New challenges:

Synthetic genome technologies

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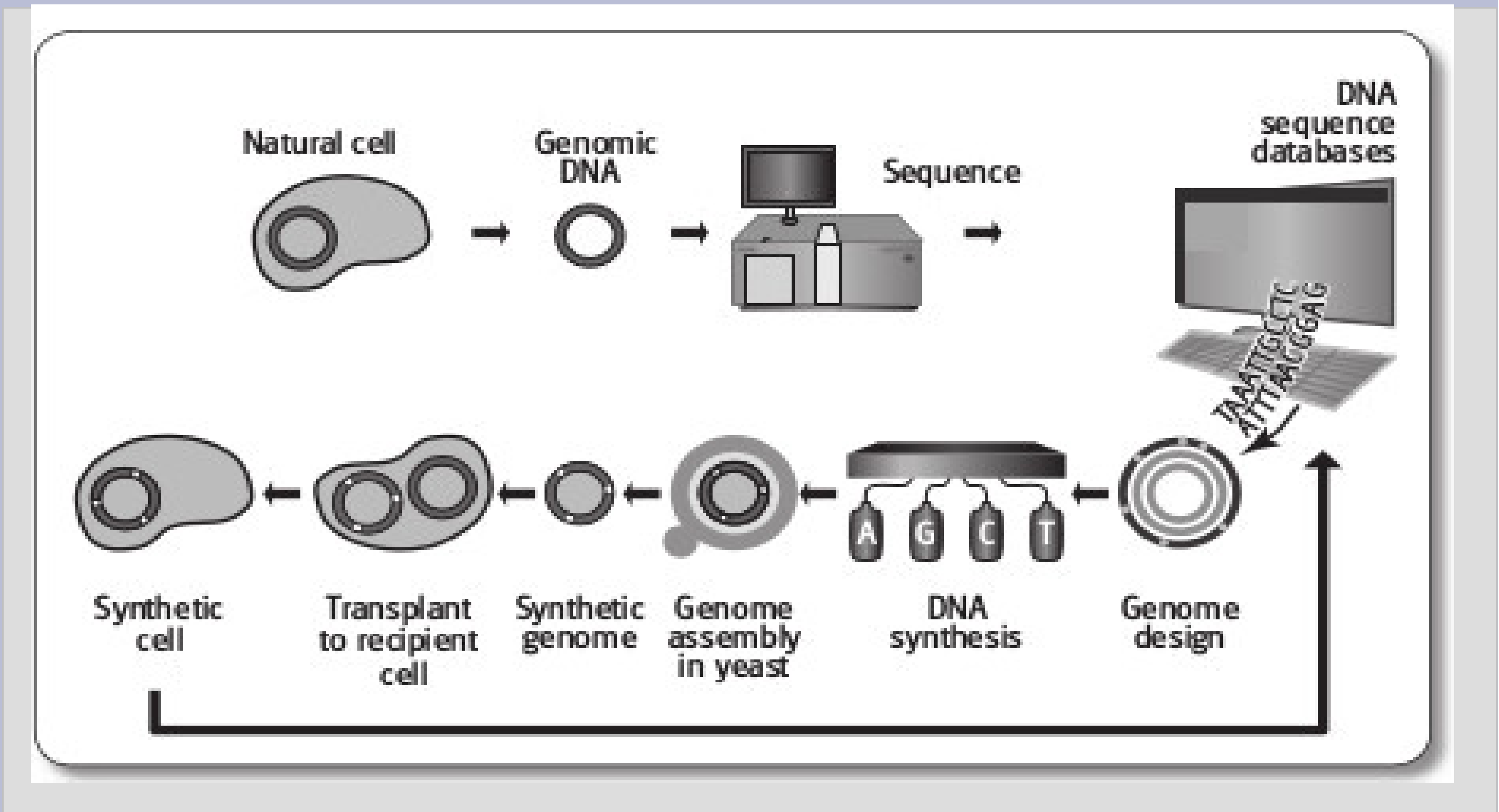
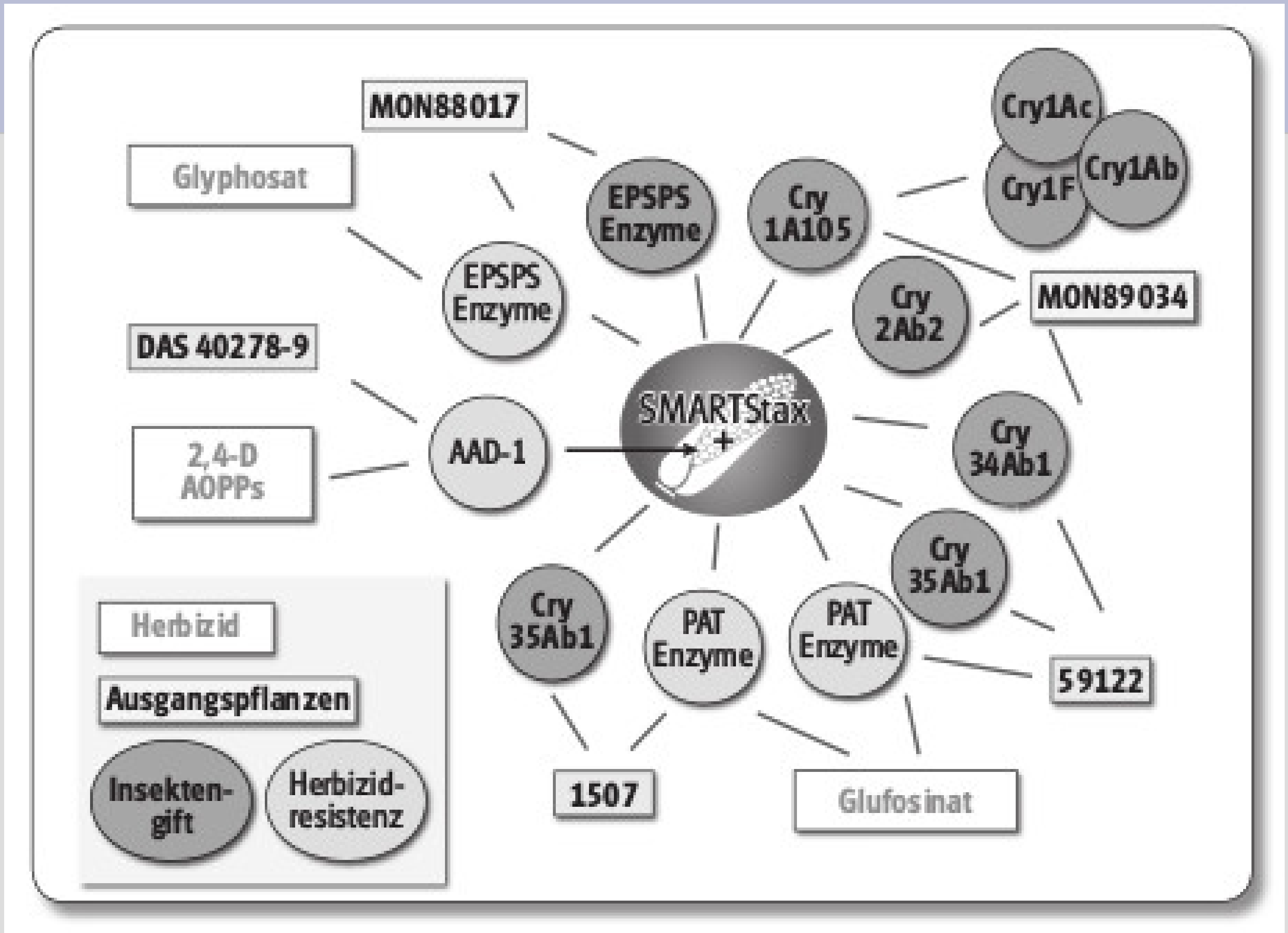
The future is now: Large scale DNA synthesis



Source: US PRESIDENTIAL COMMISSION FOR THE STUDY OF BIOETHICAL ISSUES

Synthetic DNA is used to produce genetically engineered plants



This variation of „Smartstax Maize“ sold by companies Monsanto / Dow Agrosciences produces 6 insecticidal toxins and is resistant to 4 groups of herbicides (Source: Handbuch Agrogentechnik, Oekom Verlag).

Insects with synthetic DNA to be released soon in the EU?

the olive oil times

oliveoiltimes.com
http://www.oliveoiltimes.com/olive-oil-making-and-milling/spain-considers-trial-release-of-genetically-modified-olive-flies/35987

Spain Considers Trial Release of Genetically-Modified Olive Flies

By Julie Butler
Olive Oil Times Contributor | Reporting from Barcelona

Oxitec olive fly:

DNA, synthetisized from sponge, bacteria, virus and other insects. Male offsprings are supposed to survive

Company Intrexon (US): Genetically engineered fish, trees, apples and patented mammals with synthetic DNA

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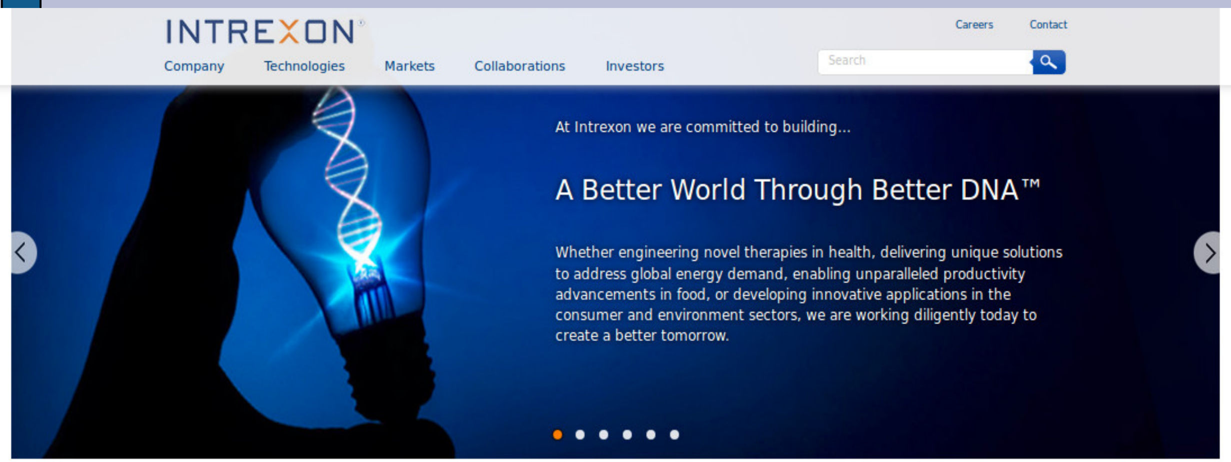


Intrexon Corporation is [....] focused on the industrial engineering of synthetic biology [....] across multiple industry sectors, including: human therapeutics, protein production, industrial products, agricultural biotechnology, and animal science. The company's advanced bioindustrial engineering platform enables [....] unprecedented control over the function and output of living cells.

http://www.dna.com/

Some methods used in Synthetic Genome Technologies / genome editing

> O**ligonucleotids**

> Multiplex Automated Genome Engineering, **MAGE**

> **Nucleases** to 'knock out' and 'knock in' such as **CRISPR-Cas**

> interfering with **epigenetics**

> insertion of whole artificial **chromosomes** / **genomes**

> **Mutagenic chain reaction** / Gene Driver

Synthetic Genome Technologies: Insertion of Oligonucloetids

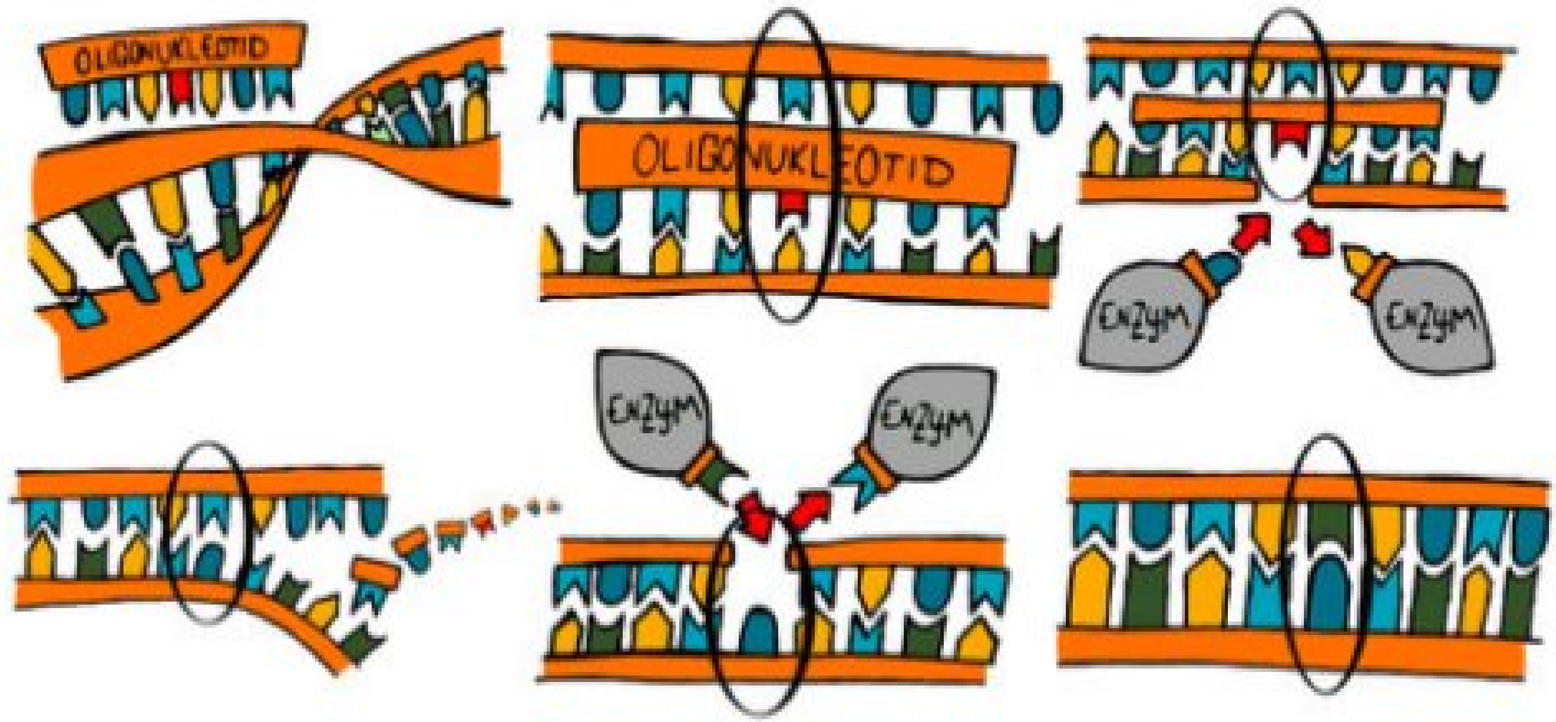


Figure 17: Model of the mode of action of oligonucleotides: 1. The oligonucleotid is inserted into cells 2. The oligonucleotid is fixed at the position with high similarity in the genome. 3. The difference between the plant´s genome and the oligonucleotide induces enzyme repair mechanisms in the cells, one strand of DNA is changed at the relevant position. 4. The oligonucleotid is removed from the plant´s DNA (mechanisms not known). 5. The difference between the two strands of DNA are repaired by the plant's own repair mechanism. 6. The specific alteration within the genome is achieved. Source: http://www.keine-gentechnik.de/dossiers/neue_technologien.html

Synthetic Genome Technologies: MAGE

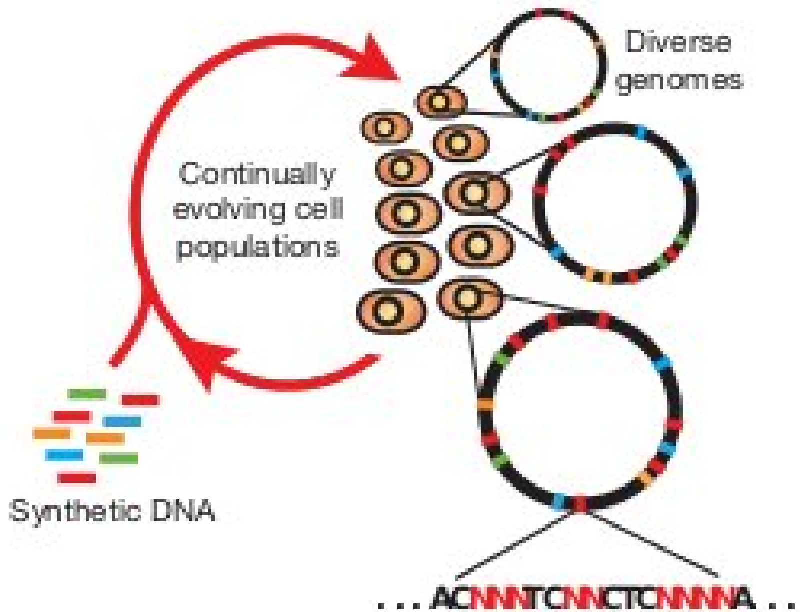


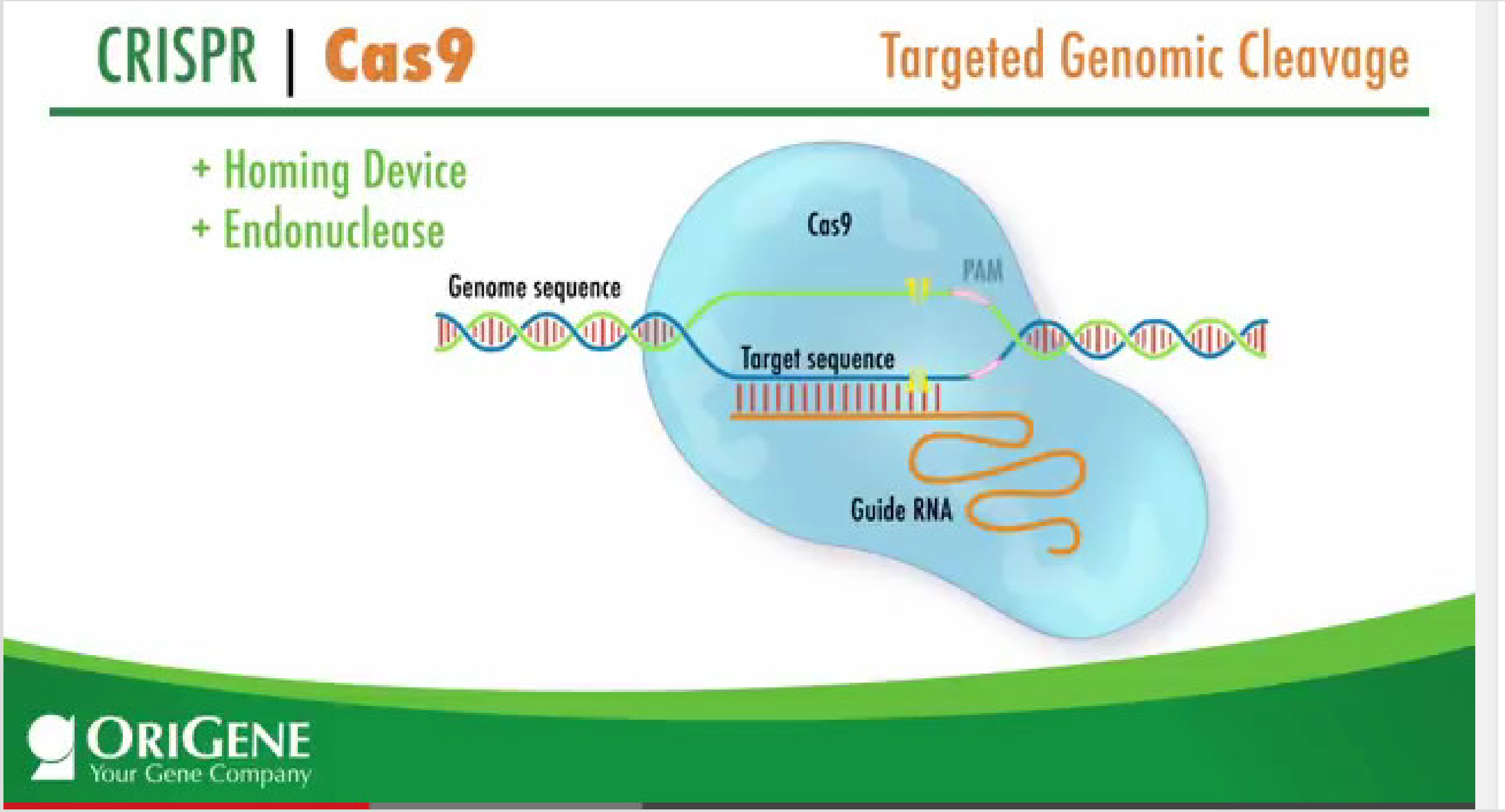
Figure 1 | Multiplex automated genome engineering enables the rapid and continuous generation of sequence diversity at many targeted chromosomal locations across a large population of cells through the repeated introduction of synthetic DNA. Each cell contains a different set of mutations, producing a heterogeneous population of rich diversity (denoted by distinct chromosomes in different cells). Degenerate oligo pools that target specific genomic positions enable the generation of a diverse set of sequences at each chromosomal location.

(Source: Wang et al., 2009, Nature)

... even small steps if repeated enable radical changes in the genome

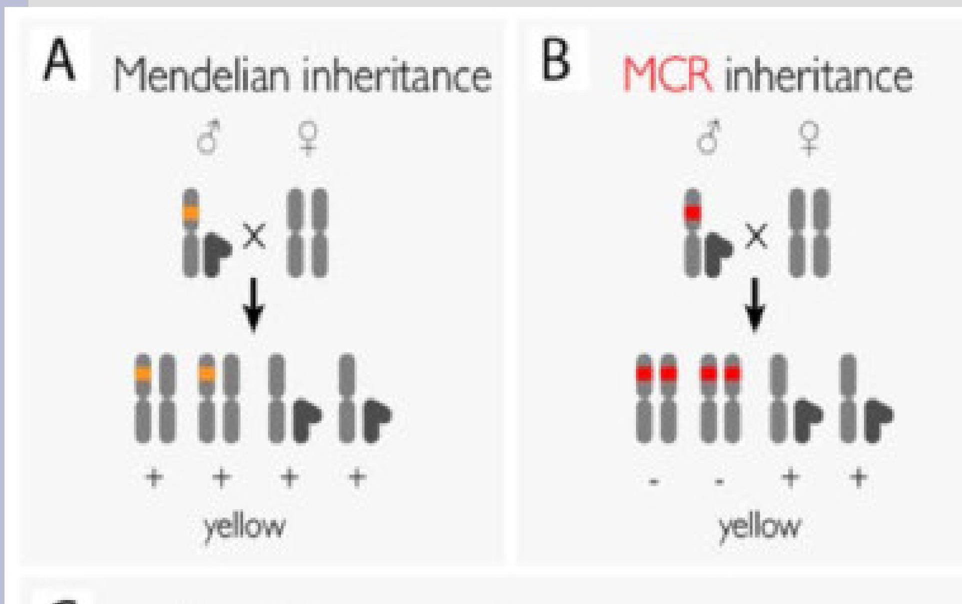
„The same technique would work for the Neanderthal, except that you'd start with a stem cell genome from a human adult and gradually reverse-engineer it into the Neanderthal genome or a reasonable close equivalent.“ (Church & Regis, 2012)

Nucleases: CRISPR / CAS
Clustered Regularly Interspaced Short Palindromic Repeats

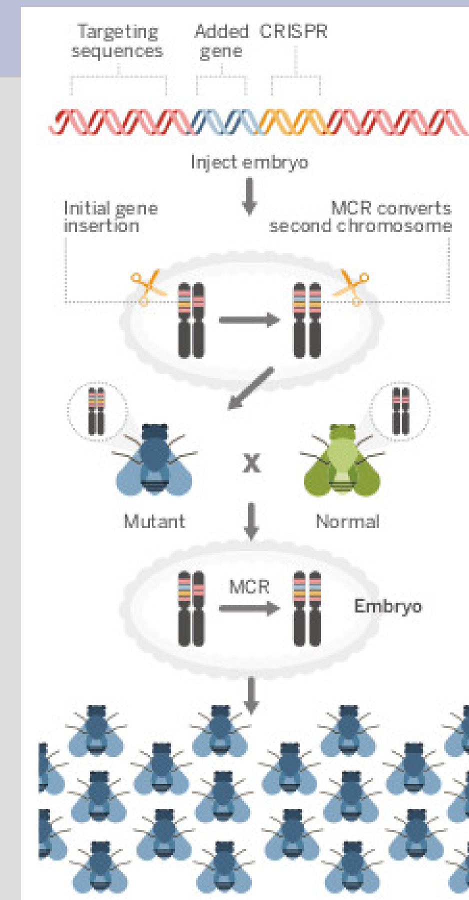


https://www.youtube.com/watch?v=0dRT7slyGhs

Mutagenic Chain Reaction / Gene Driver



Gantz & Bier, 2015, sciencemag.org SCIENCE



Bohannon, 2015, sciencemag.org SCIENCE

„Perhaps, in analogy to the famous Asilomar meeting (...) a similar conference could be convened to consider Biosafety measures and institutionalpolicies appropriate for limiting the risk of engaging in MCR research (...).“

Germany: controversy about oilseed rape of US company Cibus produced by oligonucleotides (RTDS).

Source: www.testbiotech.org/cibus-raps

Controversy about TTIP: Genetically engineered plants can escape regulation in the US

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CROPPING OUT REGULATION

Since 2010, the US Department of Agriculture has told at least 10 groups that their genetically modified (GM) crops would not be regulated because a plant pest was not used to do the engineering.

SOURCE: APHIS

Crop	Trait	Developer	Technique
Switchgrass	Easier conversion to biofuels	Ceres	Gene gun
Grapes	Red colour	University of Florida	Gene gun
Turf grasses	Herbicide tolerant	Scotts Miracle-Gro	Gene gun
Maize (corn)	Improved nutrition	Dow AgroSciences	Zinc-finger nuclease
Plums	Faster breeding	Appalachian Fruit Research Station	Non-transgenic offspring of GM parents
Tobacco	Faster breeding	North Carolina State University	Non-transgenic offspring of GM parents
Sorghum grass	Higher yields	University of Nebraska–Lincoln	Epigenetics
Not disclosed	Faster breeding	New Zealand Institute for Plant and Food Research	Non-transgenic offspring of GM parents
Ornamental plants	Not disclosed	BioGlow	Not disclosed
Not disclosed	Not disclosed	Cellectis	Meganuclease-targeted gene deletions

Table 4: Crops derived from genetic engineering and Synthetic Genome Technologies that did not undergo regulatory control in the US (source: Ledford, 2013)

Some demands

We need regulation to **protect** existing life forms as well as integrity of future evolution of life / biodiversity.

We need **control**: No release into environment without tempo-spatio control.

We need to **know the risks**: full registration of all relevant organisms and much stronger independent risk assessment.

We need more **power for civil society to participate** in decision making.