

CG920 Genomics

Lesson 11

Practical Applications

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INVESTICE DO ROZVOJE VZDĚLÁVÁNÍ

Tato prezentace je spolufinancována
Evropským sociálním fondem
a státním rozpočtem České republiky

Literature

- Literature resources for Chapter 11:



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Outline

- **Medicine**
 - Molecular Diagnosis
 - Personalized Medicine
 - Gene Therapy
- **Biotechnology**
- **Genetically Modified Organisms**
 - Transgenesis
 - Genome Editing
- **Model Organisms**
- **Principles of PCR**



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 - Molecular Diagnosis



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Molecular Diagnosis

- around 10,000 disorders in humans resulting from a single mutation
 - cystic fibrosis
 - sickle cell disease
 - muscular dystrophy
 - beta thalassemia
 -
- Early molecular diagnosis
 - mutations or infections
 - PCR
 - DNA (chip) hybridization
 - Cas-based



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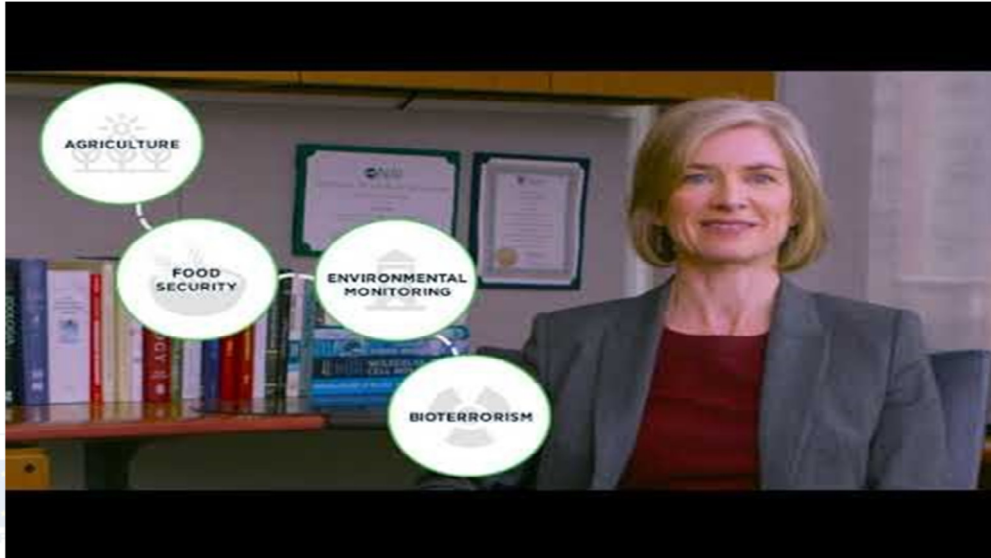
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Molecular Diagnosis

- Mammoth Biosciences

- Co-founded by Jenifer Doudna

<https://youtu.be/lPe4ldgKGdQ>



Outline

- Medicine
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 - Personalized Medicine



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Personalized Medicine

- uses **knowledge** of the **genome** for:
 - prediction of **health risks**
 - **diagnosis**
 - selection of the **most appropriate** type of **treatment**
 - **minimizing** the **side effects** of treatment
 - **prevention**



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<http://www.personalizedmedicinecoalition.org/>

Personalized Medicine

What is Personalized Medicine?

Current Practice



One size fits all

Trial and error

Personalized Medicine



The **right treatment** for
the **right person** at the
right time



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<http://www.personalizedmedicinecoalition.org/>

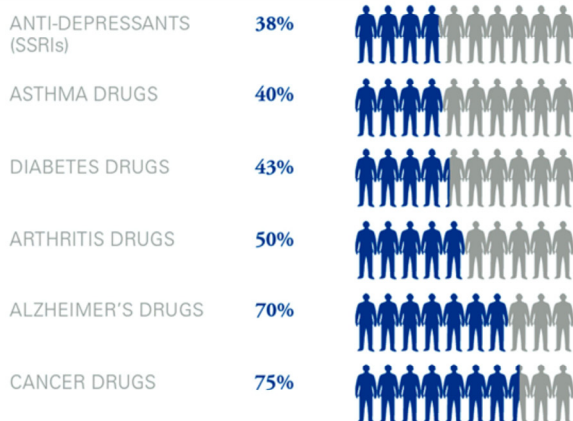


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Personalized Medicine

PERCENTAGE OF THE PATIENT POPULATION FOR WHICH A PARTICULAR DRUG IS INEFFECTIVE, ON AVERAGE



• Just in hospitals: about 6.7% of patients (2.2 million) experience serious adverse drug reactions



Serious adverse drug reactions in even smaller percentages of treated populations have led to the withdrawal of several drugs from the market

Zelnorm Vioxx Cylert

"Are good drugs going to the wrong people?"

Rezulin Baycol Lotronex*

Source of data: Brian B. Spear, Margo Heath-Chiozzi, Jeffery Huff, "Clinical Trends in Molecular Medicine," Volume 7, Issue 5, 1 May 2001, Pages 201-204.

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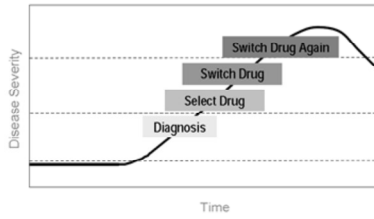
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Personalized Medicine

The Old Paradigm: Treatment of Disease

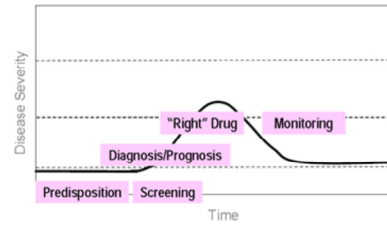
Reactive Medical Care



Diagnose Disease; Treat Symptoms; Costly, Trial and Error Treatment

Personalized Medicine Paradigm: Health Management

Efficient Medical Care



Health Management; Molecular Screening; Early Detection; Rapid Effective Treatment; Improved Quality of Care



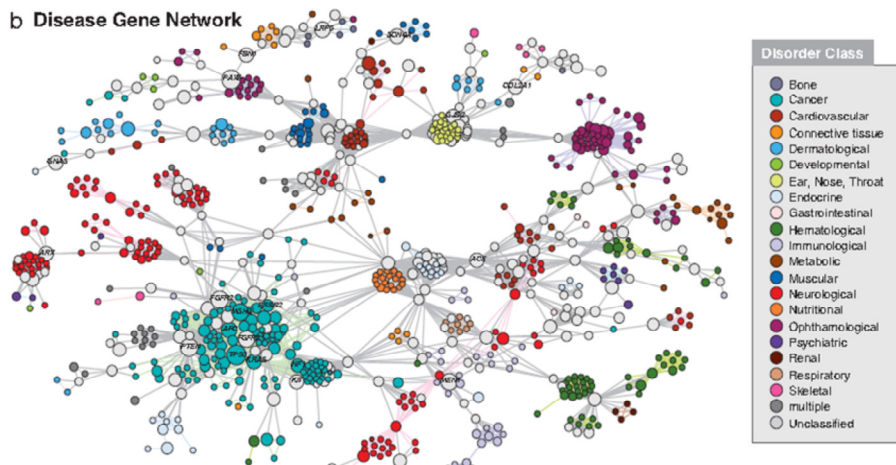
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Personalized Medicine

o Problem:

- multigene conditionality of most human diseases

b Disease Gene Network



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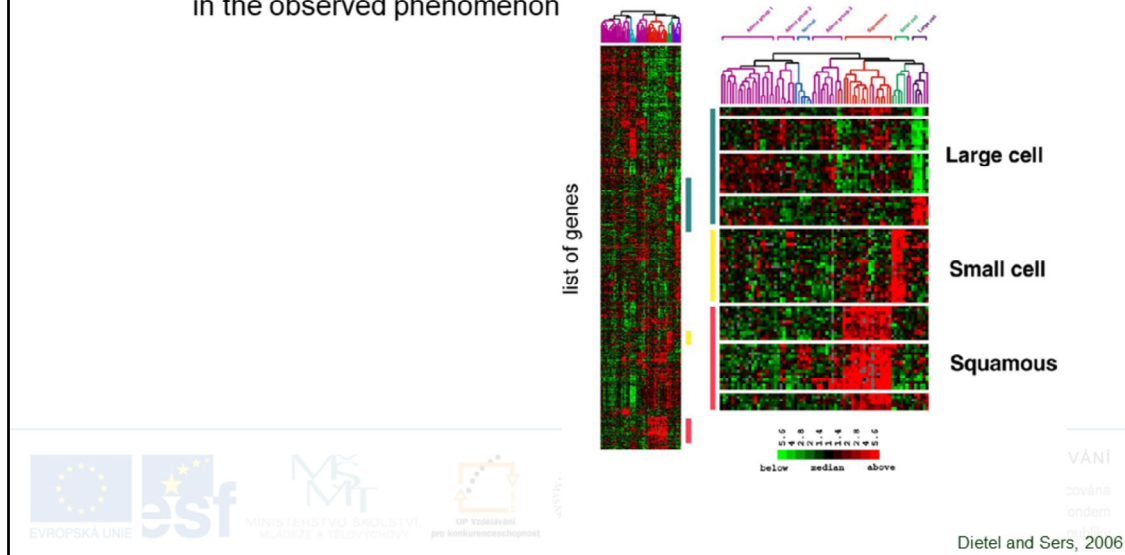


ŠLAVÁNÍ

Projekt financován ze strukturálních fondů
Goh et al., 2007 in fondem
a státním rozpočtem České republiky

Personalized Medicine

- Problem solving
 - **systems biology** - uses e.g. gene clustering to identify genes involved in the observed phenomenon



Hierarchical clustering analysis exemplified for Topotecan-resistant (R) and Topotecan-sensitive (S) cell lines. All cell lines resistant to Topotecan (left panel) and all cell lines sensitive to Topotecan (right panel) express a unique set of genes. Each row in the cluster indicates the expression profile of a specific gene across all 19 cell lines. Each column

indicates the individual cell line in which the gene is expressed.

Red, green, and black squares indicate that expression of the gene is greater than, less than, or equal to the median level of expression across all cell lines, respectively. The scale bar reflects the fold increase (red) or decrease (green) for any given gene relative to the median level of expression across all samples.

Dietel and Sers, 2006.

Personalized Medicine

- Problem solving
 - biomarkers
 - tests

Table: Selected Personalized Medicine Drugs, Treatments and Diagnostics as of September 2011*

Indications in quotes and otherwise unattributed, are cited from the therapeutic or diagnostic product label.

Therapeutic product labels contain pharmacogenomic information as:

- Information only
- Recommended
- Required
- Unhighlighted products have no pharmacogenomic information, recommendations or requirements in the label.

THERAPY	BIOMARKER/TEST	INDICATION
Mivacron® (mivacurium)	Cholinesterase gene	Anesthesia adjunct: "Mivacron is metabolized by plasma cholinesterase and should be used with great caution, if at all, in patients known to be or suspected of being homozygous for the atypical plasma cholinesterase gene."
Ansid® (flurbiprofen)	CYP2C9	Arthritis: "In vitro studies have demonstrated that cytochrome P450 2C9 plays an important role in the metabolism of flurbiprofen to its major metabolite, 4'-hydroxy-flurbiprofen."
Depakote® (divalproex)	UCD (NAGS, CTS, ASS; OTC, ASI, ARG)	Bipolar disorder: "Hypersensitivity encephalopathy, sometimes fatal, has been reported following initiation of valproate therapy in patients with urea cycle disorders (UCDs), particularly ornithine transcarbamylase deficiency (OTCD)."
Aromasin® (exemestane) Arimidex® (anastrozole) Nolvadex® (tamoxifen)	Estrogen Receptor (ER)	Breast cancer: Exemestane is indicated for adjuvant treatment of post-menopausal women with ER-positive early breast cancer. Anastrozole is for treatment of breast cancer after surgery and for metastases in post-menopausal women. Tamoxifen is the standard therapy for estrogen receptor-positive early breast cancer in pre-menopausal women.
Chemotherapy	Mammastrat®	Breast cancer: Prognostic immunohistochemistry (IHC) test used for postmenopausal, node-negative, estrogen receptor-expressing breast cancer patients who will receive hormonal therapy and are considering adjuvant chemotherapy.
Chemotherapy	MammaPrint®	Breast cancer: Assesses risk of distant metastasis in a 70-gene expression profile.
Chemotherapy	Oncoscore DX® 16-gene signature	Breast cancer: A 16-gene signature (plus five reference genes) indicates whether a patient has a low, intermediate, or high risk of having a tumor return within 10 years. Low-risk patients may be treated successfully with hormone therapy alone. High-risk patients may require more aggressive treatment with chemotherapy.
Chemotherapy	CompanDx® 31-gene signature	Breast cancer: The test predicts "time to event" for metastasis of breast cancer, following surgery or biopsy.
Falodex® (fulvestrant)	Hormone Receptor (HR)	Breast cancer: Fulvestrant is indicated for the treatment of hormone receptor positive metastatic breast cancer in post-menopausal women with disease progression following anti-estrogen therapy.
Herceptin® (trastuzumab) Tykerb® (lapatinib)	HER-2/yes receptor	Breast cancer: "...for the treatment of patients with metastatic breast cancer whose tumors overexpress the HER-2 [Human Epidermal growth factor Receptor 2] protein and who have received one or more chemotherapy regimens for their metastatic disease." High levels of HER-2 expression have been associated with increased disease recurrence in breast cancer, but show a better response to trastuzumab.
Pharmaceutical and surgical prevention options and surveillance	BRCA 1/2	Breast cancer: Guides surveillance and preventive treatment based on susceptibility risk for breast and ovarian cancer.
Nolvadex® (tamoxifen)	Breast Cancer Index® (HOXB13, IL17BR)	Breast cancer: Calculates a combined risk analysis for recurrence after tamoxifen treatment for ER-positive, node-negative breast cancer.



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The Case for Personalized Medicine, 3rd edition

Personalized Medicine

o Other problems

• Ethical Issues

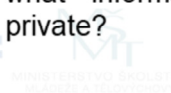
- the condition is genetic testing or **knowledge of the genome** - easily **abused**
- risk: **insufficient data security**
- in some countries, employers or insurance companies do not have access to such data

• High Costs

- medicine could be divided into **first-class** and **low-class** services
- **globalization gap** could grow even larger - poor countries would not be able to afford this

• Privacy

- crucial and complex issue
- what information about oneself can/should be considered private?



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Gene Therapy

Procedure in which the DNA sequence is inserted into the patient genome to replace or supplement the original gene

- Options:
 - replace the mutated gene
 - repair the mutation
 - deliver DNA encoding a therapeutic protein
 - antisense therapy
- In the future useful for treating e.g. hereditary diseases
- Types:
 - somatic gene therapy
 - gene therapy of germ cells



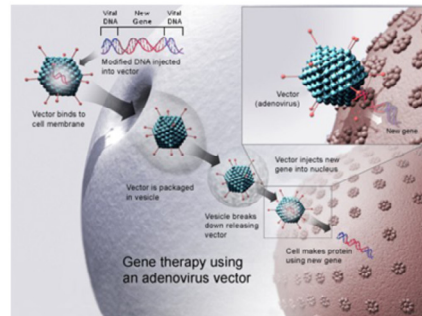
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Gene Therapy

○ Methods

- **viral vectors**
 - retroviruses
 - adenoviruses
 - herpes simplex virus
- **non-viral methods**
 - injection of plasmid DNA into muscle
 - increased efficiency of DNA delivery
 - electroporation
 - sonoporation
 - „gene gun“ (biolistic)
 - magnetofection
- **genome editing**



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Ethical Issues

- **International Commission on the Clinical Use of Human Germline Genome Editing**
 - convened by the U.S. National Academy of Medicine (NAM), the U.S. National Academy of Sciences (NAS), and the Royal Society of the U.K. ...
 - ...to identify a number of scientific, medical, and ethical requirements that should be considered, and could inform the development of a potential pathway from research to clinical use — if society concludes that heritable human genome editing applications are acceptable
 - more details at <https://nationalacademies.org/gene-editing/international-commission/index.htm>



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Ethical Issues

- Alliance for Regenerative Medicine

- **international group** representing the **cell** and **gene therapy sector**
- put out a “**statement of principles**” on **genome editing** endorsed by **13** of the **most active companies** in this field
- changing **heritable DNA** in sperm, eggs or a new embryo — came true in November 2018 when **He Jiankui**, a Chinese biophysicist, said that his lab had edited **two baby girls** to make them **resistant to HIV infection**. This mutation will be inherited by their descendants.
- **31 clinical trials** for gene edited therapies **are in progress around the world**, **20** of which are in **oncology**. None is yet close to commercialisation. The US has the largest number of trials (19) followed by China (10) and the UK (6)

FT, Clive Cookson, Science Editor August 27 2019



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- **Biotechnology**



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BIOTECHNOLOGY

- It uses living organisms, cells or parts of cells (enzymes) for research, leading to new products and applications in medicine, agriculture, food, environmental protection
- Also used in developing better/sustainable production methods for the chemical industry and other industrial processes
- An **interdisciplinary approach** requiring knowledge of chemistry, biology, physics, material sciences, engineering and informatics
- The origin of biotechnology can be traced 4,000 years back, when the Sumerians (although not knowingly) used microbes for the production of alcoholic beverages.

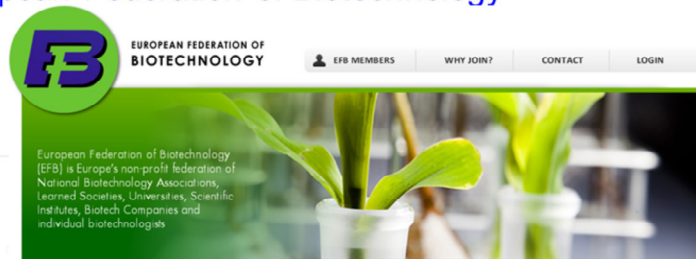


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BIOTECHNOLOGY

- Examples
 - effective utilization of **plant biomass** for **fuel production**
 - acquisition of starting material (**monomers**) for the **production of polymers** from living organisms instead of from fossil sources
 - **phytopharmaceuticals** – using plants in new vaccination methods such as expression of **antibodies** or **antigens** suitable for **immunization**
- **European Federation of Biotechnology**



TOJE VZDĚLÁVÁNÍ

stace je spolufinancována
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opětovně Českou republikou

<http://www.efb-central.org>

Outline

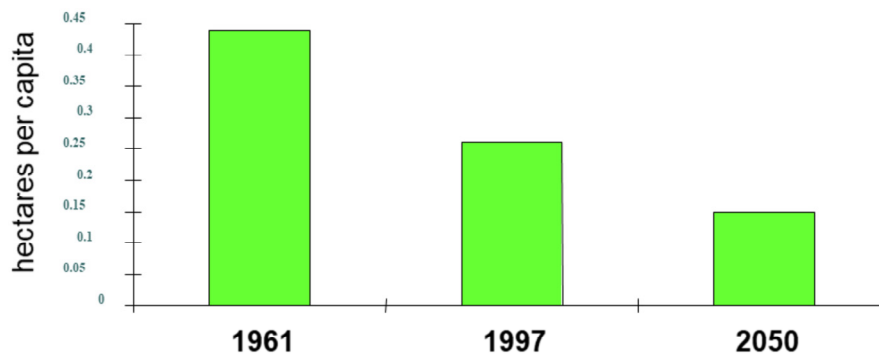
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 - Transgenesis



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Human Population vs Arable Land Availability



Source: UN Millennium Ecosystem Assessment



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Our civilization is built on farming, the surface area needed for feeding people has decreased by 90% over 10,000 years .

To prevent collapse, it is necessary to reduce this area from the current 0.45 ha/person to 0.2 ha/person by the year 2050. Return to original methods of agriculture would be a return to the original demands on area and therefore would be unsustainable Intensive farming = conversion of water and oil into food.

goal of plant biotechnology is to use all the available scientific knowledge to **breed varieties with higher yield** with lower inputs (of land, water, fertilizers, sprays ...)

Nutrition Deficiency



<https://qz.com/africa/1064653/the-world-could-run-out-of-food-two-decades-earlier-than-thought/>

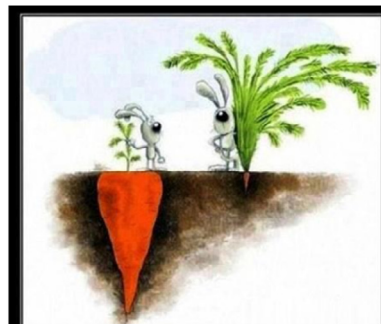
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EVROPSKÝ SOCIÁLNÍ FOND a státním rozpočtem České republiky

Announced recently by Quartz server, the world could be facing a 214 trillion calorie deficit in the food production (announced **as soon as in 2027**).

Breeding

- organisms naturally vary due to **mutations**
- before the era of genetic engineering - **question of chance**
- breeding tools
 - **selection** and **crossing**
- **modern breeder** learned to **change hereditary information** – **increase the mutants allele frequency**
 - **chemicals, radiation ...**
- results are **incidental/non-targeted**



Success
is not always visible at a glance



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Genetic Engineering

- Targeted modification ("targeted breeding")
 - ability to transfer genes = **transgenesis**
- the first practical application: production of **human insulin** in bacteria - 1978

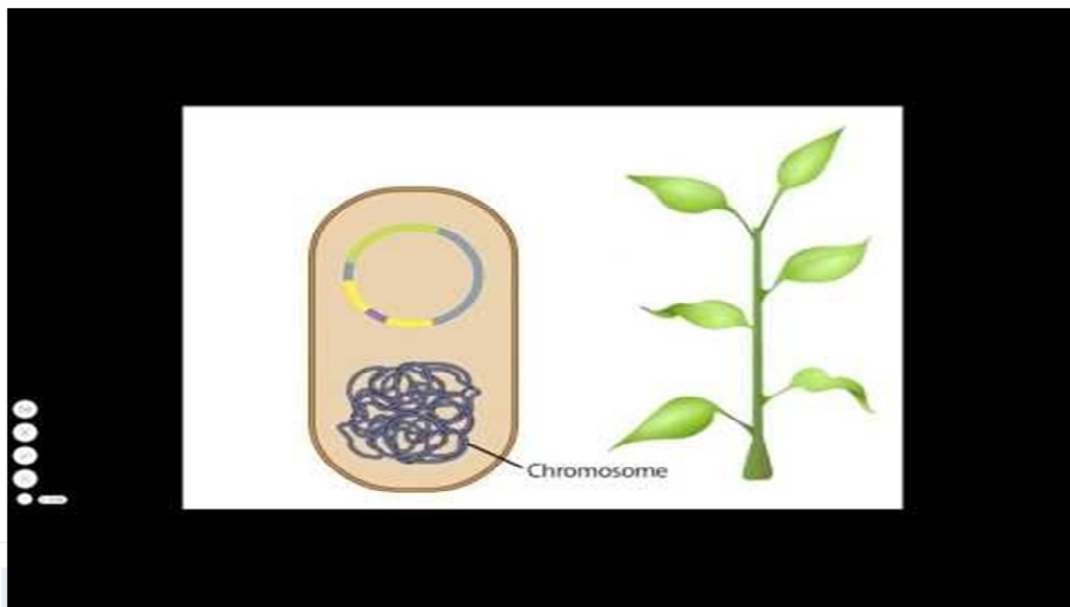


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Boyer a Swanson – firma Genentech

Plant Transgenesis



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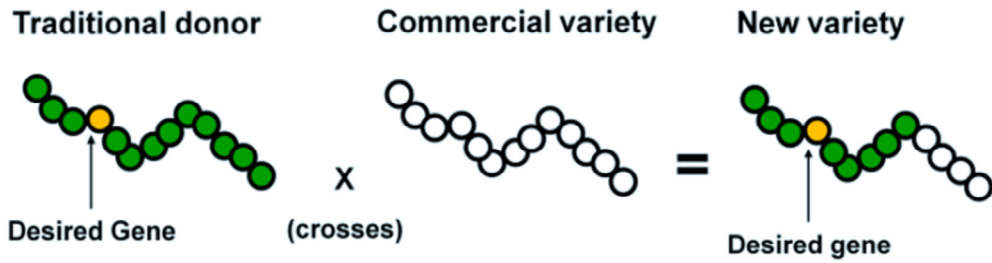
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<https://www.youtube.com/watch?v=yesNHd9h8k0>
a státním rozpočtem České republiky

Breeding Vs. Genetic Engineering



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Genetically Modified Organisms (GMOs)

- Organisms carrying **modified genetic information** – either **own** or **foreign** (from another organism), enabling **targeted changes** in the organism and its use for **specific purposes**
- **GMOs**
 - plants
 - bacteria
 - animals

<http://www.gmo-compass.org/>



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Genetically Modified Plants

- resistance to **pests**
- **herbicide** resistance
- resistance to **drought**
- resistance to **cold**
- resistance to **salinity**
- more efficient **nitrogen utilization**
- increasing **nutritional quality**



<http://ipbo.vib-ugent.be/>



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Bt Plants

- resistance to insect pests
- corn, cotton, rice
- genes from *Bacillus thuringiensis* (**Bt**)
- Expression of crystalline delta-endotoxins - **Crystal (Cry)** proteins
- increasing yields, reducing the amount of chemical sprays



European corn borer damage and fungal infection in non-Bt (left) and Bt hybrids (right)

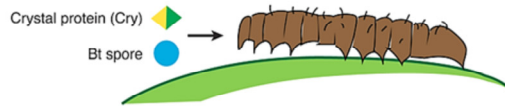


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Bt Plants

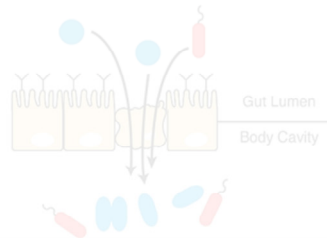
(A) Larvae ingest Bt spores and Cry proteins



(B) In larval midgut, proteolytic digestion of proteins release Cry toxins, which bind to epithelial receptors



(C) Toxin binding causes cell lysis destroying barrier to body cavity



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When the Cry protein reaches the gut, it is partially degraded, releasing a smaller and potentially toxic part of the protein [6]. But this toxin will only be active if it finds the right matching protein receptor sticking off the cells lining the gut of a larval insect. This is the most important aspect of the Cry toxin mechanism. Much in the same way that a certain key will only open a certain lock, the Cry toxin can only exert its toxic effect on a particular cell receptor. Consequently, the toxin tends to only impact insects within a particular taxonomic order.

Once the toxin is bound, the process is fairly straightforward. The toxin recruits other Cry toxins to the same cell and together they form a hole in cell's membrane that ultimately causes the cell to burst [6]. The cumulative effect of this happening to many cells is the irreversible destruction to the midgut membrane, compromising the barrier between the body cavity and gut. Without this barrier, *Bt* spores and other native gut bacteria can infiltrate and grow within the nutrient-rich body of the insect [4-5].

What makes *Bt* such a great candidate for pesticide and GM applications is that while these Cry toxins are highly effective against insects, they have been shown to be safe for consumption by mammals. Tests by the EPA have demonstrated that Cry proteins, like any other benign dietary protein, are very unstable in the acidic stomach environment. Furthermore, an oral toxicity test, which involves giving mice exceptionally high doses of purified toxic *Bt* proteins, showed no significant health impacts. In their 2001 reassessment of several *Bt* Cry proteins, the EPA concluded from these findings that "there is reasonable certainty that no harm will result from aggregate exposure to the U.S. population, including infants and children, to the Cry1AB and Cry1F proteins and the genetic material necessary for their production." Similar conclusions were drawn about the Cry1Ac protein of *Bt* cotton [7]. Other mouse studies on have shown that even high doses of truncated Cry proteins, such that only the toxic region is conserved, have no deleterious effects [8]. A paper in Annual Review of Entomology from 2002 also makes the strong point that, in addition to no demonstrated toxicity of *Bt* toxins, their use provides important health benefits to livestock and humans by preventing certain insect-caused crop diseases that produce toxic and carcinogenic compounds [13].

Ht Plants

- resistance to systemic herbicides
- glyphosate
 - interferes with the synthesis of aromatic amino acids; animals without the appropriate enzymatic apparatus = harmless
 - blocks the enzyme 5-enolpyruvylshikimate-3-phosphate synthase (EPSPS) in chloroplasts – affects green plants
 - ineffective for bacterial EPSPS - evolutionarily divergent
 - soya, maize, sugar beet, canola, cotton, alfalfa - added enzyme for tolerance
 - company Bayer (Monsanto), trade name Roundup



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Ht Plants

- resistance to systemic herbicides
- glufosinate (phosphinothricin)
 - prevents processing of ammonium - toxic
 - *Streptomyces hygroscopicus* synthesizes and transforms it: acetylation by the enzyme phosphinothricin acetyltransferase – coding gene isolated in 1987 - named *bar*
 - trade names: Basta, Liberty, Finale, Radical ...



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Multiresistant Plants

- Bt resistance + herbicide
- multiresistant corn - the majority of total production in the USA
- example of multiresistant corn:
 - three Bt genes for resistance to air pests
 - three Bt genes for resistance against soil pests
 - two genes for herbicide resistance



INVESTICE DO ROZVOJE VZDĚLÁVÁNÍ

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Disease-Tollerant Plants

- **viruses** - no chemical agents available
- gene encoding **non-infectious viral envelope** protein - increases resistance to viral infection
 - **banana; papaya** - Hawaii, Southeast Asia
 - **cassava** - a basic food ingredient for more than **500 million people** + **animal feed**



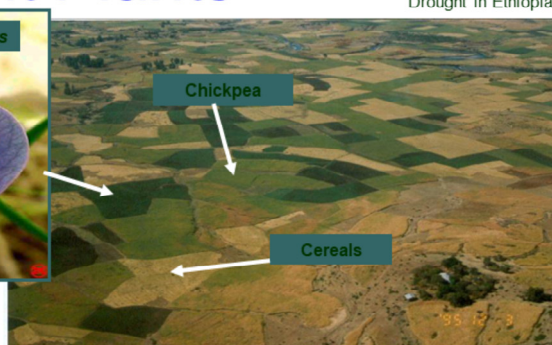
Left: Papaya with Papaya ringspot disease
Right: Biotech Papaya resistant



Hlízy manioku (cassava) tvoří základní potravinovou složku pro více než 500 milionů lidí. Rovněž se využívá jako krmivo - zkrmuje se v podobě maniokové moučky hlavně prasatům, skotu, ovčím a kozám.

Disease- and Stress-Tolerant Plants

Drought in Ethiopia



New drought-tolerant maize (right) needs less water.

- Chickpeas - more resistant to drought, but toxic
 - GMOs with inactivated toxin
- Corn resistant to drought

ČESKÁ REPUBLIKA

OP Vzdělávání pro konkurenceschopnost



MINISTERSTVO ŠKOLSTVÍ, MLÁDEŽE A TĚLOVÝCHOVY

OP Vzdělávání pro konkurenceschopnost

Evropský sociální fond

Evropským sociálním fondem a státním rozpočtem České republiky

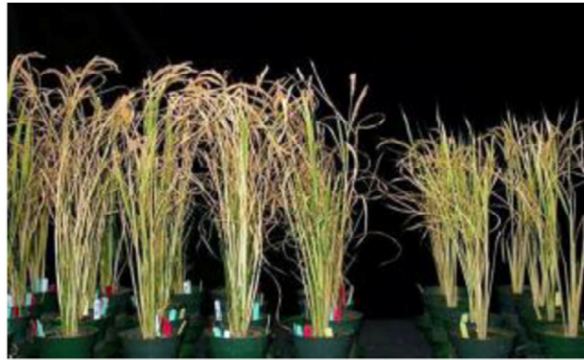
Hrachor – Lathyrus sativus

Cizrna – Chickpea

Obiloviny - Cereals

Nitrogen Use Efficiency

- use of nitrogen from fertilizers
 - rice with gene from barley - 3x higher nitrogen utilization under oxygen deficiency



The effect of Nitrogen Use Efficiency (NUE) in rice growth with reduced N applications. Left: rice engineered

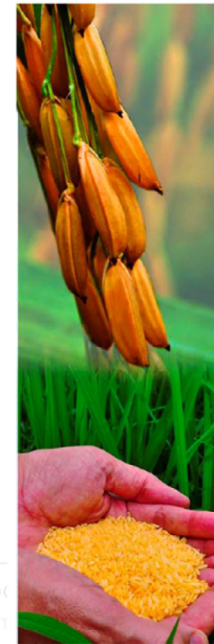
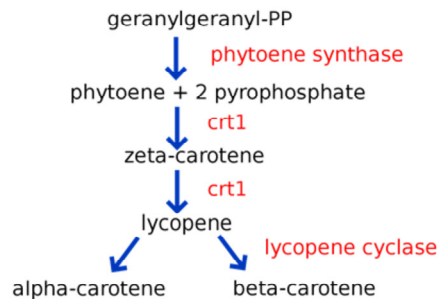


When crops are supplied with excess nitrogen fertilizer to gain maximal yields the excess nitrogen is converted into the gas nitrous oxide (N₂O) and also leaches into rivers. N₂O has 300x the Global Warming Potential of CO₂ and nitrogen fertilizer runoff creates marine dead zones, such as in the Gulf of Mexico at the mouth of the Mississippi river. Crops that have the ability to grow well with less nitrogen, because of enhanced uptake or similar characteristics, result in less N₂O release and less N runoff. This lessens the effect of fertilizer nitrogen on global warming and lake and marine pollution.

Improved Nutrition Value

o Golden rice

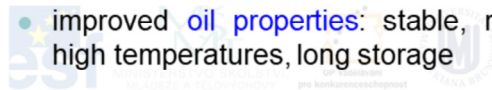
- several genes from maize encoding enzymes for the biosynthesis of β -carotene (precursor of vitamin A)



Golden Rice
8. listopadu 2009, Česká republika

o Canola and Soybean

- improved oil properties: stable, resistant to high temperatures, long storage



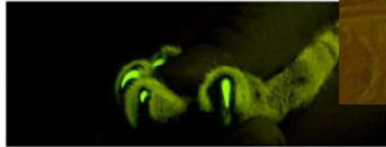
INVESTICE DO

While most biotech crops have characteristics that enhance their cultivation, those with enhanced consumer characteristics are being developed. For example many children in SE Asia develop blindness because of a deficiency of vitamin A. Golden rice is engineered with genes from maize to be high in the precursor of vitamin-A that when eaten is converted to vitamin-A in order to prevent blindness in developing countries. High oleic soybean and canola oil are now available. Oil with this fat profile is more stable, allowing for greater heat tolerance and longer shelf life.

GMO Animals

○ Transgenic cats

- **lentiviruses** are **sensitive to restriction factors**
 - specific **restriction factor**: rhesus macaque **TRIMCyp + eGFP**
- uniform expression, no mosaicism and no silencing in F1 generation
- **lymphocytes** of transgenic animals **resistant to replication of FIV**



EVROPSKA UNIJA

EVROPSKI SODIŠČNIK

EVROPSKI SODIŠČNIK

Wongsrikeao *et al.*, 2011, Nature Methods

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Outline

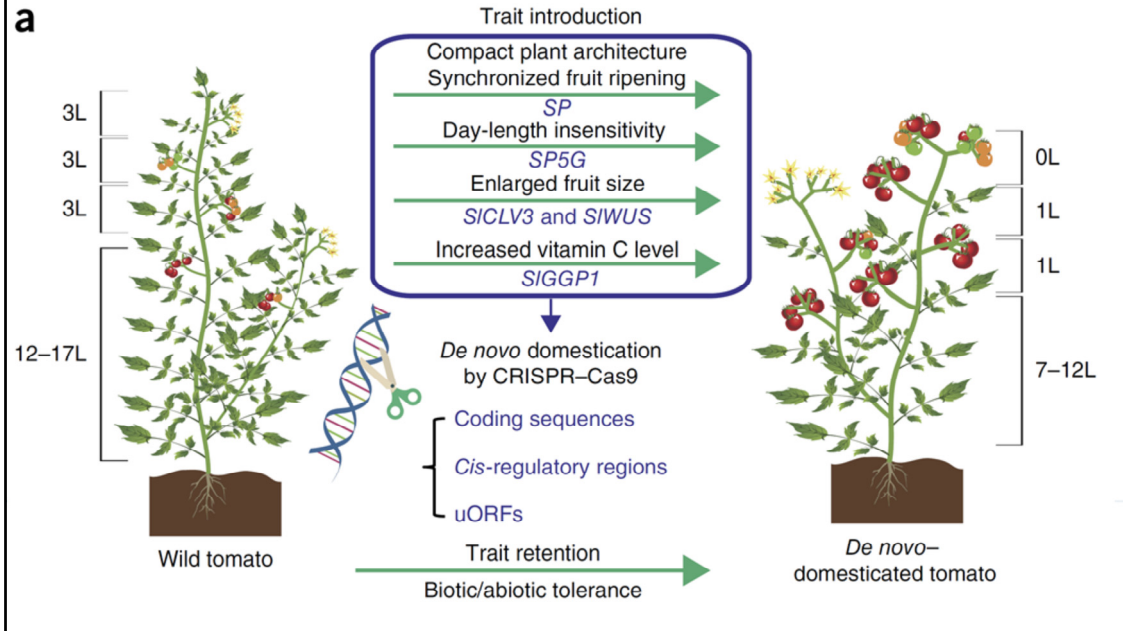
- **Medicine**
 - Molecular Diagnosis
 - Personalized Medicine
 - Gene Therapy
- **Biotechnology**
- **Genetically Modified Organisms**
 - Transgenesis
 - **Genome Editing**



INVESTICE DO ROZVOJE VZDĚLÁVÁNÍ

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Gene Editing in Plant Domestication



Outline

- **Medicine**
 - Molecular Diagnosis
 - Personalized Medicine
 - Gene Therapy
- **Biotechnology**
- **Genetically Modified Organisms**
 - Transgenesis
 - Genome Editing
- **Model Organisms**



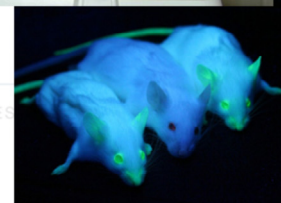
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Mus musculus

house mouse

- Low requirements for area
- Relatively large number of offspring (3-14, 6-8 on average)
- Genome size is close to the size of human genome (about 3000 Mbp), the number of genes as well (about 24K)
- 20 chromosomes (19+1)
- Suitable for a wide range of physiological experiments (anatomical and physiological similarity to human)
- Possibility to obtain (quite easily) KO mutants and transgenic lines



INVE

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More info about mouse at

<http://www.informatics.jax.org/greenbook/index.shtml>.

Mus musculus

house mouse

- Genome known since 2002 (<http://www.ncbi.nlm.nih.gov/projects/genome/assembly/grc/mouse/>)

Mouse Genome Overview
Information concerning the continuing improvement of the mouse genome.

The GRC is working hard to provide the best possible reference assembly for mouse. We do this by both generating multiple representations (alternate loci) for regions that are too complex to be represented by a single path. Additionally, we are releasing regional fixes known as patches. This allows users who are interested in a specific locus to get an improved representation without affecting users who need chromosome coordinate stability.

Getting Data
GRCm38.p1 (latest minor release from the GRC): [FTP](#)
GRCm38 (latest Major release from the GRC): [FTP](#)
Alignments of MGSv37 to GRCm38: [GRC FTP](#)
Information on regions under review: [FTP](#)
Annotated clone assembly problems: [FTP](#)

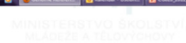
Next assembly update
The next assembly update (patch release 2) will be a minor update (only patches) and will happen in March 2013.

GRCm38.p1
Release date: 23 Aug 2012
Release type: minor

GRC Blog
The GRC and the 10th International Zebrafish Genetics and Development Meeting (June 20-24, 2012 - Madison, Wisconsin) 26 Jul 2012
Hidden assembly problems exposed 06 Jul 2012
The human reference genome GRCh37 represents th... see all

Recently Resolved Mouse Issues
Mouse (MG-4136) Nov 16, 2012
Inversion found in the assembly has been corrected in component AL611930.25.
Mouse (MG-4212) Nov 16, 2012
There is an assembly gap between AC132093.3 and AC235617.4, originally described in MG-3584, and then updated in MG-4143. This duplicate Jira issue is being used to manage an update at this gap that is being considered for patch release. see all

References
Whole Genome Papers
The Mouse Genome WGS Assembly
The Mouse Genome: Clone based assembly

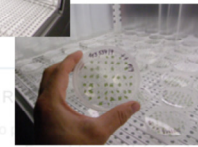


VZDĚLÁVÁNÍ
spolufinancována
Evropským sociálním fondem
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Arabidopsis thaliana

mouse-ear cress

- **Low requirements** for cultivation area
- High **number of seeds** (20.000 per plant and more)
- **Small and compact genome**, (125 MBp, about 25.000 genes, average size 3 kb)
- **5 chromosomes**
- Suitable for **wide range of physiological experiments**
- **High natural variability** (approximately 750 ecotypes (Nottingham Arabidopsis Seed Stock Centre))



Columbia 0

Landsberg 0

Wassilewskija 0



<http://seeds.nottingham.ac.uk/>



INVESTICE DO

INVESTICE DO Vzdělávání a odborné přípravy pracovníků a státním rozpočtem České republiky

Arabidopsis thaliana

mouse-ear cress

- Genome known since 2000 (<http://www.arabidopsis.org/>)

The screenshot shows the homepage of the Arabidopsis Information Resource (TAIR). The page features a navigation menu with options like Search, Browse, Tools, Portals, Download, Submit, News, and ABRIC Stocks. The main content area is titled "The Arabidopsis Information Resource" and provides a detailed overview of the database, including its history and the types of data it contains. A prominent graphic in the center encourages users to "Click here to try our new online submission form" and lists the types of data that can be submitted, such as molecular function, biological process, and gene localization. To the right, there is a "Breaking News" section with several recent updates, including the availability of a new set of confirmed T-DNA lines and a new protein chip. The bottom of the page includes a footer with the European Union logo and the text "EVROPSKA UNIJA" and "Evropská unie".

Outline

- **Medicine**
 - Molecular Diagnosis
 - Personalized Medicine
 - Gene Therapy
- **Biotechnology**
- **Genetically Modified Organisms**
 - Transgenesis
 - Genome Editing
- **Model Organisms**
- **Principles of PCR**



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PCR



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Discussion



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