CG020 Genomika

Přednáška 12

Praktické aplikace genomiky

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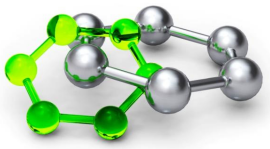

Literatura

- Literární zdroje ke kapitole 12:

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Osnova

- Lékařství
  - Molekulární diagnostika
  - Individualizovaná medicína
  - Genová terapie
- Biotechnologie
- Geneticky Modifikované Organismy
  - Transgenoze
  - Editování genomu
- Modelové organismy
- Principy PCR

Osnova

- Lékařství
  - Molekulární diagnostika

Molekulární Diagnostika

- Cca 10,000 onemocnění u člověka je podmíněno mutací v jediném genu
  - cystická fibróza
  - srpkovitá anémie
  - svalová dystrofie
  - β-talasémie
  - ….
- Časná molekulární diagnostika
  - mutace nebo infekce
    - PCR
    - Hybridizace na DNA čipu
    - Cas-based

Molekulární Diagnostika

- Mammoth Biosciences
  - Spoluzakladatelka Jenifer Doudna

https://youtu.be/IPe4ldgKGdQ

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It has been fouynd that binding of gRNA=targeted CRIPSR to the target sequence activates ssDNA cleavage activityt of Cas12. “By combining Cas12a ssDNase activation with isothermal amplification, we create a method termed DNA endonuclease-targeted CRISPR trans reporter (DETECTR), which achieves attomolar sensitivity for DNA detection. DETECTR enables rapid and specific detection of human papillomavirus in patient samples, thereby providing a simple platform for molecular diagnostics.” (Chen et al., 2018). The approach was used also for designing the CRISPR-based detection of SaRs-Cov-2 (Broughton et al., 2020).

Osnova

- Lékařství
  - Molekulární diagnostika
  - Individualizovaná medicína

Individualizovaná Medicína

- Využívá znalost genomu pro:
  - Předpověď zdravotních rizik
  - Diagnositku
  - Výběr nejvhodnějšího typu léčby
  - minimalizuje nežádoucí efekty léčby
  - prevence

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http://www.personalizedmedicinecoalition.org/

Individualizovaná Medicína

What is Personalized Medicine?

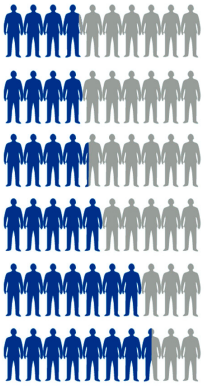
Current Practice	Personalized Medicine
	
Trial and error	The right treatment for the right person at the right time

http://www.personalizedmedicinecoalition.org/

Individualizovaná Medicína

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

ANTI-DEPRESSANTS (SSRIs)	38%
ASTHMA DRUGS	40%
DIABETES DRUGS	43%
ARTHRITIS DRUGS	50%
ALZHEIMER'S DRUGS	70%
CANCER DRUGS	75%



- 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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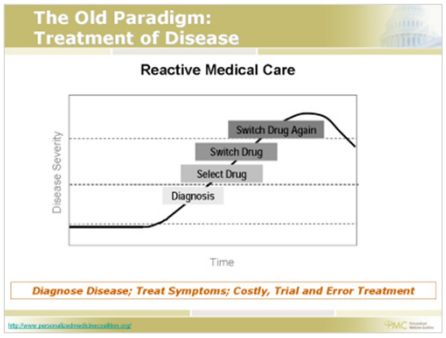
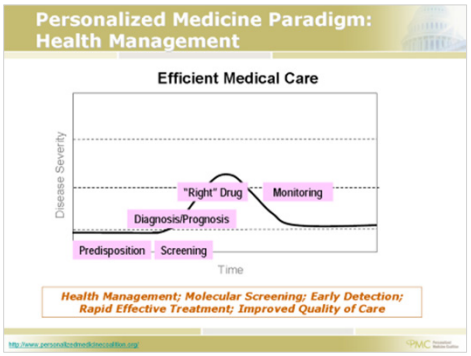
Individualizovaná Medicína





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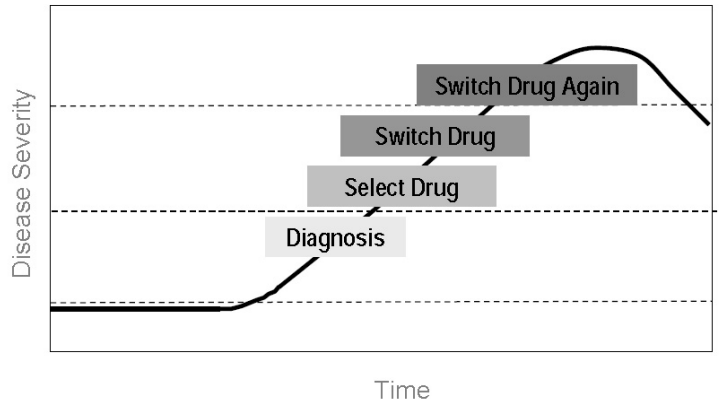
The Old Paradigm: Treatment of Disease

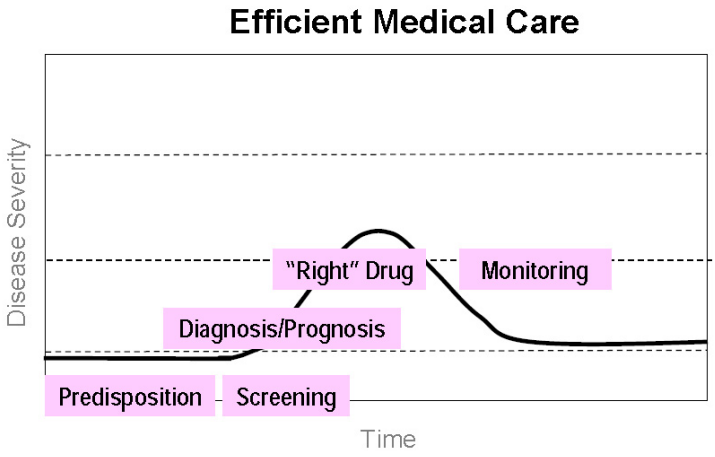
Reactive Medical Care



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

http://www.personalizedmedicinecoalition.org/

Personalized Medicine Paradigm: Health Management

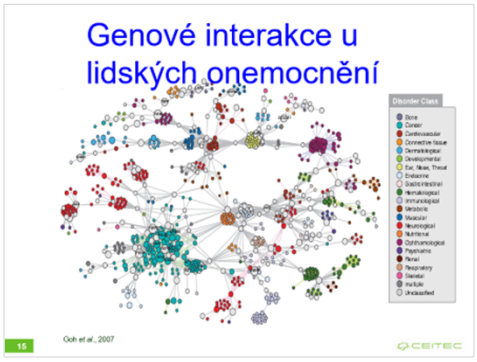


Health Management; Molecular Screening; Early Detection; Rapid Effective Treatment; Improved Quality of Care

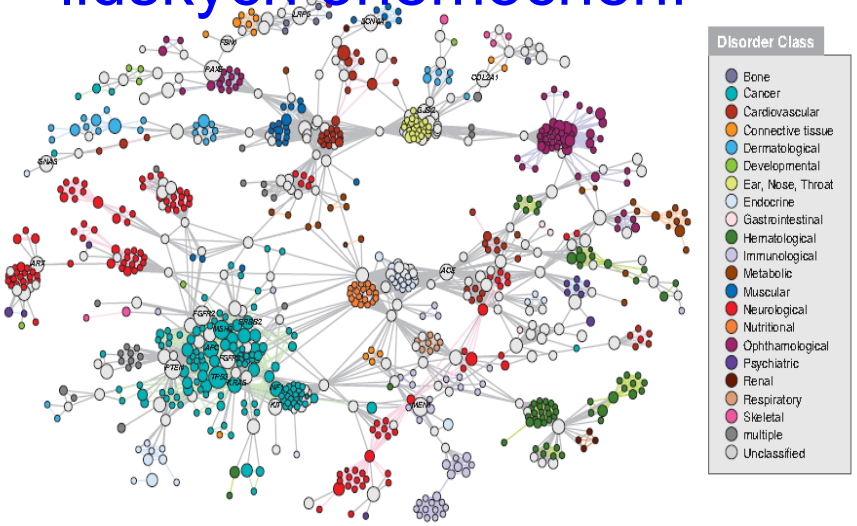
http://www.personalizedmedicinecoalition.org/

Individualizovaná Medicína

- Problém:
  - Mnohofaktoriální podmíněnost většiny lidských onemocnění



Genové interakce u lidských onemocnění



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Goh *et al.*, 2007

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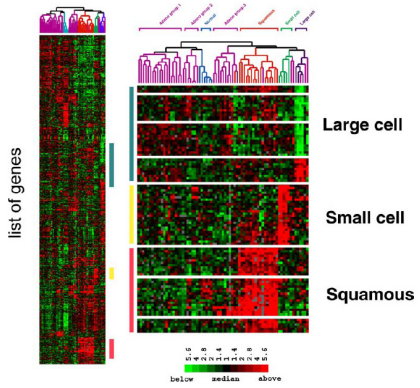
In the disease gene network, each node is a gene, with two genes being connected if they are implicated in the same disorder. The size of each node is proportional to the number of disorders in which the gene is implicated (see key). Nodes are light gray if the corresponding genes are associated with more than one disorder class. Genes associated with more than five disorders, and those mentioned in the text, are indicated with the gene symbol. Only nodes with at least one link are shown.

Individualizovaná Medicína

- Řešení problému:
  - **Systémová biologie** – využívá např. genové klastrování k identifikaci genů asociovaných s pozorovaným jevem (nemocí, poruchou, ..)



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Dietel and Sers, 2006

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.

Topotecan, sold under the brand name **Hycamtin** among others, is a chemotherapeutic agent medication that is a topoisomerase inhibitor. It is a synthetic, water-soluble analog of the natural chemical compound camptothecin. It is used in the form of its hydrochloride salt to treat ovarian cancer, lung cancer and other cancer types (Wikipedia).

Individualizovaná Medicína

- Řešení problému:
  - **Systémová biologie** – využívá např. genové klastrování k identifikaci genů asociovaných s pozorovaným jevem (nemocí, poruchou, ..)
    - biomarkery
    - testy

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."
Ansaid® (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, CPS, ASS, OTC, ASL, ARG)*	**Bipolar disorder:** "Hyperammonemic encephalopathy, sometimes fatal, has been reported following initiation of valproate therapy in patients with urea cycle disorders (UCDs), particularly ornithine transcarbamylase deficiency (OTC)."
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	Mammostrat®	**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	Oncotype 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.
Faslodex® (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/neu 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

Aplikace přístupů systémové biologie (včetně genového klastrování na předchozím snímku) pak umožní identifikovat specifické markery a testy, které umožní testovat odpověď na různé typy terapií.

Individualizovaná Medicína

- Další problémy
  - Etické otázky
    - Možnost zneužití znalosti genomu
    - riziko: nedostatečná ochrana dat
    - V některých zemích je uzákoněn omezený přístup pro určité typy zaměstnanců nebo pojišťovací společnosti
  - Vysoké náklady
    - Dělení medicíny na first-class and low-class služby
    - Zvětšování problému globalizačního handikapu – chudé země si nemohou takto pokročilý typ léčby dovolit
  - Soukromí
    - Zásadní a komplikovaná otázka
    - Jakou informaci lze považovat za soukromou?

Osnova

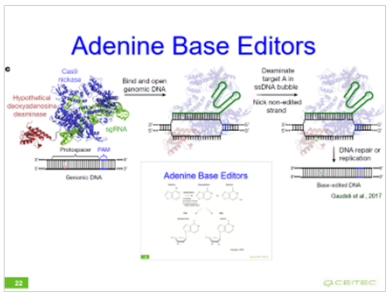
- Lékařství
  - Molekulární diagnostika
  - Individualizovaná medicína
  - Genová terapie
- Biotechnologie

Gene Therapy

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

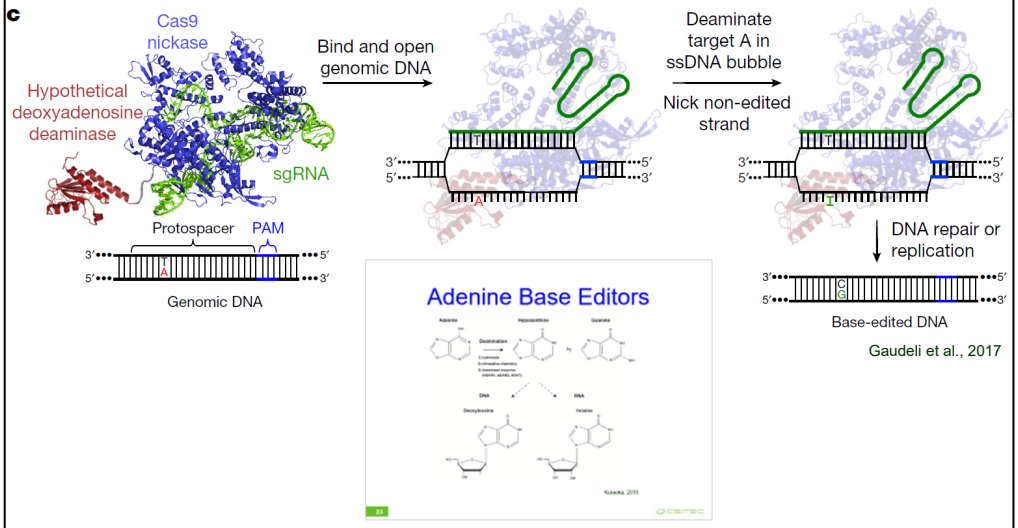
- Options:
  - replace the mutated gene
  - repair the mutation
  - deliver DNA encoding a therapeutic protein
  - antisense therapy
- In the future useful for treating e.g. hereditary diseases
- Types:
  - somatic gene therapy
  - gene therapy of germ cells

Gene Therapy



- Hutchinson–Gilford progeria syndrome
  - C•G-to-T•A mutace (c.1824 C>T; p.G608G) v genu pro laminin (*LMNA*)
  - Defekt v sestřihu RNA vede k tvorbě toxického proteoinu progerinu
  - Věk dožití cca 14 let
  - In vivo oprava pomocí ABEs potvrzena u myší a lidských fibroblastů (Koblan et al., 2021)

Adenine Base Editors



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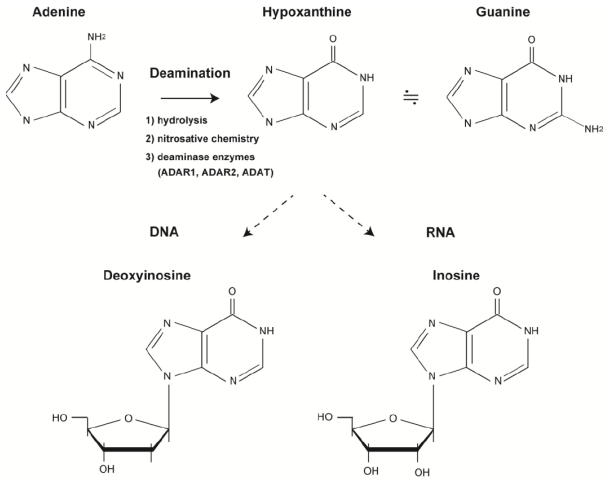
Adenine Base Editors



Kuraoka, 2015

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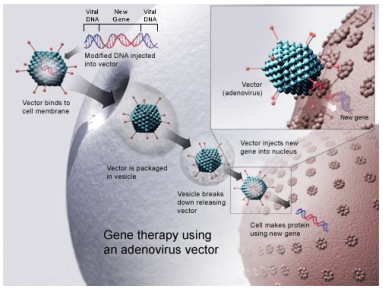
Formation of deoxyinosine and inosine. Deamination of adenine to hypoxanthine results in the formation of deoxyinosine in DNA and inosine in RNA. Hypoxanthine, which is recognized as guanine, pairs with cytosine. Deoxyinosine and inosine are nucleosides that form when hypoxanthine is attached to a deoxyribose ring or ribose ring, respectively.

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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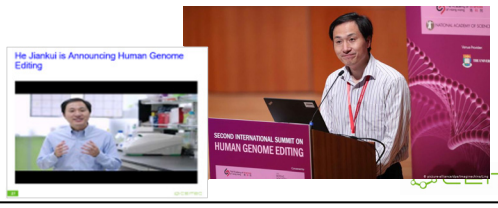
Ethical Issues

- Regulace editace genomu v zemědělství a lidském zdraví
  - https://crispr-gene-editing-regs-tracker.geneticliteracyproject.org/
- 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

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 commercialization. The US has the largest number of trials (19) followed by China (10) and the UK (6)

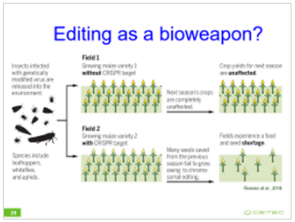
FT, Clive Cookson, Science Editor August 27 2019



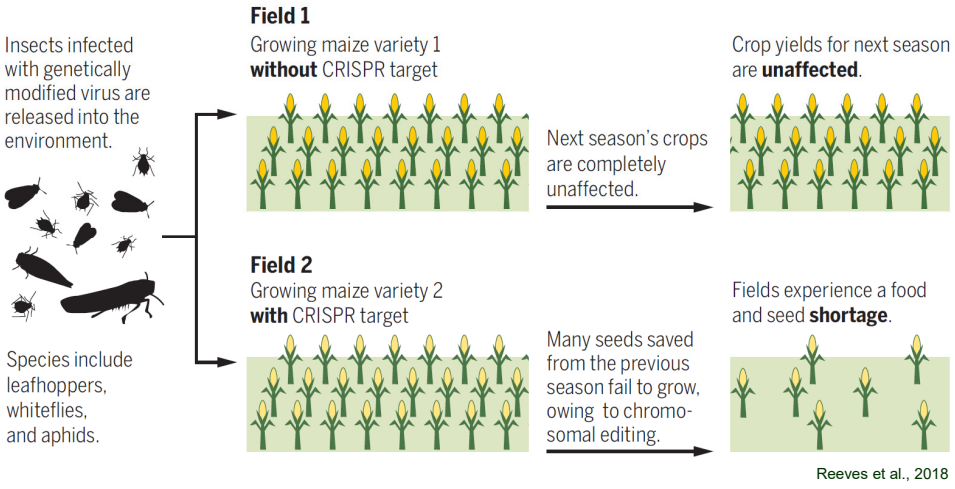
He Jiankui is Announcing Human Genome Editing

Ethical Issues

- Genome editing as a bioweapon?
  - ongoing research program funded by the U.S. Defense Advanced Research Projects Agency (DARPA)
  - aims to disperse infectious genetically modified viruses that have been engineered to edit crop chromosomes directly in fields
  - the means of delivery of these viral horizontal environmental genetic alteration agents (HEGAAs) into the environment should be insect-based dispersion
  - Part of scientific community does not find the program useful for the U.S. agriculture, but points to its possible misuse



Editing as a bioweapon?



Reeves et al., 2018

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Outline

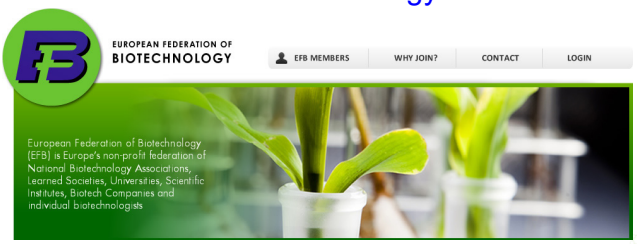
- Medicine
  - Molecular Diagnosis
  - Personalized Medicine
  - Gene Therapy
- Biotechnology

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.

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

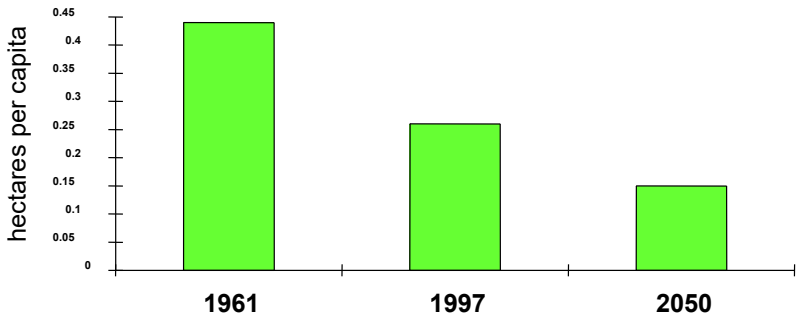


http://www.efb-central.org

Osnova

- Lékařství
  - Molekulární diagnostika
  - Individualizovaná medicína
  - Genová terapie
- Biotechnologie
- Geneticky Modifikované Organismy
  - Transgenoze

Human Population vs Arable Land Availability



Source: UN Millennium Ecosystem Assessment

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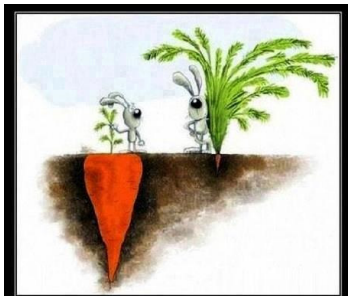
Announced recently by Quartz server, the world could be facing a 214 trillion calorie deficit in the food production (announced **as soon as in 2027.**

Breeding

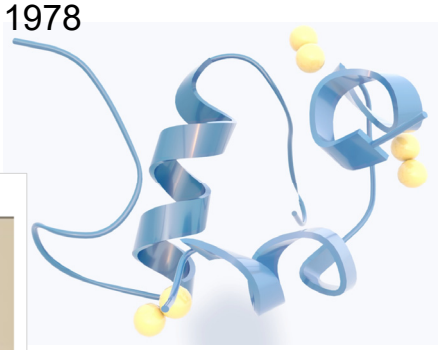
- organisms naturally vary due to mutations
- before the era of genetic engineering - question of chance
- breeding tools
  - selection and crossing
- modern breeder learned to change hereditary information – increase the mutants allele frequency
  - chemicals, radiation ...
- results are incidental/non-targeted



Success
is not always visible at a glance

Genetic Engineering

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



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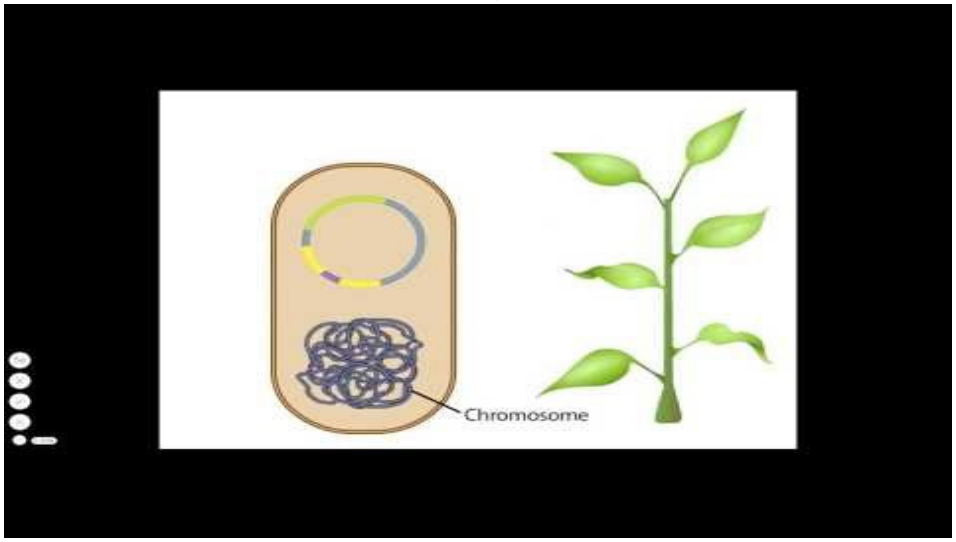
Insulin, a peptide hormone composed of two polypeptide chains connected via two disulfide bridges (in yellow, the third one is not involved in the linkage).

The Story of Insulin

Plant Transgenosis



https://www.youtube.com/watch?v=yesNHd9h8k0

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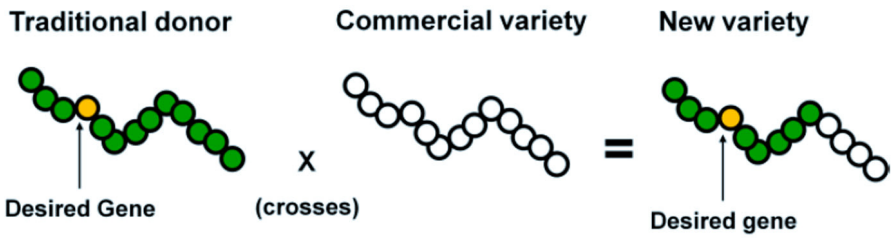
Breeding Vs. Genetic Engineering



Geneticaly 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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Geneticaly 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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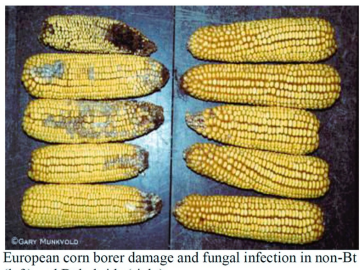
Bt Plants

- 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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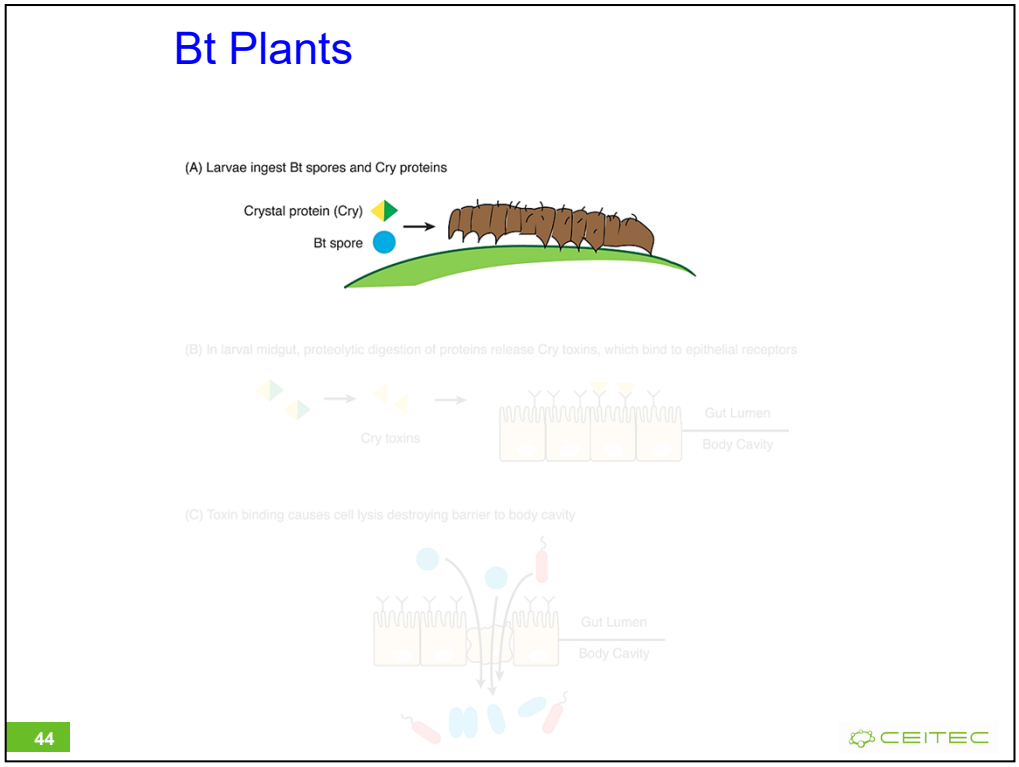


When the Cry protein reaches the gut, it is partially degraded, releasing a smaller and potentially toxic part of the protein [6]. But this toxin will only be active if it finds the right matching protein receptor sticking off the cells lining the gut of a larval insect. This is the most important aspect 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-enolpyrovylshikimate-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

Ht Plants

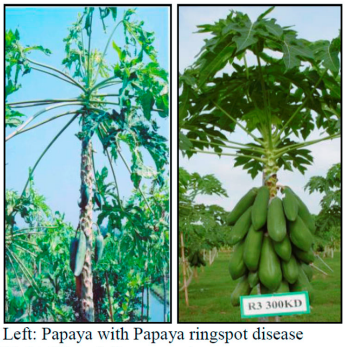
- resistance to systemic herbicides
- glufosinate (phosphinothricin)
  - prevents processing of ammonium - toxic
  - *Streptomyces hygroscopicus* synthesizes and transforms it: acetylation by the enzyme phosphinothricin acetyltransferase – coding gene isolated in 1987 - named *bar*
  - trade names: Basta,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

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

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

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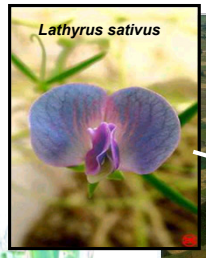
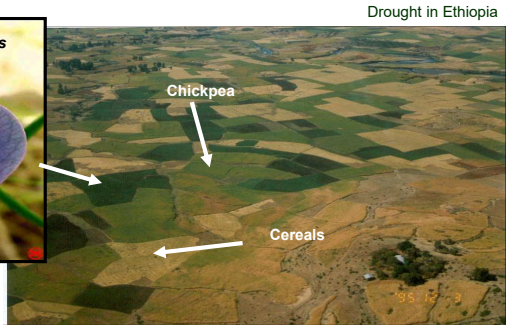
Hlízy manioku (cassava) tvoří základní potravinovou složku pro více než 500 milionů lidí. Rovněž se využívá jako krmivo - zkrmuje se v podobě maniokové moučky hlavně prasatům, skotu, ovcím a kozám.

Disease- and Stress-Tollerant Plants

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





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

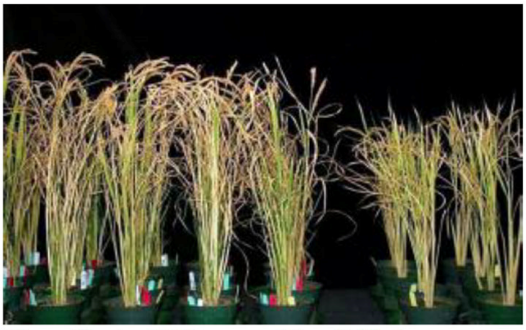
Hrachor – Lathyrus sativus

Cizrna – Chickpea

Obiloviny - Cereals

Nitrogen Use Efficiency

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

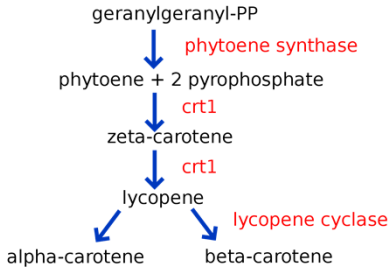


The effect of Nitrogen Use Efficiency (NUE) in rice growth with reduced N applications. Left: rice engineered

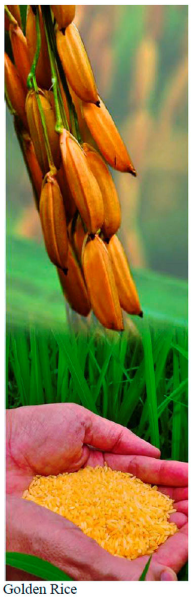
When crops are supplied with excess nitrogen fertilizer to gain maximal yields the excess nitrogen is converted into the gas nitrous oxide (N2O) and also leaches into rivers. N2O has 300x the Global Warming Potential of CO2 and nitrogen fertilizer runoff creates marine dead zones, such as in the Gulf 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

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



- **Canola and Soybean**
  - improved oil properties: stable, resistant to high temperatures, long storage


Golden Rice

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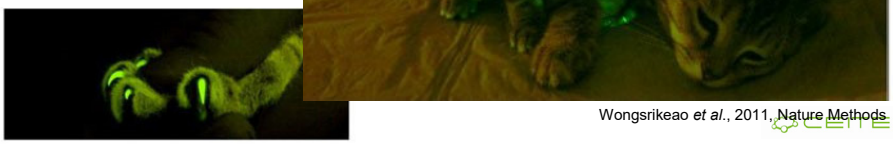
While most biotech crops have characteristics that enhance their cultivation, those with enhanced consumer characteristics are being developed. For example many children in SE Asia develop blindness because of a deficiency of vitamin A. Golden rice is engineered with genes from maize to be high in the 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 mosaicity and no silencing in F1 generation
  - lymphocytes of transgenic animals resistant to replication of FIV



Wongsrikeao *et al.*, 2011, Nature Methods

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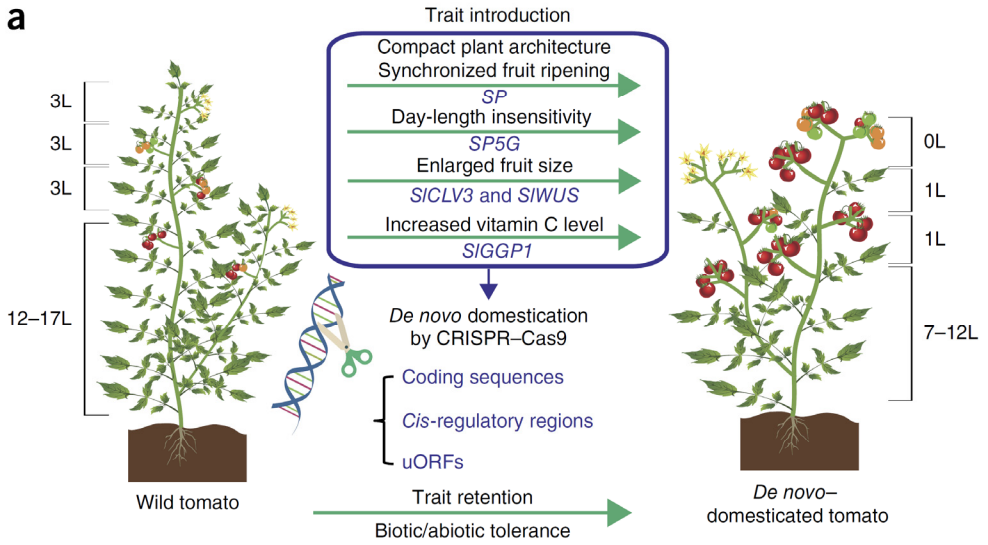
Feline immunodeficiency virus (***FIV***), the “cat AIDS" is a *Lentivirus* that affects cats worldwide, with 2.5% to 4.4%[1][2] of felines being infected (Wikipedia)

Osnova

- Lékařství
  - Molekulární diagnostika
  - Individualizovaná medicína
  - Genová terapie
- Biotechnologie
- Geneticky Modifikované Organismy
  - Transgenoze
  - Editování genomu

Gene Editing in Plant Domestication



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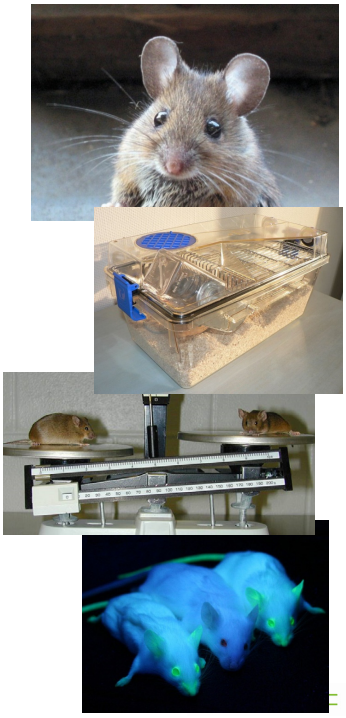
- Modelové organismy

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



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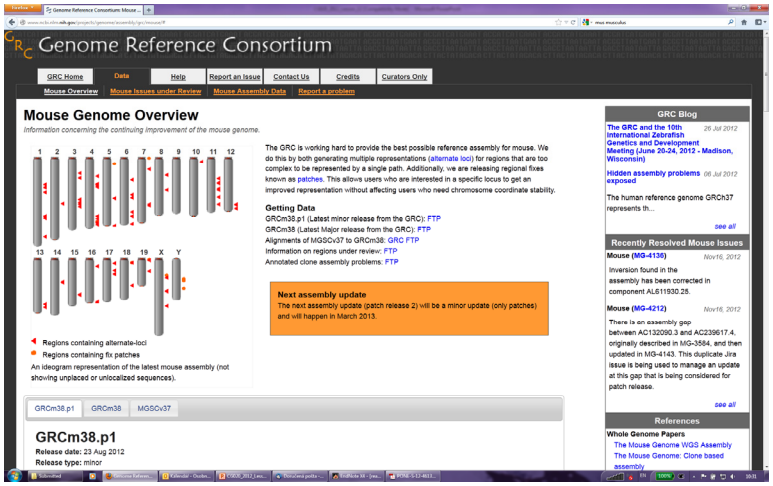
More info about mouse at http://www.informatics.jax.org/greenbook/index.shtml.

Mus musculus
house mouse

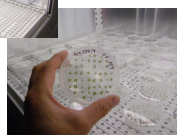
- Genome known since 2002 (http://www.ncbi.nlm.nih.gov/projects/genome/assembly/grc/mouse/)



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 od physiological experiments
- High natural variability (approximately 750 ecotypes (Nottingham Arabidopsis Seed Stock Centre))



Columbia 0

Landsberg 0

Wassilewskija 0

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

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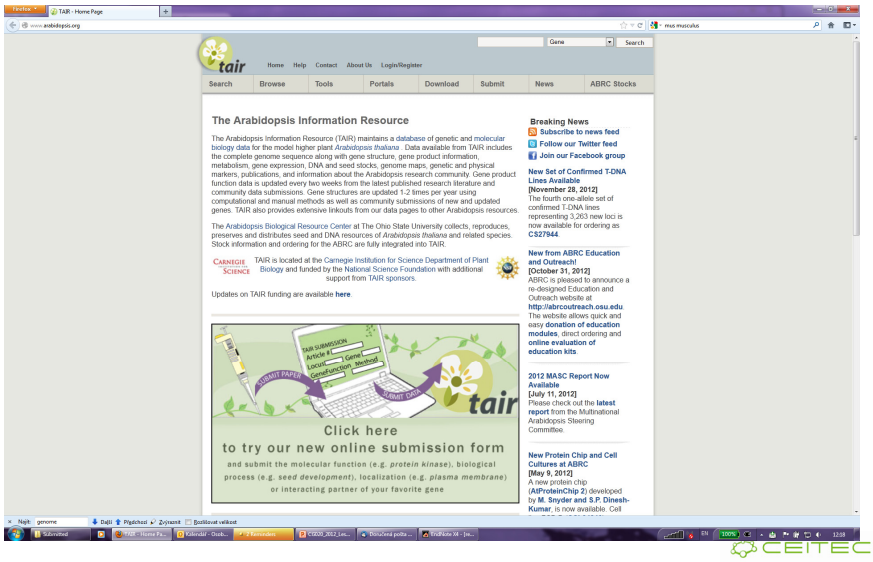
Arabidopsis thaliana

mouse-ear cress

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



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  - Transgenoze
  - Editování genomu
- Modelové organismsy
- Principy PCR

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Polymerase Chain
Reaction

Klíčové koncepty

- Techniky využívající pokročilé genetické a genomické přístupy zásadním, způsobem mění naše možnost dosahovat požadovaných cílů v medicíně i zemědělství.
- Možnost programovatelné editace genomu slibuje zásadní obrat v léčbě zejména dědičně podmíněných chorob a ve šlechtění nových odrůd i ras
- Je nezbytná přísná kontrola s jasně nastavenými pravidly pro všechny, ale nikoliv úplný zákaz

Diskuse