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Functional genomics

• To define genes’ functions and understand the relationship between genotype and phenotype
Outline

• Resources, approaches, technologies, and tools used in functional genomics studies
  – Chemical, physical, and insertional mutagens induced mutations
  – Reverse genetics
  – Site-specific mutation
  – Forward genetics
  – Gene expression profiling (Dr. Jason Fiedler)
  – Gene expression regulation
    ✓ Post gene expression regulation and RNA editing
    ✓ Epigenetic modification
Final exam

• About 10 questions (100 points)

  – Basic terms and knowledge: mutagens, restriction enzyme, gene editing, RNA editing, QTL mapping, small RNA, etc.

  – Methods and applications: methods/mutagens used for inducing mutation and their advantages, gene editing methods, QTL mapping, map based clone, etc.
Why is functional genomics important?

- **Weeds control by herbicide**
  - Glyphosate (Roundup) kills plants by inhibiting 5-enolpyruvylshikimate-3-phosphate synthase (EPSPS)
  - EPSP is an essential precursor for some amino acids, which are used to produce protein

![Glyphosate mechanism diagram]
Why is functional genomics important?

- Some micro-organisms have a version (allele) of EPSPS resistant to glyphosate inhibition
Why is functional genomics important?

- Genetic modified (GM) crops
  - The resistant EPSPS gene was transferred into crops, then the genetic modified (GM) crops have glyphosate resistance
  - The success of glyphosate is due in large part to the high specificity of this simple small molecule towards EPSPS
  - In 2015, 89% of corn, 94% of soybeans, and 89% of cotton produced in the US were genetically modified to be herbicide-tolerant
  - Over 250 million pounds of glyphosate sprayed on American crop fields each year are used on genetically engineered (GE) crops like corn and soybean

Using genetic modified cultivars, weeds can be well controlled by herbicide, reducing cost and yield loss
Why is functional genomics important?

• Disease control
  – Insecticide to kill mosquitoes
    o In 1977, a child was dying of malaria (caused by a parasite) every 10 seconds; mosquitoes carry and spread the parasite.
    o Pyrethroids, an insecticide, has played an outsize role in the global fight against malaria in the last decades
      ✓ “Between 2000 and 2015, ~633 million malaria deaths were averted, with 78% of that decline due to the insecticide; treating people with antimalarial drugs accounted for the remaining 22%.”
    o First detected in Ivory Coast in 1993, resistance to pyrethroids was rare until about 10 years ago, when it began racing across the continent of Africa
Why is functional genomics important?

- **Disease control**

After 40 years, the most important weapon against mosquitoes may be failing

**BY KAI KUPFERSCHMIDT** | **OCT. 13, 2016**

As mosquitoes develop resistance to pyrethroid insecticides, researchers are forced to look for alternatives.

Brazil will release billions of lab-grown mosquitoes to combat infectious disease. Will it work?

**BY KELLY SERVICK** | **OCT. 13, 2016**

Desperate health officials are investing in new control strategies, but the evidence—and the economics—are still hazy.
Why is functional genomics important?

• Disease control
  – The excess tTAV protein in genetically modified mosquitoes may tie up the cell's protein production machinery
  – Oxitec mosquitoes bearing the lethal gene grow up feeding on tetracycline, an antibiotic that blocks tTAV activity and keeps them alive
Why is functional genomics important?

• **Clinical care**
  – Pharmacogenomics to genomic (personalized) medicine
    » Study of genetic variation on drug responses
    » Using an individual’s genome to determine whether or not a particular therapy, or dose of therapy, will be effective

http://imagenetics.sanfordhealth.org/genetic-medicine/
Why is functional genomics important?

• Clinical care
  – More than 100 Food and Drug Administration (FDA)-approved drugs have pharmacogenomics information in their labels, in diverse fields such as analgesics, antivirals, and anti-cancer therapeutics

• [http://www.fda.gov/Drugs/ScienceResearch/ResearchAreas/Pharmacogenetics/ucm083378.htm](http://www.fda.gov/Drugs/ScienceResearch/ResearchAreas/Pharmacogenetics/ucm083378.htm)
Why is functional genomics important?

- **Gene therapy**
  
  - Uses genes to treat or prevent disease. Inserting a gene into a patient’s cells instead of using drugs or surgery.
  
  - Several approaches to gene therapy, including:
    
    - Replacing a mutated gene that causes disease with a healthy copy of the gene.
    - Inactivating, or “knocking out,” a mutated gene that is functioning improperly.
    - Introducing a new gene into the body to help fight a disease.

  - Although gene therapy is a promising treatment option for a number of diseases, the technique remains risky and is still under study to make sure that it will be safe and effective. Gene therapy is currently being tested only for diseases that have no other cures.

Why is functional genomics important?

- **Gene therapy**
  - [https://agtc.com/science/](https://agtc.com/science/)
  - [https://www.youtube.com/watch?v=GGEiaDau7hU](https://www.youtube.com/watch?v=GGEiaDau7hU)
CRISPR will change humanity forever?

• Genome editing is a type of genetic engineering, where DNA is inserted, replaced, or deleted for a target site in the genome using artificially engineered nucleases followed by DNA repairing

• http://www.sciencealert.com/this-video-explains-perfectly-why-crispr-really-will-change-humanity-forever

• https://crisprcas.pioneer.com
References


