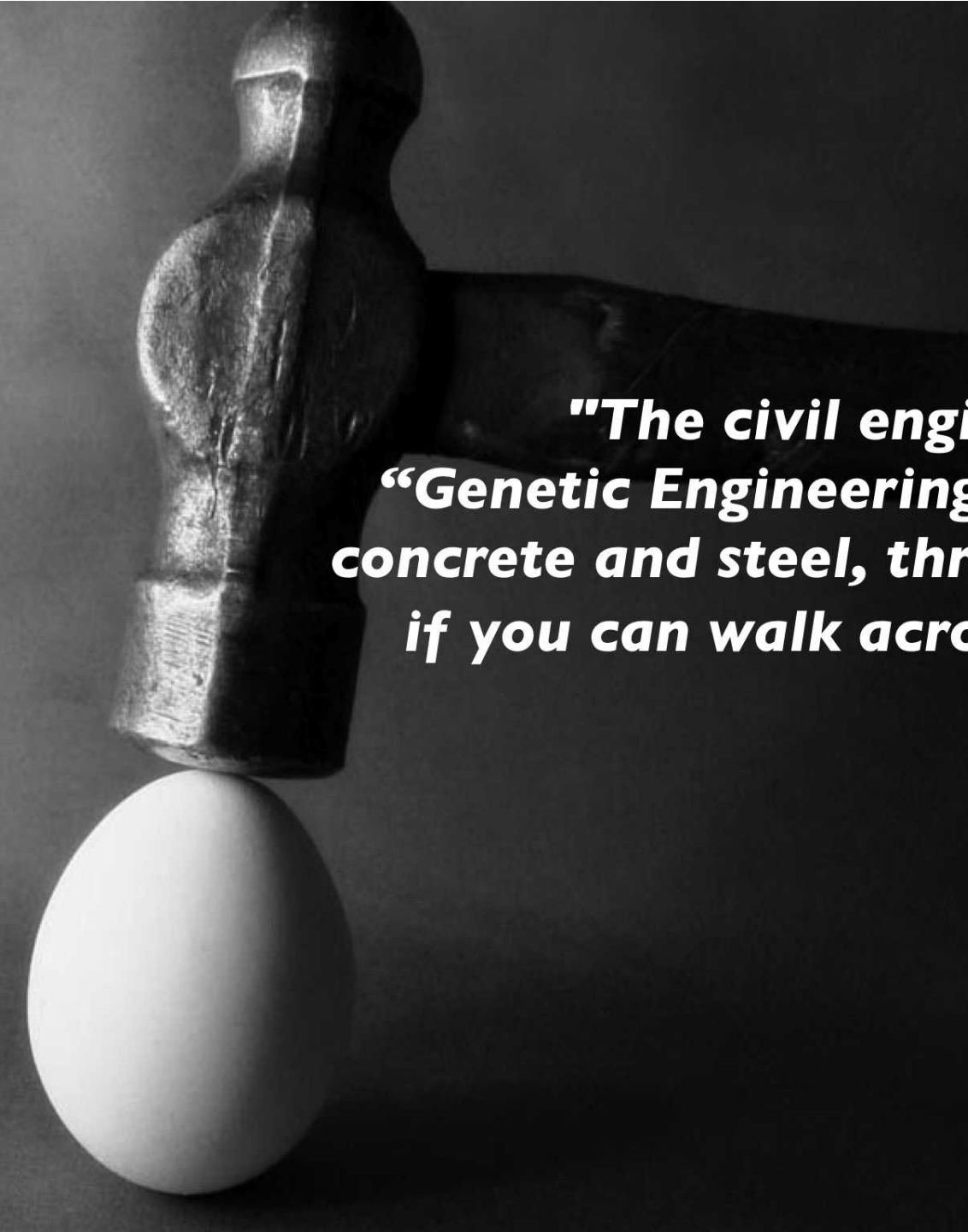


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A black and white photograph showing a hammer with its head resting on a white egg. The hammer is positioned vertically, with the egg directly beneath it. The background is dark and out of focus.

**"The civil engineering equivalent of
"Genetic Engineering" is to get a bunch of
concrete and steel, throw it into a river, and
if you can walk across it, call it a bridge."**

Simon Munnery, Comedian

Is Synthetic Biology Dangerous?

- Practically
- Ethically

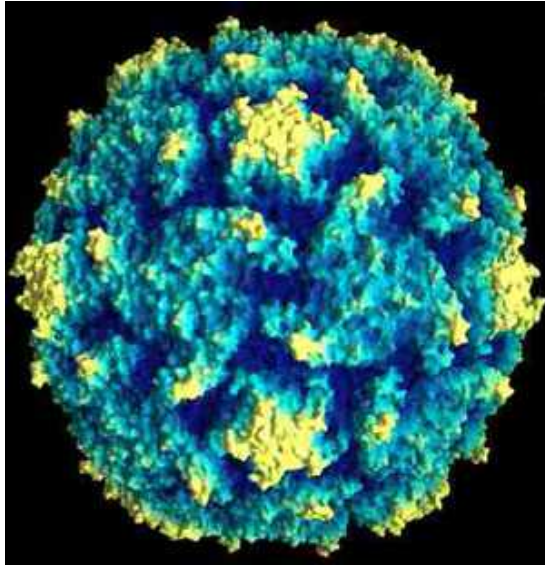


Practical

- 1) Deliberate Misuse (Terrorism)
- 2) Organism escaping lab
- 3) Testing in the open environment



Bio-terrorism

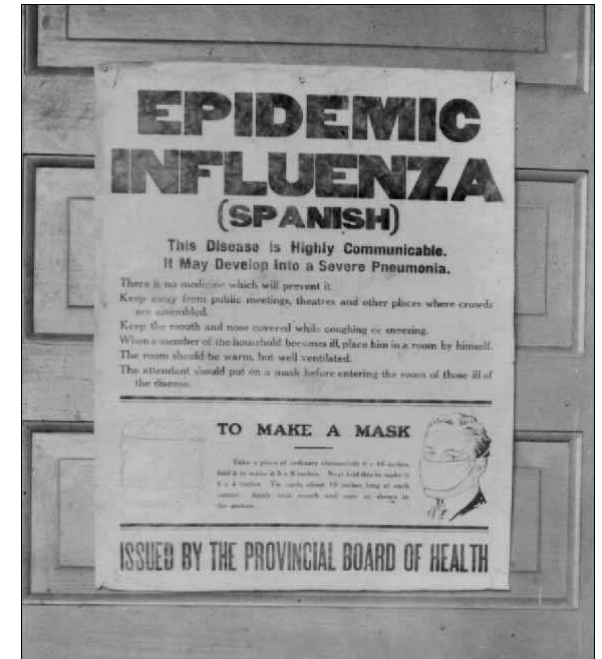


Polio Virus synthesis

Cello et al. 2002

H5N1 'Spanish Flu' synthesis

Tumpey et al. 2005



Not a serious threat though??

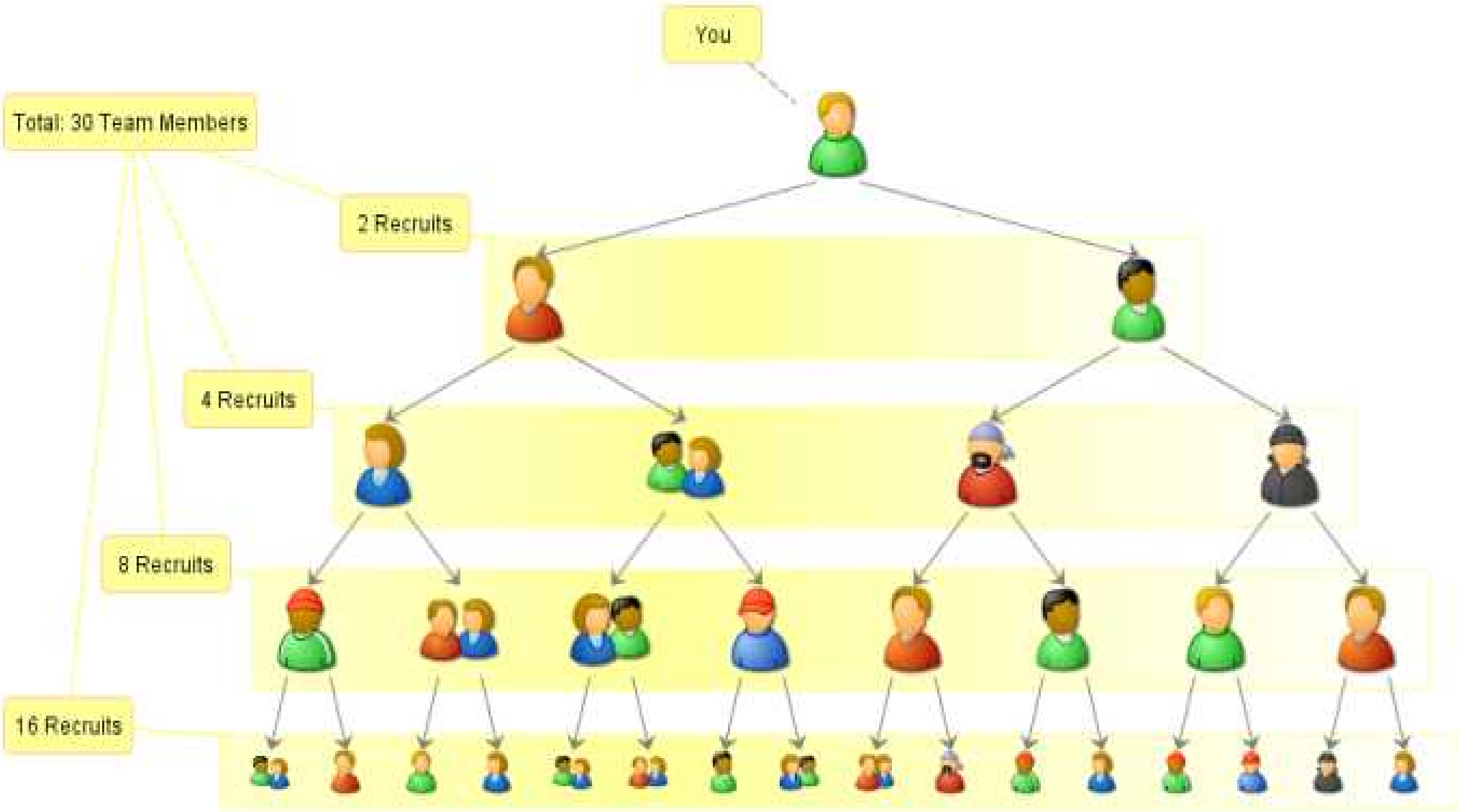
Polio was created from mail order Oligonucleotides..

- Short nucleic acid polymer, <50 bases
- 1. Expertise to assemble these is available worldwide
- 2. Open-Source Nature

But... complex system, not just simple infectious agent

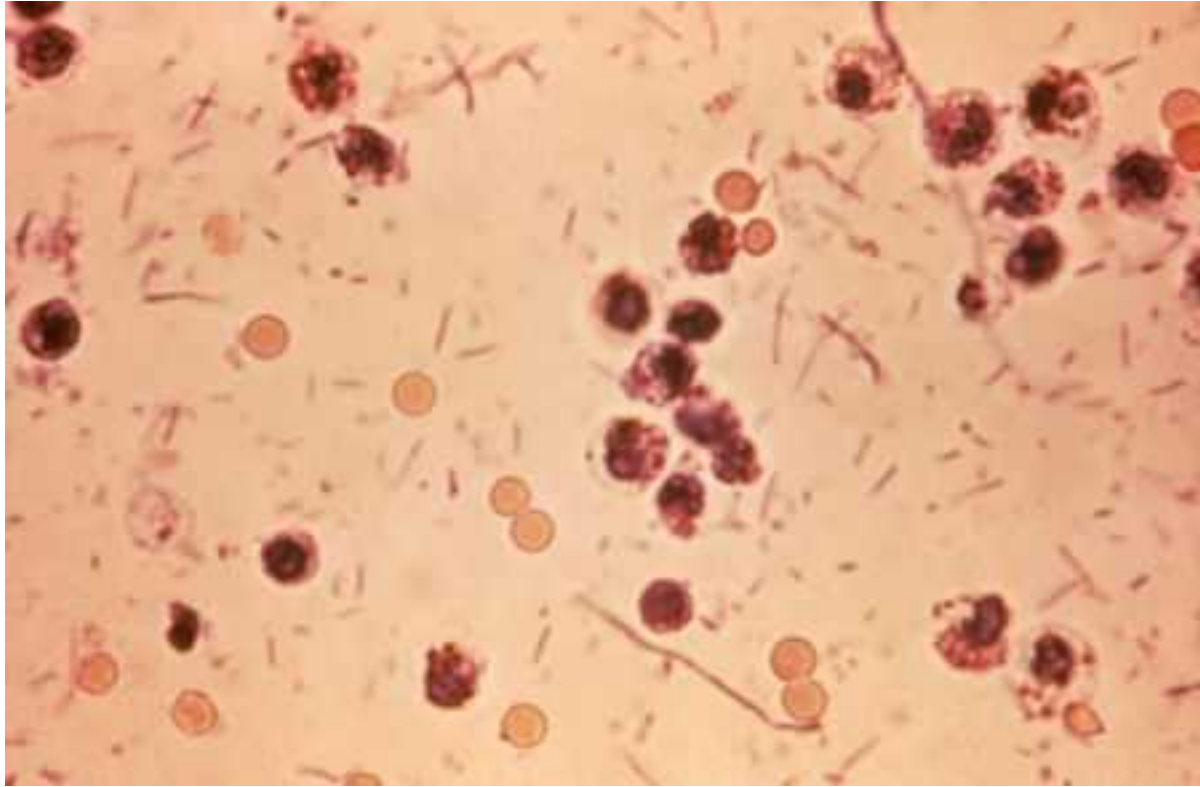
- 1. Supply of pathogen
 - Chemicals required to stabilise and preserve virulence and infectivity during storage
 - Storage and transportation
 - Effective dispersal mechanism

"It not very likely that synthetic biology will lead to an increase in bioterrorism." (Tucker and Zilinkas, 2006)





The 'Biohacker'



Diane Thompson - Shigella attack, 1996

Organism Escaping Lab

At the moment low risk

- Simple circuits placed into well understood bacterial hosts

10 years time...

- Complex synthetic genomes could be used, resulting in 'emergent properties' from interactions between genes.
- until organism actually exposed to humans / other species, we cannot know whether it is pathogenic.

3. Testing in open environment

By definition, some engineered organisms would have to be released to be useful

- disrupt local organisms or fauna through competition or infection - could lead to the extinction of one or more wild species.
- once a synthetic organism has successfully established itself in the environment it might become endemic and thus impossible to eliminate.
- the synthetic organism might damage or disrupt some aspect of the habitat into which it was introduced - degrading local environment.

Categories of Ethical Concern

- Malevolent Risk
- Undermine/Fail to respect Moral Status of living thing
- Accidental Harm
- Enhancement of Human Beings
- "Playing God"



TOM DOUGLAS - Oxford Uehire Centre for Practical Ethics

The meaning of life..

The minimal genome project..

Definition of 'Life'

- Something purely for natural scientists?
 - Are the dimensions of human life purely physiological?
 - Life reducible just to DNA?
-
- Wide ranging implications - Abortion, 'Special' life status





Humans

Rights
Interests
Intrinsic Value

GE organisms??

Animals

eg. 'Human Brain'
Computer?

Machines

no rights/interests
instrumental value only

TIME

FICTION BONUS
"CLONE ON THE RANGE"
BY DOUGLAS COUPLAND



**Will There Ever
Be Another You?**

A SPECIAL REPORT ON CLONING



Scientists...

enjoy a right to absolute freedom of enquiry



But...

Should they engage in all research
that they have a right to engage in?

Playing God

We have long been able to influence genetic makeup..

- Selective Breeding
- Genetic Engineering

BUT these rely on using existing living templates.

Synthetic Biology allows us to create living organisms from non-living, inorganic matter.

Design and Create life, not just tinker with it.

What's the 'Playing God Concern'

Religious Concern - humans taking on 'God' role of designing and creating organisms.

Secular Concern - humans tampering with large organism systems they don't fully understand.



Creation of a dual use dilemma

Risk of harmful use becomes so high that pursuit of knowledge no longer is desirable.

- Nuclear Fission Experiments

Summary

- Physical Concerns
- Ethical Concerns

Never too early to consider these, they're unlikely to be easy to solve.

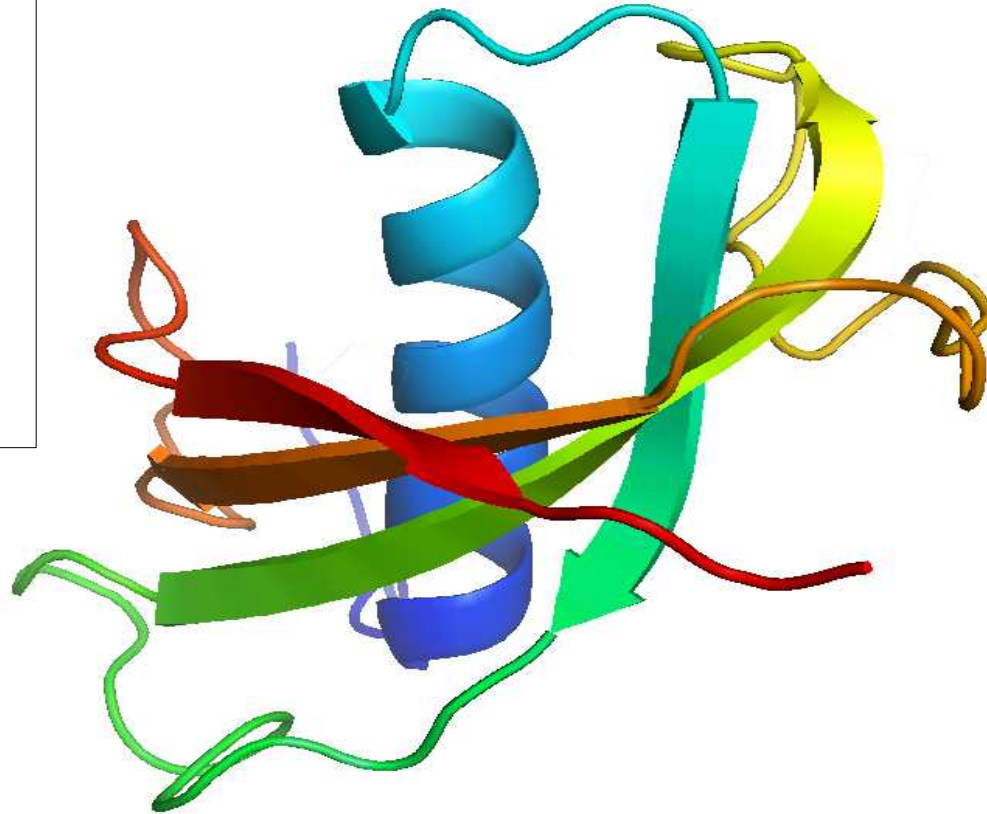
"Engineered bacteria attack lethal infection with its own weapons."

Nature 2011

Great promise, big questions still to be solved.

So... what are we doing?

Designing a 'kill switch' using Protogrin-1



Specifications



Design

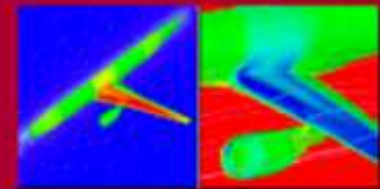


Testing/Validation



**Standard
Engineering
Practice**

Modelling



Implementation

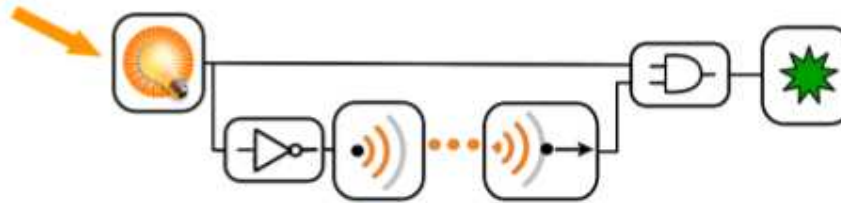


Standard, Interchangeable Parts

Applications

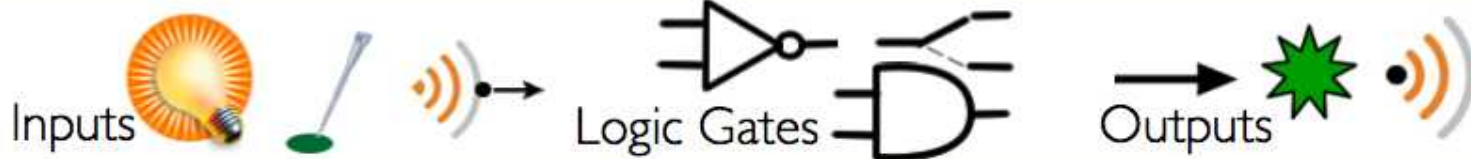


Systems



IF dark
signal-out
ELSEIF (signal-in AND light-in)
MAKE Pigment

Devices



Parts

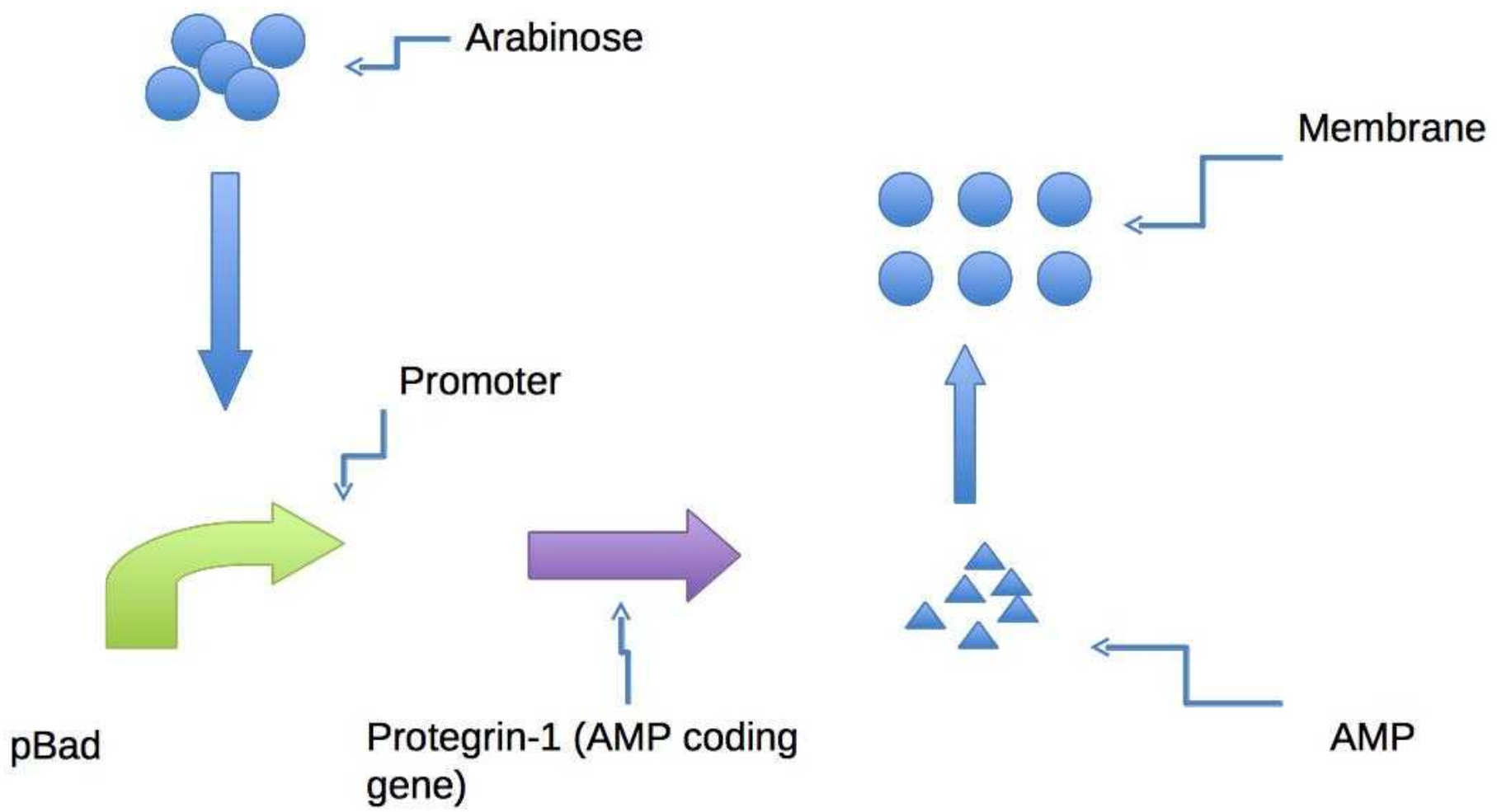


DNA



```
ATGCTTACCGGTACGTTTACGACTACGTAGCTAGCAT  
GCTTACCGGTACGTTTACGACTACGTAGCTAGCATG  
CTTACCGGTACGTTTACGACTACGTAGCTAGCATGCT  
TACT...
```

Switch Theory



What are AMPs?

- Potent, broad-spectrum antibiotics
- Amphiphatic design¹
 - Distinct hydrophobic / cationic regions
- Protogrin-1 is a rapidly bactericidal in vitro²
 - E. Coli is susceptible

¹Zasloff – *Nature Review* 2002, ²Lam et al *J. Phys. Chem. B* 2006, 110, 21282-21286

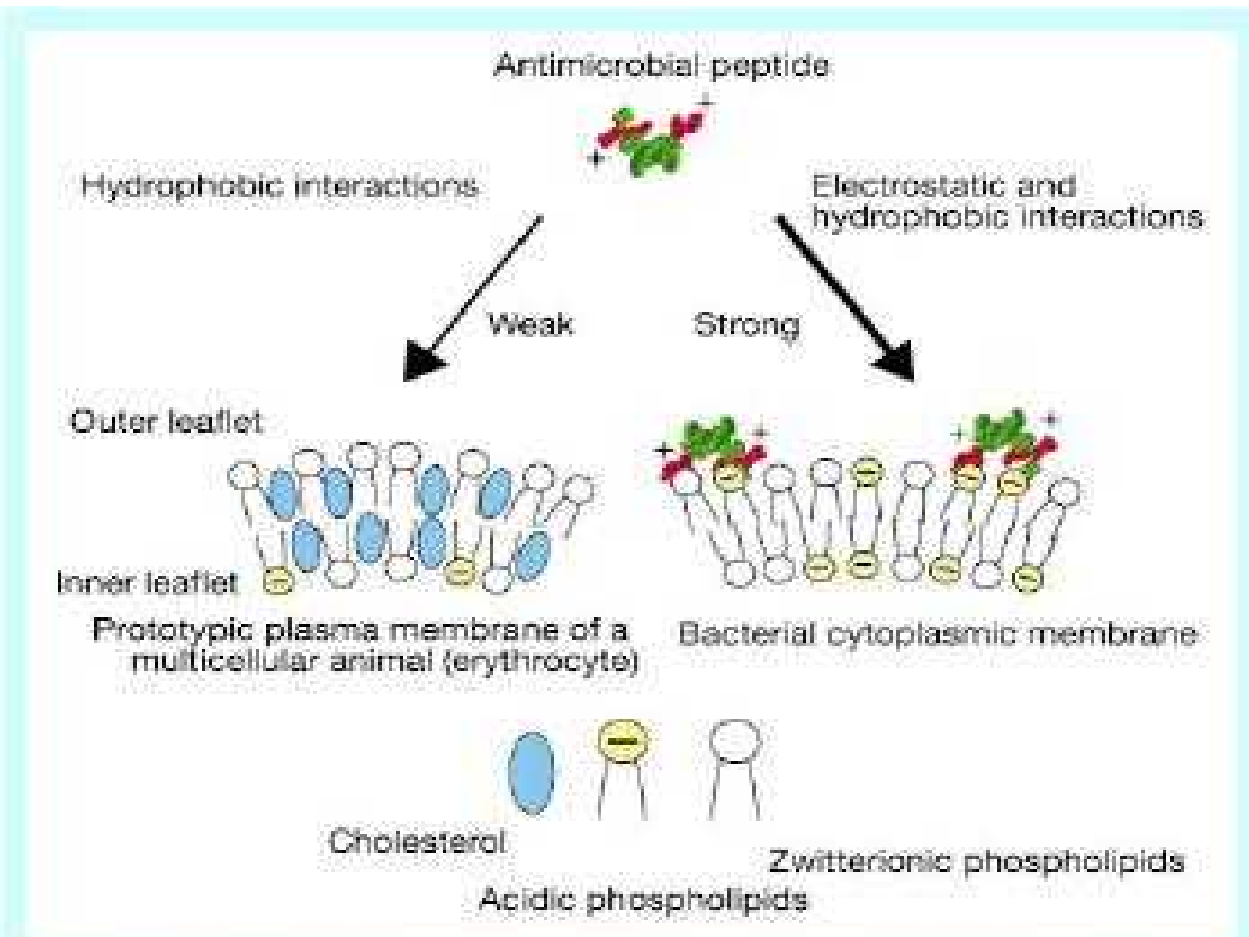
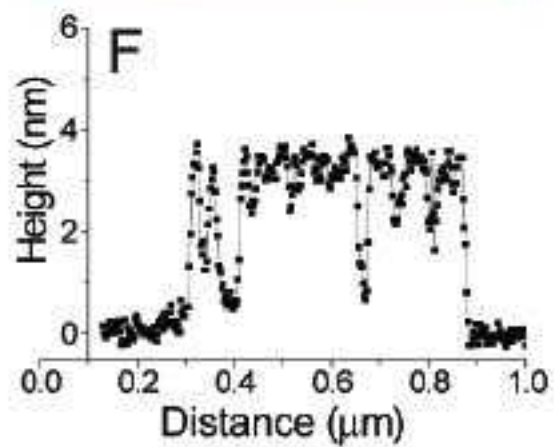
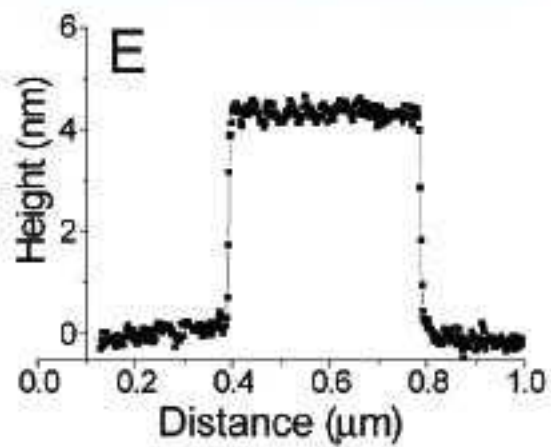
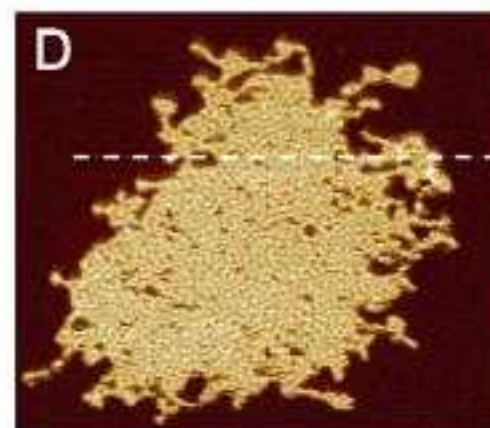
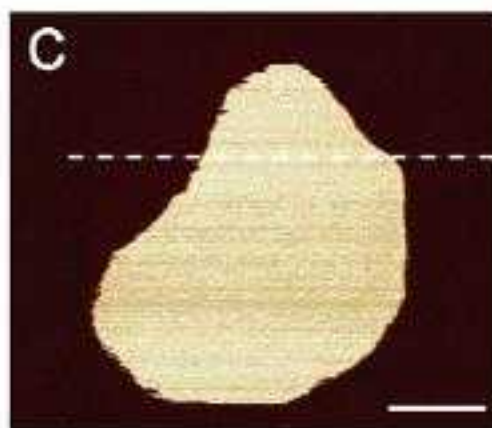
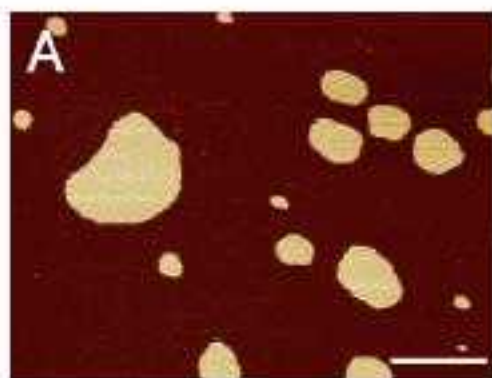


Figure 2 The membrane target of antimicrobial peptides of multicellular organisms and the basis of specificity. (Modified from ref. 21.)



Applications

Environmental safety...

- Using either +ve or -ve promoters
- Or make cell kill itself after certain number of cycles

Applications in Drug Therapy

- very specific delivery
- Drug only produced in certain conditions
- exportation from cell enabled

- conjugation (pass on ability to self destruct selectively)



Many Thanks