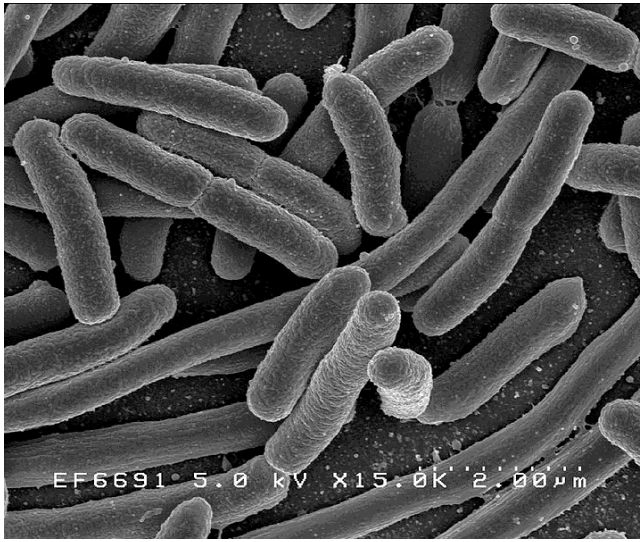
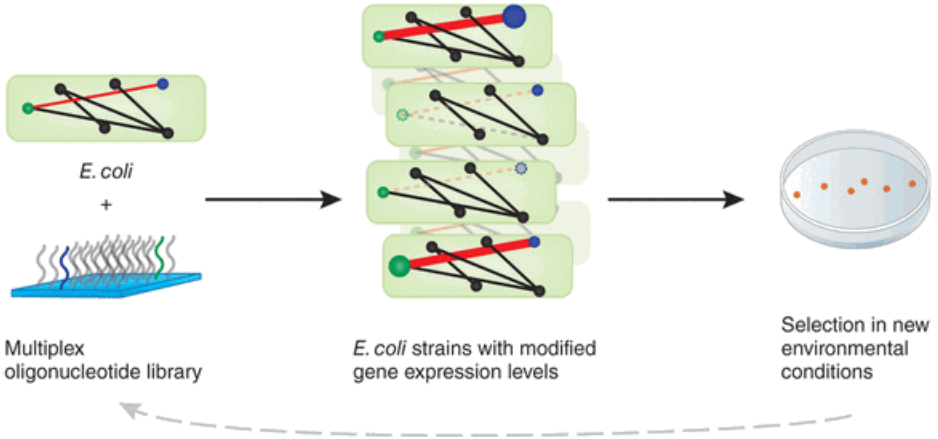
Tool Development for Transformational Biotechnology Advances

Breakout Session:
Genetic Tools

Genetic Tools

Model systems have powerful, well established tools.





Nature Biotechnology ***28, 812–813 (2010)***

Whole genome modification can be readily performed in E. coli using MAGE (Multiplex automated genome engineering), TRMR (trackable multiplex recombineering), and other techniques.

Goals

The focus of this session is to:

1) Discuss briefly the most powerful genetic tools that have been developed in model systems for transformation and manipulating their genomes.

2) Clarify to ARPA-E what are the most valuable genetic tools from model systems for plant manipulations, and what challenges are involved in translating them for use in plants.

3) Identify multiple tools that could be utilized together to dramatically increase the ability of researchers to manipulate plant's genome or control its metabolism.

Please try to consider…

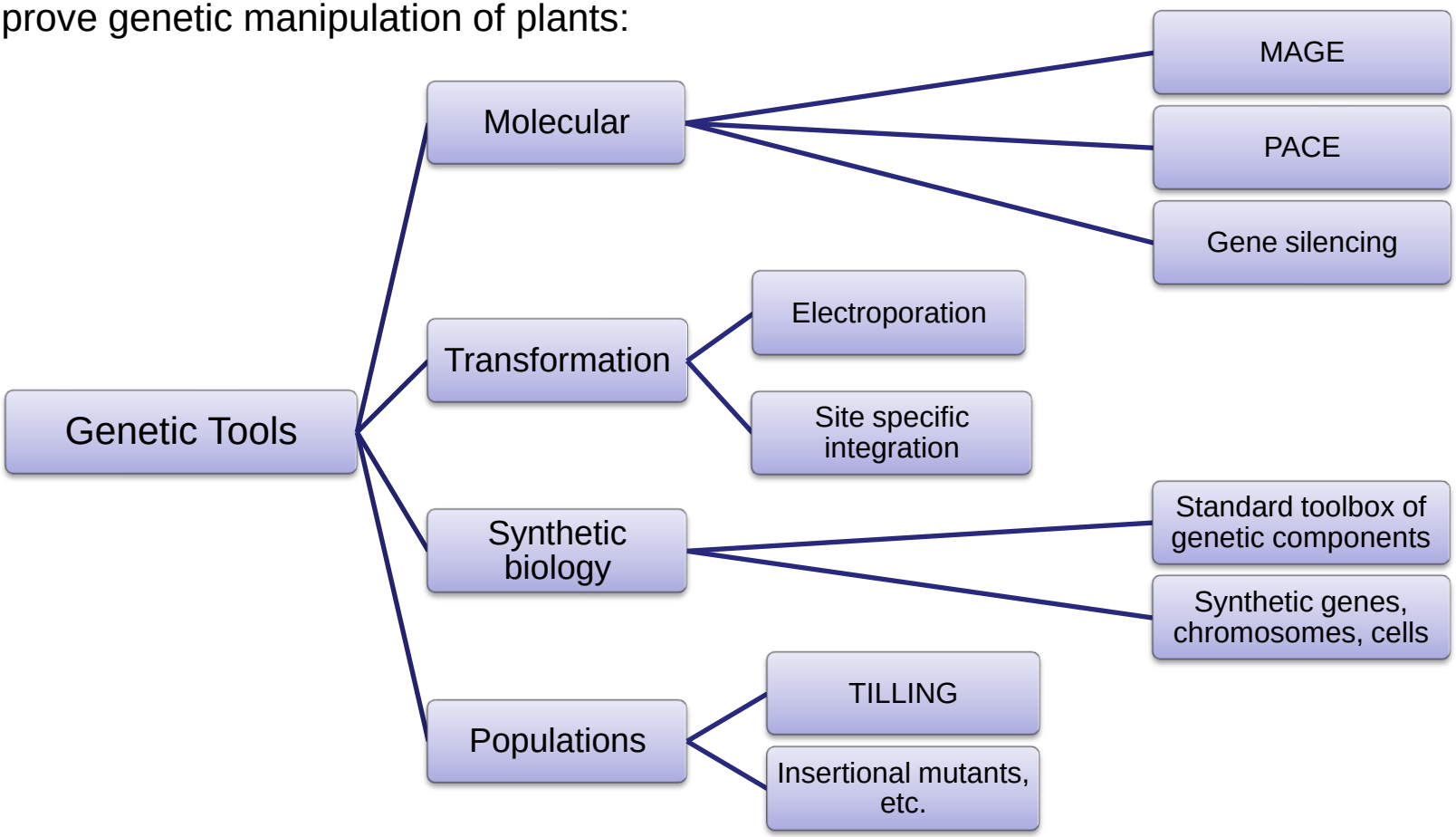
- **What are the quantitative (theoretical) limits of technologies?**
- **How can we reduce these ideas to practice?**
  - What is the current and target TRL (technology readiness level)?
  - What tools/techniques are needed to move the concept up the TRL scale and what recent breakthroughs have been made to support the expectation this is possible?
- **Is a technology breakthrough in a 3-5 year timeframe realistic?**
  - What are the aspects of the technology that constrain development?
  - Are there advances in related fields that could shorten the timeline?
- **Creative IP strategies to encourage wide adoption of ARPA-E funded technologies.**

Please try to consider…

ARPA-E is not looking to fund basic research into better understanding the processes behind these techniques to improve manipulation of plant genomes or phenotypes.

Genetic Tools in Model Systems

Potentially promising tools from model systems to improve genetic manipulation of plants:



Questions to Address on Genetic Tools

1) Identify some of the most powerful tools available to model organisms (E. coli, S. cerevisiae, Arabidopsis) and select the three that would be most desirable to have in crop plants. How likely are these tools able to be adapted for plants?

Questions to Address on Genetic Tools

2) What is needed to produce a completely synthetic plant chromosome (> 250 kb) routinely and ensure that it stably persists in plant cells? How close to deployment is this capability, both for specific plant species and for general plants? Would it be a significant advantage if 1 Mb chromosomes could be produced?

Questions to Address on Genetic Tools

3) What would be necessary to produce a synthetic cell/virus/?? that could persist symbiotically in a plant? How many of these components are well characterized now, or demonstrated in a plant? What sorts of applications would this capability be preferable over stable plant transformation.

Questions to Address on Genetic Tools

4) What are the key tools necessary to achieve predictable incorporation, expression, and function of a foreign gene/protein in a plant? Discuss both in terms of specific genetic components and modifications to the plant host.

Questions to Address on Genetic Tools

5) What biological factors in plant cells prevent homologous recombination from occurring? Can an efficient system be developed so that genes or regions of chromosomes can be deleted or replaced?

Questions to Address on Genetic Tools

6) Are there approaches that would allow easy identification of transformed cells at the single cell level or assess gene expression?

Questions to Address on Genetic Tools

7) How could you make multiple modifications to specific genes throughout the plant genome? Are there non-transformation methods to control gene expression?

Questions to Address on Genetic Tools

8) What capabilities will cheap, large scale sequencing allow? Would being able to readily generate large quantities of sequence data allow novel high throughput methods of genotyping?