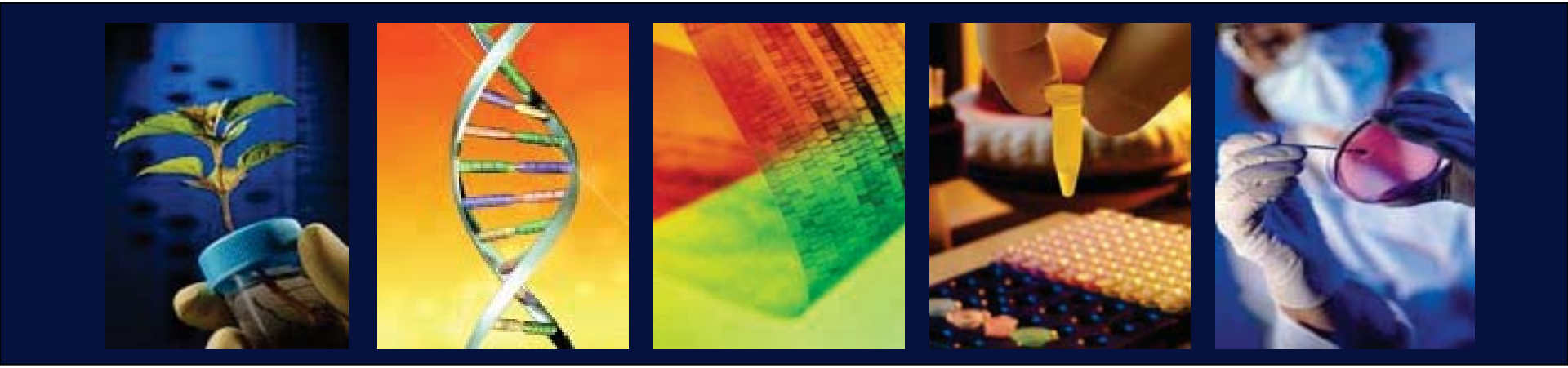
Synthetic Biology and Dual Use



Marcus Schmidt, Ph.D.

Co-Founder

Organization for International Dialogue and Conflict Management

Synthetic Biology and Dual Use

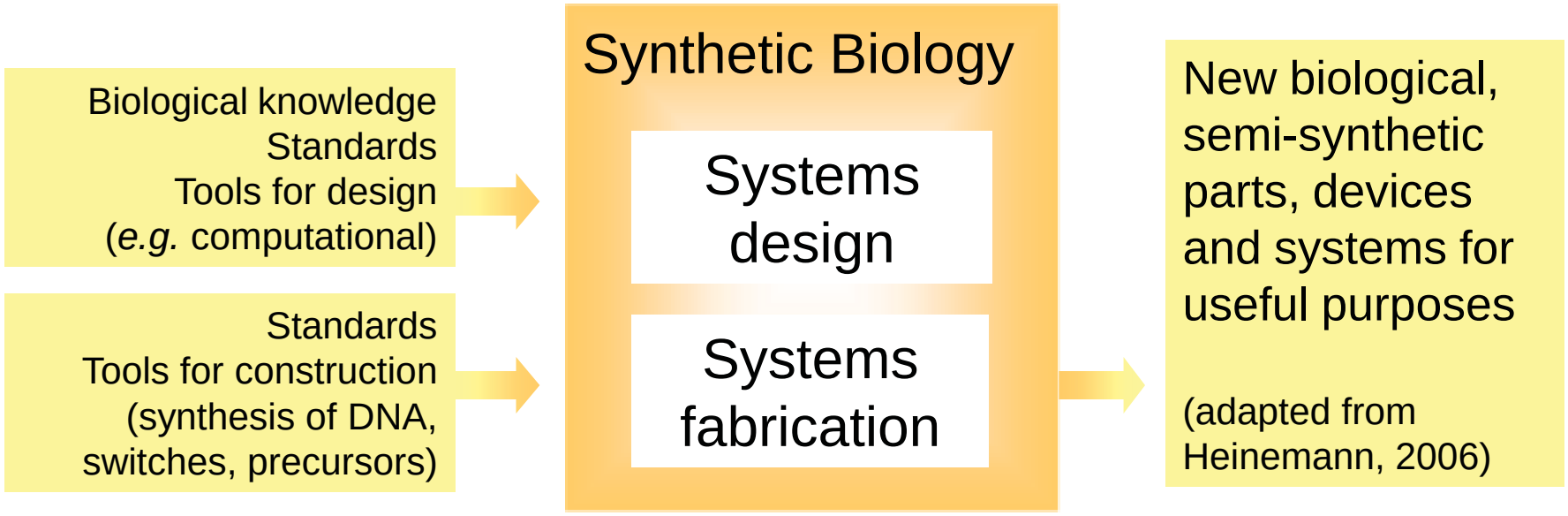
Promises and risks

Oscar Kuipers
Molecular Genetics
Center for Synthetic Biology
Instutute of Molecular Biology
and Biotechnology
University of Groningen
o.p.kuipers@rug.nl

Markus Schmidt
Biosafety Working Group
Organisation for International Dialogue and
Conflict Management
Vienna, Austria
Markus.schmidt@idialog.eu

What is synthetic biology ?

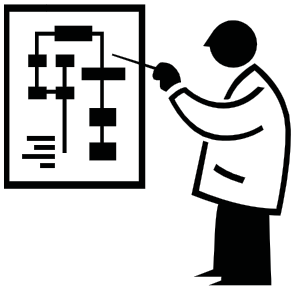
- Design and construction of new biological parts, devices, and systems
- Re-design of existing, natural biological systems for useful purposes.
- Top-down ('subtraction') *and* Bottom-up ('addition') approach for constructing new devices and materials
- Orthogonal and/or xenobiological systems



Synthetic Biology

Classical Engineering

- Idea



- Design

GENEART
THE GENE OF YOUR CHOICE

- Construction

DNA molecules with any desired sequence can be ordered overnight by labworkers
In near future cells expressing desired sequences can be ordered

Synthetic biology: *in vivo* versus *in vitro*

In vivo:
- top-down
- cell-based engineering (chassis)
- driven by developments in systems biology, recombinant-DNA, synthesis of genes, ..

In vitro:
- bottom up
- bio-inspired materials, devices
- driven by developments in synthetic and systems chemistry

Engineering principles and standardization are relevant for both *in vivo* and *in vitro* approaches

Examples of useful applications:

- New drugs
- Drugs produced in novel more efficient way
- Novel drug delivery systems (Red Biotech)
- Cell factories for biofuel
- Cell factories for platform chemicals (White Biotech)
- Bacteria for bioremediation (Green Biotech)
- Designer bacteria
- Fast evolution methods
- Electronic devices; biosensors
- Nanomotors
- Etc.

Safety and security risks posed by synthetic biology

- Pathogen engineering or design (e.g. novel genomes, MDR)
- Virus engineering or design and construction
- Toxin production, novel molecules
- Etc.

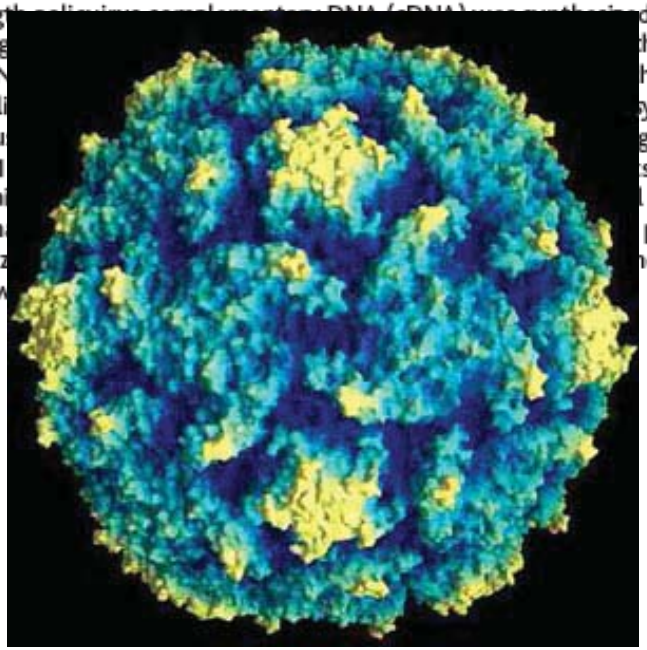
Ways of release:
- unintented release into environment (e.g. lab-accident)
- intended benign use (e.g. gene therapy, crop protection)
- bioterrorism / biowarfare (pathogens, viruses, toxins)

Synthetic virus

Chemical Synthesis of Poliovirus cDNA: Generation of Infectious Virus in the Absence of Natural Template

Jeronimo Cello, Aniko V. Paul, Eckard Wimmer*

Full-leng… by assem-
bling olig… thetic polio-
virus cDN… h translated
and repli… synthesis of
infectiou… g antibodies
and CD1… s in *CD155*
transgeni… l and patho-
genic ch… possible to
synthesiz… eans solely
by follow…



Science 2002

Characterization of the Reconstructed 1918 Spanish Influenza Pandemic Virus

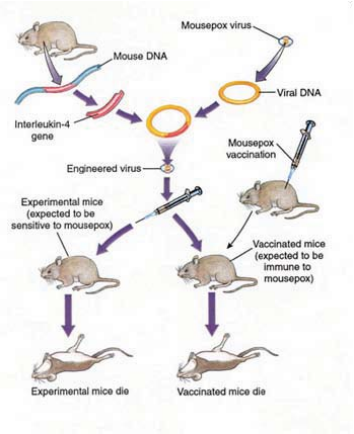
Terrence M. Tumpey,[1]* Christopher F. Basler,[2]
Patricia V. Aguilar,[2] Hui Zeng,[1] Alicia Solórzano,[2]
David E. Swayne,[4] Nancy J. Cox,[1] Jacqueline M. Katz,[1]
Jeffery K. Taubenberger,[3] Peter Palese,[2] Adolfo García-Sastre[2]

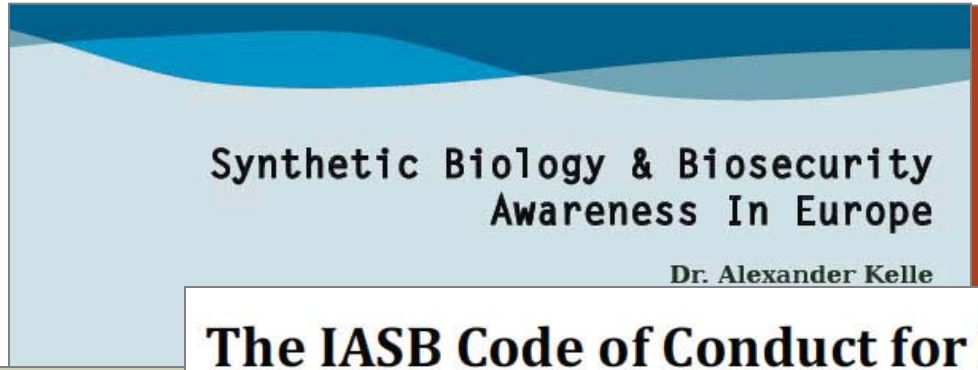
The pandemic influenza virus of 1918-1919 killed an estimated 20 to 50

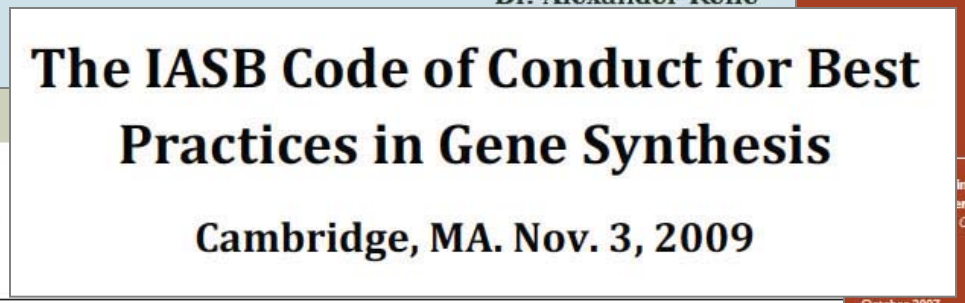
Science 2005

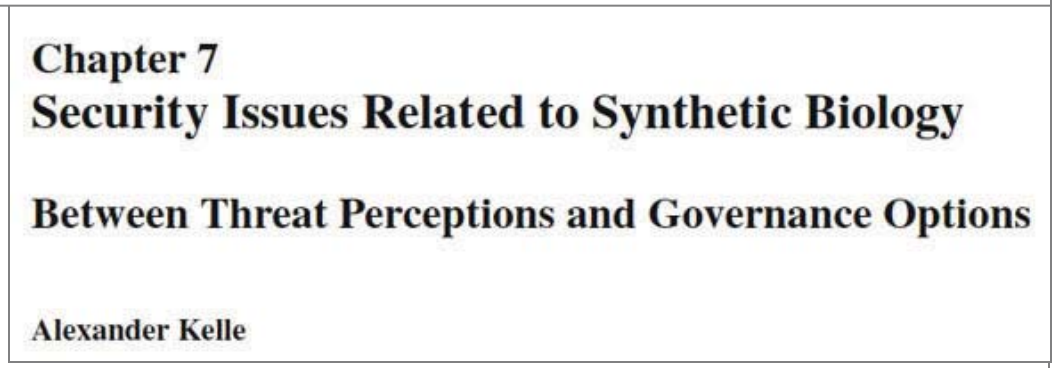
Novel (super)viruses

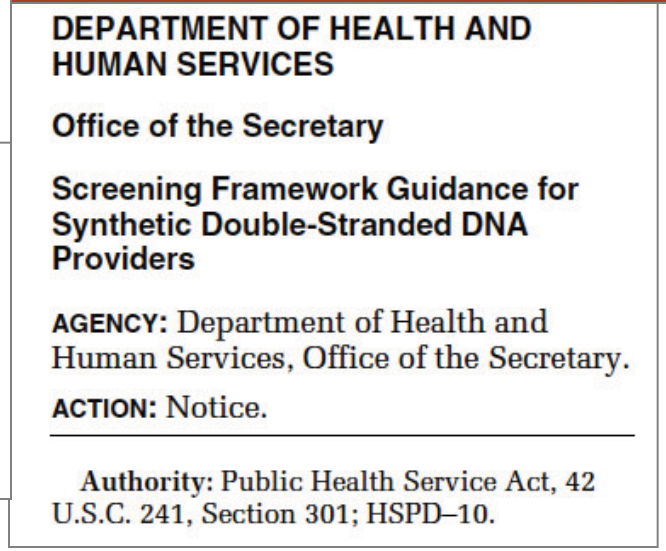
- Mousepox with Interleukin 4
  - Jackson et al. 2001. J. of Virology
  - US military
    - Rabbitpox with Interleukin 4
    - Cowpox with Interleukin 4
- Bat SARS-like coronavirus „humanized“
  - Becker et al. 2008. PNAS
- Reconstitution of infectious, human „fossil“ endogenous retrovirus
  - Wimmer et al. 2009. Nat Biotech











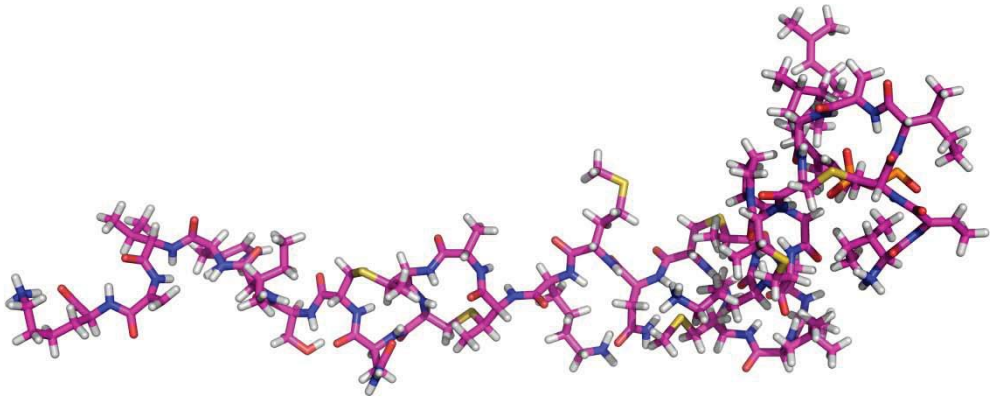
- Wellcome Trust project "Building a sustainable capacity in dual-use bioethics"

www.dual-usebioethics.net

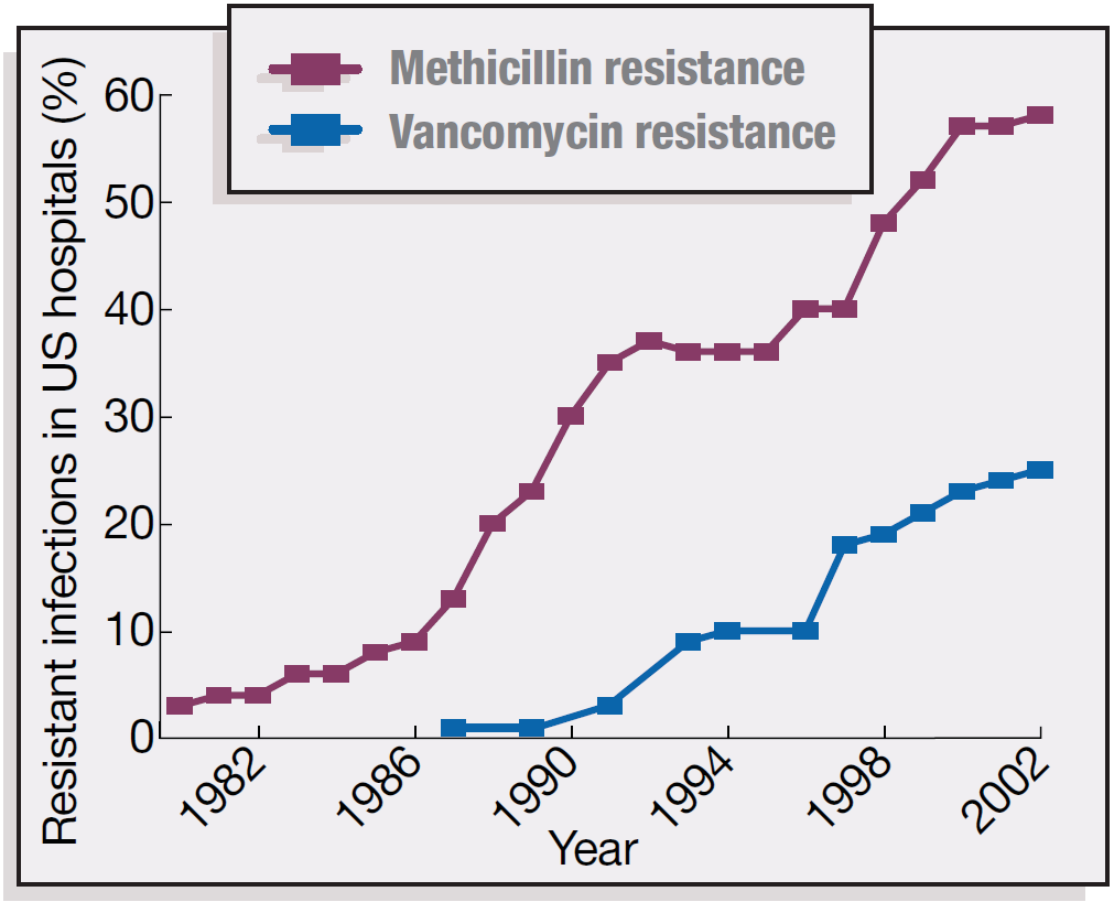
SynMod (ESF Synthetic Biology project)

Synthetic biology to obtain novel antibiotics and optimized production systems

Sven Panke (ETH, Zurich/Basel)
Oscar Kuipers (University of Groningen)
Fritz Gotz (Univ. Tuebingen)
Markus Schmidt (IDC, Vienna)
Ralf Wagner (GENEART, Germany)
Nicolas Szita (Uni. College London)

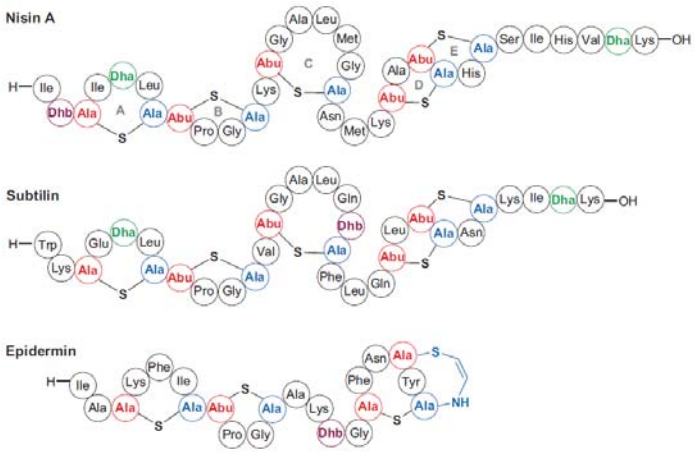


Need for novel antibiotics

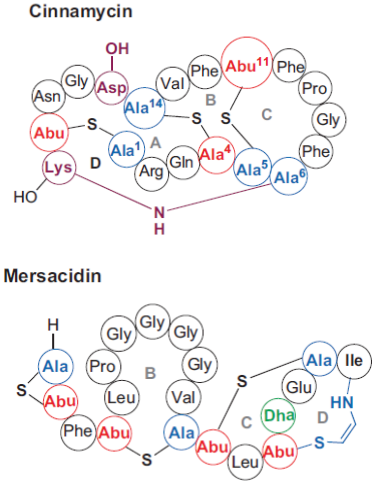


Source: CDC

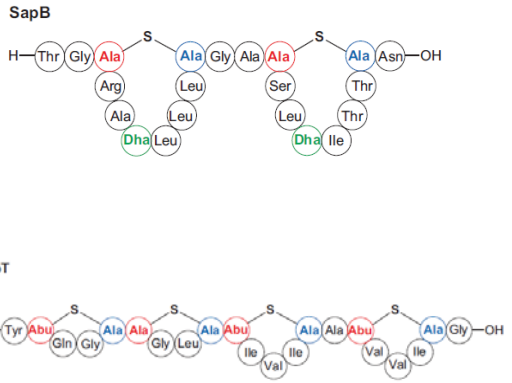
Class I



Class II



Class III



Willey et al. 2007 Annu Rev. Microbiol.

Potent antimicrobials agains Gram positive bacteria
Low resistance development
High stability
Non-toxic for eukaryotes
Enormous combinatorial potential
Ongoing clinical trials

Mode of action

- Lipid II
- Pore forming

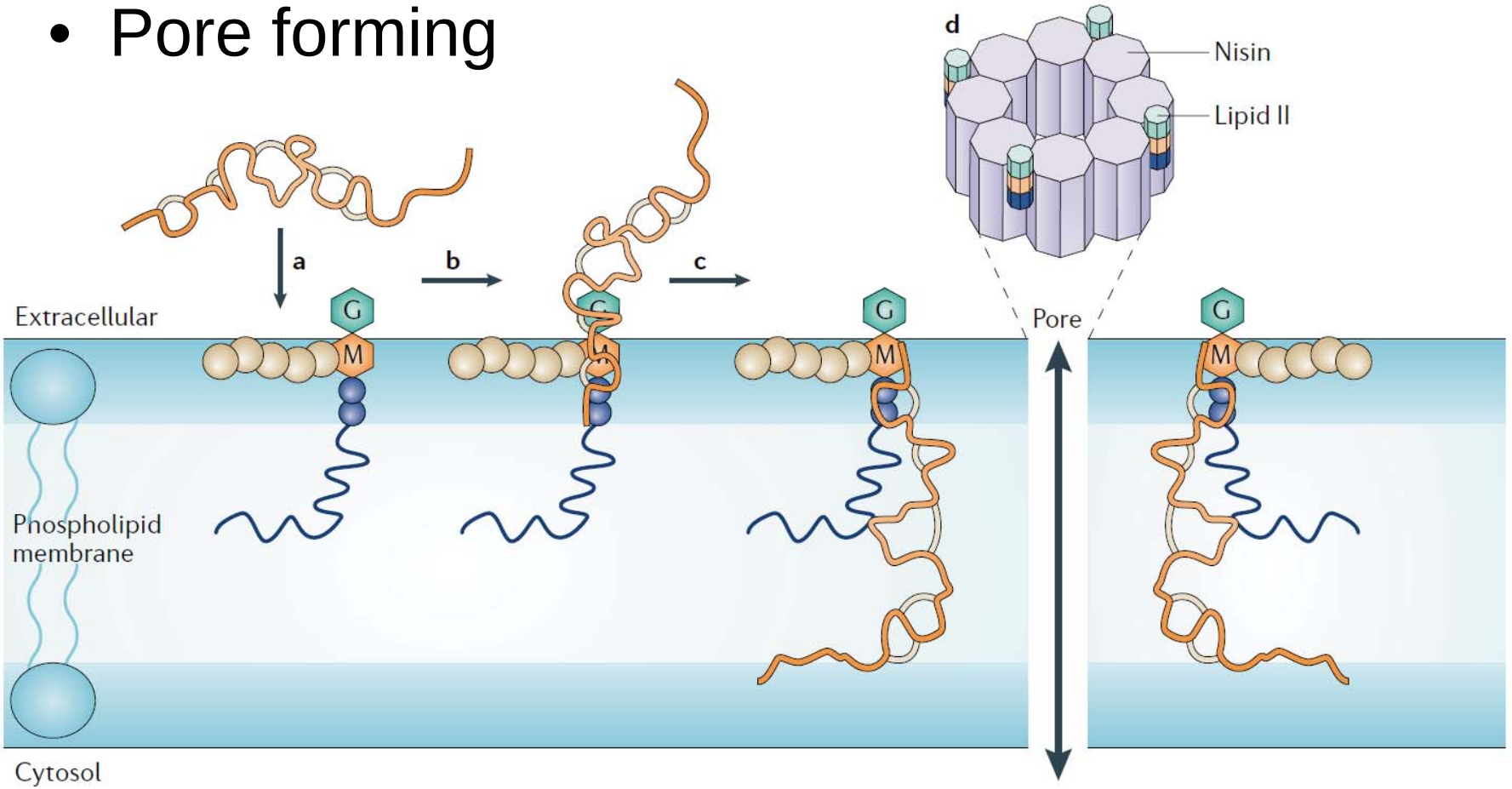


Image from Breukink et al 2004

Synthetic biology to obtain novel antibiotics and optimized production systems

Goals:

- Design, develop and produce novel antimicrobial compounds based on lantibiotic elements

- Develop and use novel HT screening methods

- Screen for desired characteristics (activity against Multidrug-resistant bacteria; low level of resistance development; stable, soluble, good pharmacokinetics)

- Develop highly efficient production host (*Staphylococcus carnosus*)

- Production of >3 highly potent antimicrobials for further (clinical) trials and structural characterization

- Address risks, ethical and societal issues

Criteria for medical use

- Pharmacokinetics
- Solubility and Stability (chemical; proteolysis)
- Toxicity, allergenicity
- Efficacy
- Safety

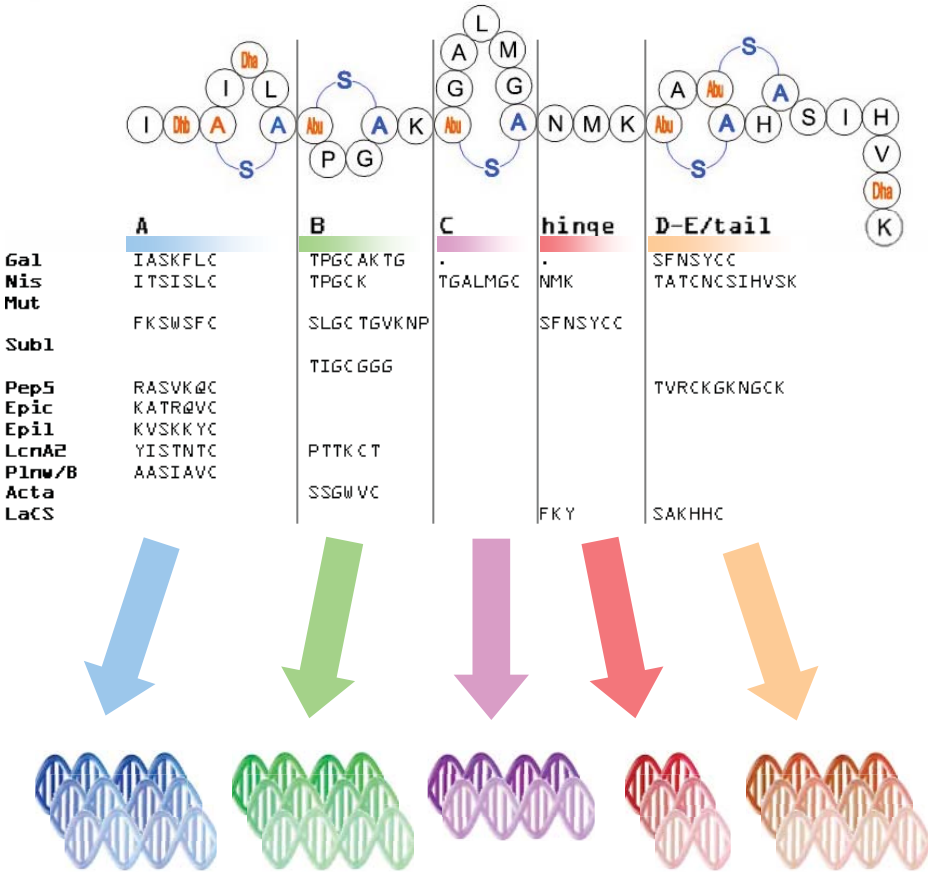
Benefits

- Novel antibiotics
- Less resistance, less MDR

Concerns and risks

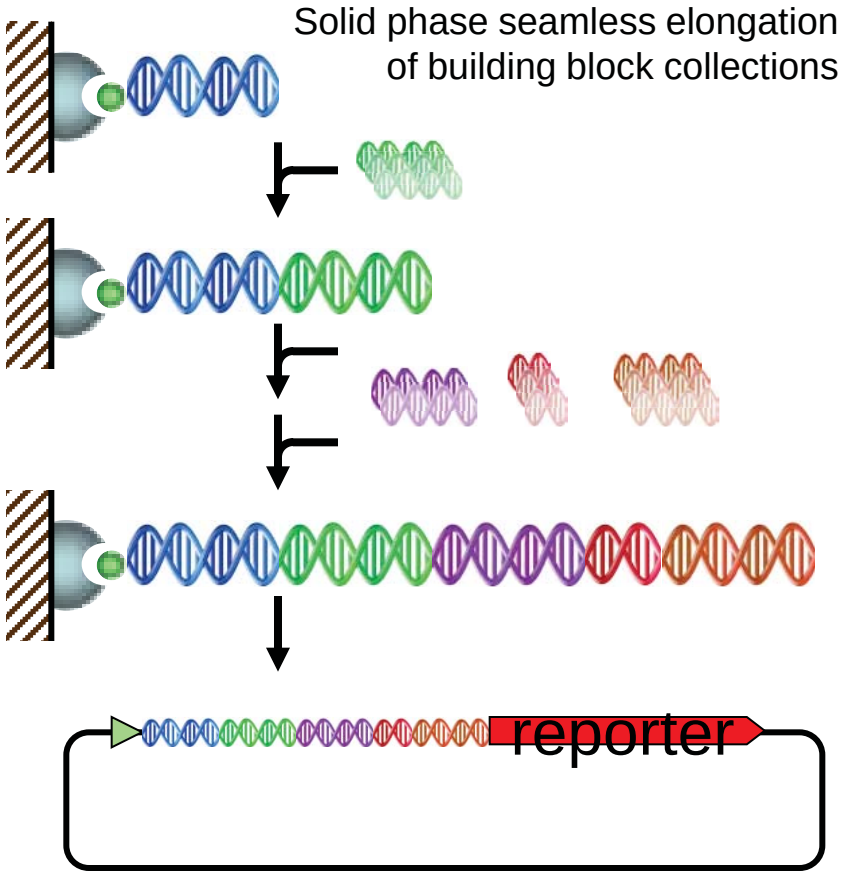
- Unwanted activity against eukaryotes (toxins)
- Too stable

Lantibiotic precursor libraries



Synthetic collections of building block modules with and without random non-wt substitutions

Ralf Wagner



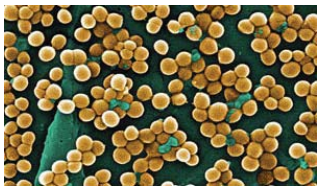
Solid phase seamless elongation of building block collections

Ligation into reporter vector and screening for constructs with open reading frames

Biosafety, Ethics, and Public Perception

Dr Markus Schmidt, Organisation for International Dialogue and Conflict Management, Vienna, Austria

Organisation for International Dialogue and Conflict Management



- Analysing safety issues in SYNMOD

- Focusing on the ethical dimension

- Collaboration with other ELSI intiatives

- Communication and Dissemination

- Public panel debates / focusgroups on novel antibiotics

- Short documentary film on synthetic lantibiotics

- Preparation of information material for the press/public

Awareness raising

- Increase awareness among life scientists, engineers, computer scientists about biosecurity, safety and ethical aspects of their work.

- Should be part of educational program

- Code of conduct / ethics

Acknowledgements:
Bert Poolman
Sven Panke
iGEM