

# Case It: Case-based Learning in Molecular Biology

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The screenshot displays the Case It! 6.06 software interface. At the top, there is a menu bar with 'Quit', 'Notes', and 'Tutorial'. The main window is divided into three horizontal sections. The top section shows a 'Heat block' on the left, a pipette in the center, and a multi-well plate on the right. The middle section features a biohazard container on the left, a central text box with the title 'Case It! 6.06' and a bulleted list of topics, and a 'Click here to begin...' button. The bottom section shows a power supply unit on the left, a gel electrophoresis apparatus in the center, and the 'MADE WITH macromedia' logo on the right.

Quit Notes Tutorial

Heat block

*Case It! 6.06*

- DNA / protein electrophoresis
- Restriction digests / mapping
- Southern / Western / Dot blots
- Multiplex PCR and ELISA
- Bioinformatics analyses
- DNA chips (microarrays)

Click here to begin...

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# Overview

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- Introduction to *Case It!* project
- New cases on honey bee biology
  - Virus detection by PCR
  - Bee virus bioinformatics
- Case It Mobile prototype
- Open-ended research applications  
(if time permits)
  - HHMI SEA-PHAGES project

# Case It! Project

URL for Case It! Home Page:

<http://www.caseitproject.org>

- Includes tutorials and download links
- Access to case descriptions

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# Case It! Project

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Electronic framework for analyzing and discussing case studies in molecular biology

- Genetic and infectious diseases and associated ethical issues
- Students gather background information on cases
- Analyze DNA and/or protein sequences using Case It! simulation
- Online poster sessions
- Role-playing



# Techniques for DNA and protein analysis

## Case It! simulation

### Features of Case It! simulation

- DNA analysis
  - PCR, Restriction enzyme digestion, electrophoresis, Southern blot, Dot blot
- Protein Analysis
  - ELISA, Western blot, protein electrophoresis
- Microarrays (SNP and Expression)
- Bioinformatics tools
  - Connection to BLAST and other NCBI tools
  - Integration with MEGA software - Alignments, Tree building
- Case studies in genetic and infectious diseases and other biology topics

# Honey bee cases

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- Collaborators:
  - Kim Mogen and Brad Mogen, UWRF Biology
  - Marla Spivak, UM Bee Lab
- Incorporating research on honey bee health and colony collapse disorder in first-year biology classes
  - Virus detection by RT-PCR
  - Effects of pesticide exposure, mite levels, etc.

# Case scenario

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Honey bees are commonly exposed to pesticides as they forage for pollen and nectar. Some pesticides are known to disorient bees and thus affect their behavior. Sub-lethal exposures of some pesticides are considered possible contributing factors to Colony Collapse Disorder (CCD). Dr. Muskiver was curious if pesticide exposure was linked to virus infection, another possible contributing factor to CCD.

To test this question, Dr. Muskiver set up test colonies, and fed the honey bees either with untreated pollen or pollen treated with sub-lethal doses of pesticides. She then tested the bees for the presence of several viruses using multiplex PCR.

# PCR Result



1.0 % agarose  
runtime = 60  
100 volts

1. 100 bp ladder 2. neg control 3. pos control all viruses  
4. Hive 1 pesticide-treated 5. Hive 2 pesticide-treated  
6. Hive 3 no pesticide 7. Hive 4 no pesticide

# Case scenario - bioinformatics

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Recent declines in honey bee populations have given rise to the syndrome named Colony Collapse Disorder (CCD). Several potential stressors have been identified. A team of research scientists, funded by the North American Honey Bee Council, decide to survey colonies from around North America for two of the notable stressors – Deformed Wing Virus (DWV), a virus that causes wing deformation, and *Varroa destructor*, a parasitic mite that feeds on the bee.

It has recently been reported that there are *V. destructor* transmit certain strains of DWV more effectively, and that long-term mite infection reduces virus diversity and leads to the prevalence of more pathogenic viruses. The scientists are interested in testing the relationship between DWV strains and the *Varroa* mite in North America.

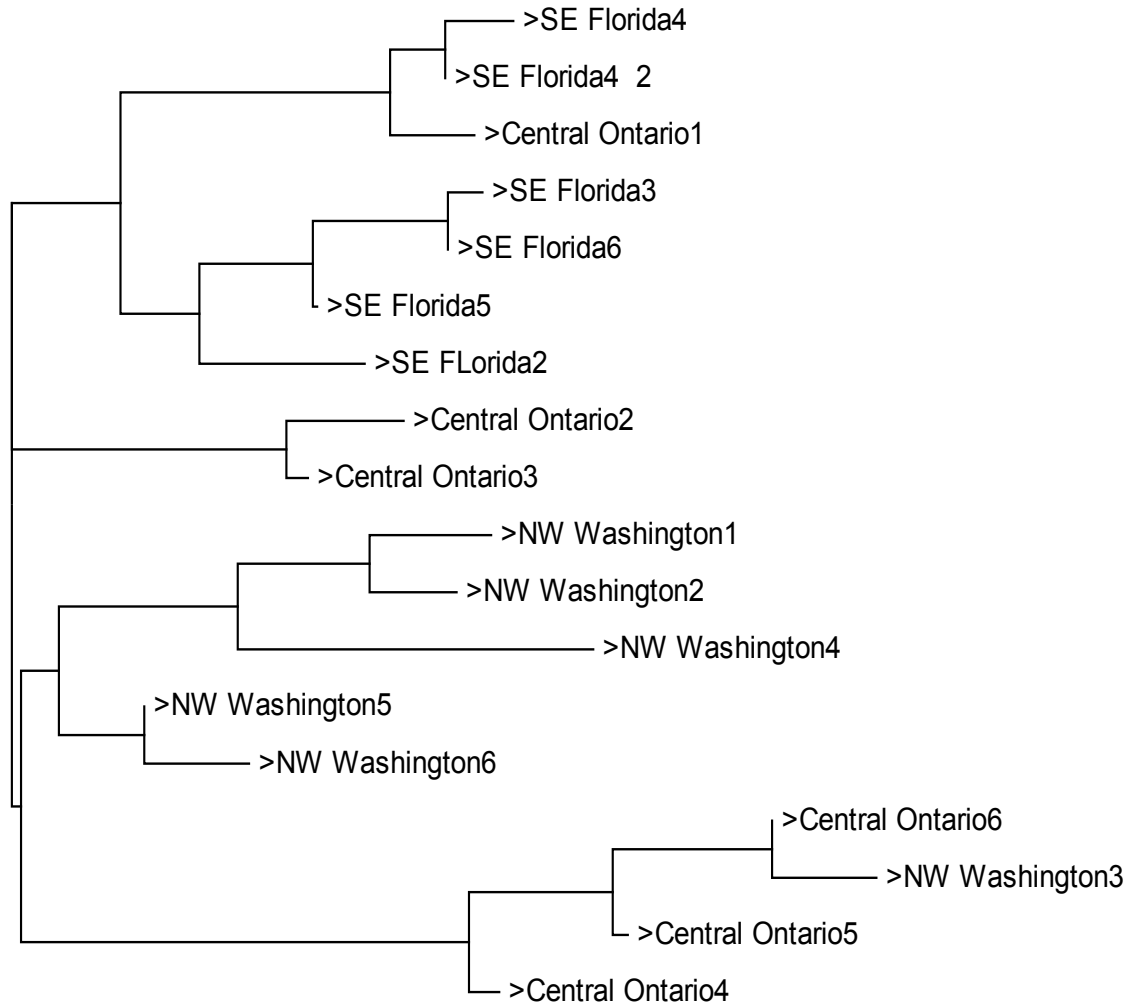
# Case scenario - bioinformatics

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Bees tested from:

- Central Ontario - low mite levels
- Northwestern Washington - low mite levels
- Southeast Florida - high mite levels
- Oahu, Hawaii - high mite levels
- Northern Arizona - moderate mite levels
- Southern British Columbia - moderate mite levels

# DNA sequence analysis





# *Case It! mobile*

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- Access to case scenarios and lab results from tablets, smart phones, and Macs
- See prototypes at [www.caseitproject.org/mobile](http://www.caseitproject.org/mobile)

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If there is time...

**ADDITIONAL SLIDES**

# Open-ended research

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- HHMI SEA-PHAGES project in General Biology course for freshmen
- Lab sequence replaced by phage research
  - Isolate mycobacteriophages from soil
  - Isolate phage DNA and analyze by restriction enzyme digestion
  - Select one phage to send for sequencing

# Open-ended research

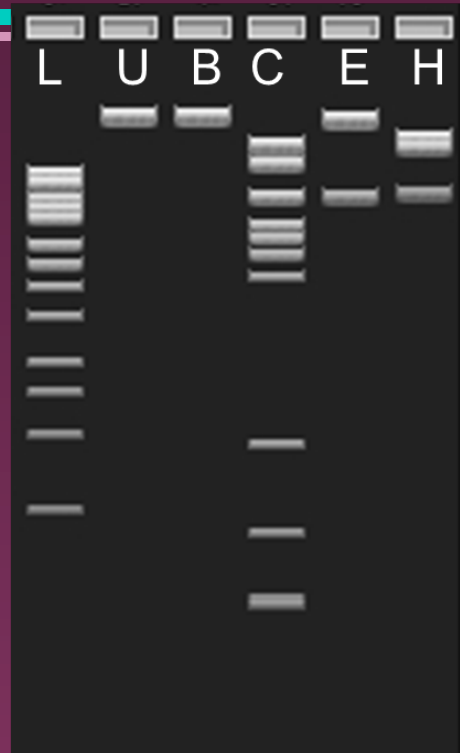
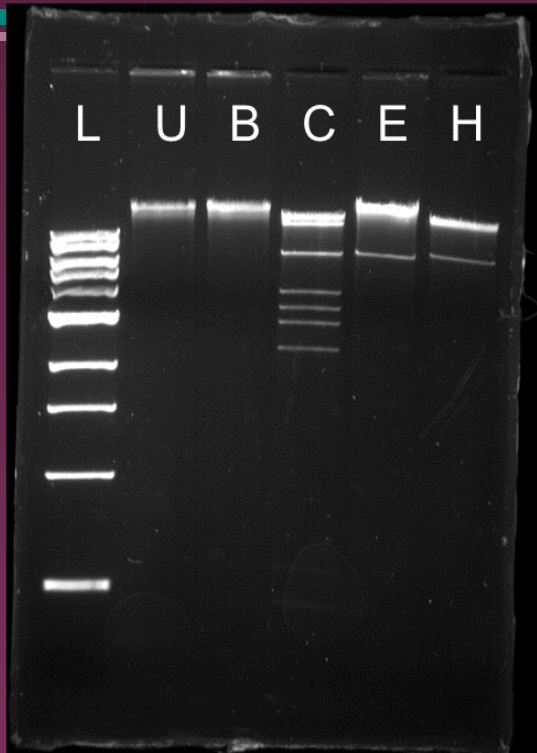
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- Spring semester – phage genomics
- Retrieve complete phage genome sequence
  - Annotate genes
  - Comparative genomics
  - Research projects on phage biology
- [www.phagesdb.org](http://www.phagesdb.org)

Abrogate lab gel

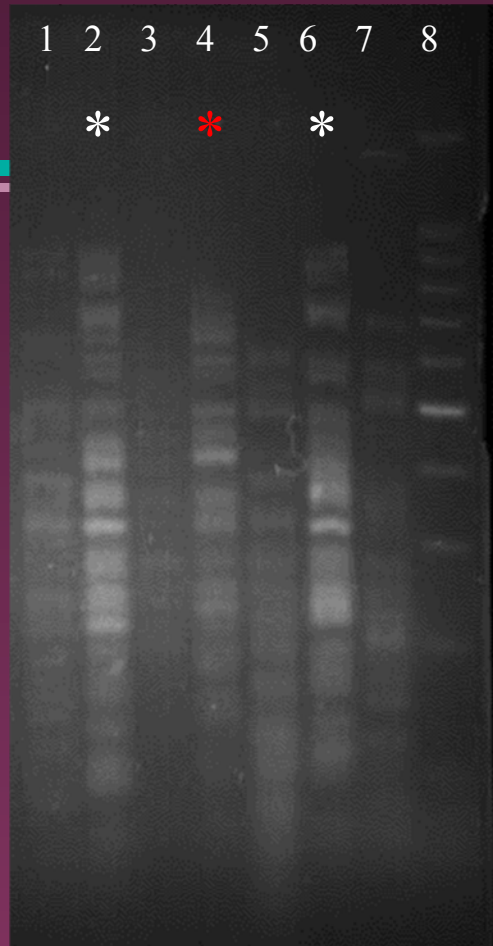
Abrogate virtual gel

Bxb1 virtual gel

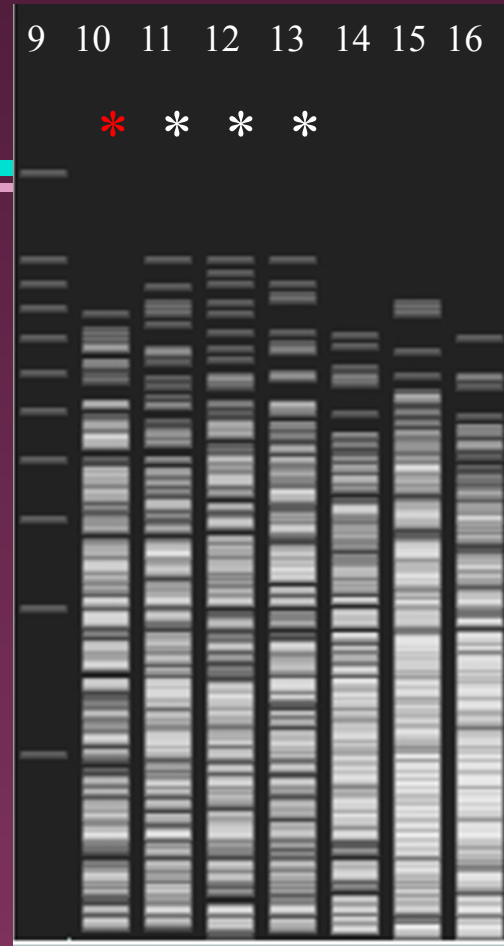


L=1 kb ladder; U=undigested; B=BamHI; C=ClaI; E=EcoRI  
H=HindIII

## HaeIII Lab Gels



## HaeIII Virtual Gel



- Ran separate in 2% agarose gel
- \* Indicates A1 phages
- \* Indicates Abrogate
- Abrogate significantly different from A1 phages

# Huntington's disease case

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Case scenario - from Case It web site

Restriction enzyme digestion and Southern blot  
or

PCR and gel electrophoresis

Sequence analysis - detect triplet base repeat,  
sequence alignment and BLAST to identify  
gene



# Sample case: Huntington's Disease

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Susan is a 23-year-old whose father, age 55, and paternal aunt, age 61, have been diagnosed with Huntington's chorea. A paternal uncle, age 66, appears to be unaffected by the disease. Susan wants to know if she inherited the mutated gene from her father so that she can prepare for that future if necessary. She arranges to undergo DNA testing for Huntington's. Her 17-year old brother, John, also decides to be tested after talking with Susan.

# Role playing

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- Students present the results of their case analysis as a web poster
  - Includes a statement to the “family”
  - Wiki system provides group web posters with associated discussions

[caseitconferencing.wikispaces.com](http://caseitconferencing.wikispaces.com)
- Visit another group’s web poster and post questions in the role of a person in the case
- Authors respond to questions in the role of a genetic or health counselor

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  - Huntington's disease example
- New – microarray cases (SNP and expression)
  - Breast cancer expression microarray
- Case It Mobile prototype
  - HIV cases with introduction to bioinformatics
- Open-ended research applications
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# Breast cancer case

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- Woman diagnosed with breast cancer, without prior risk factors
- Microarray analysis used to determine potential for aggressive growth and invasiveness of tumor

# Breast cancer microarray case

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Sarah was devastated when she received a diagnosis of breast cancer. It did not seem to run in her family, so she assumed she did not have to worry about it. She is grateful for the support of her friends, especially Molly, who is a clinical lab pathologist. Molly is helping her think about the difficult decisions regarding how aggressive her treatment should be, in terms of surgery, chemotherapy, etc.

# Breast cancer microarray case

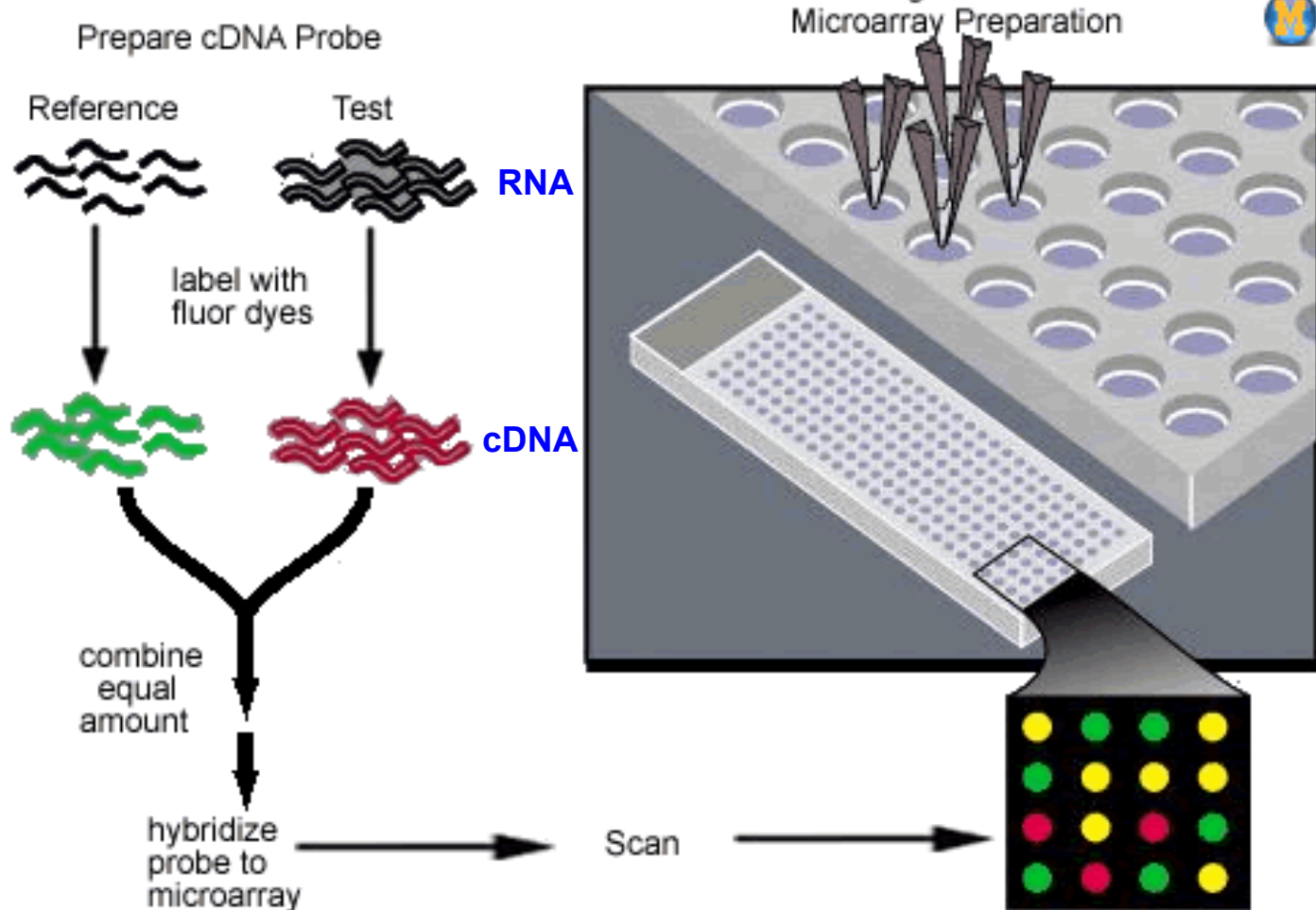
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Molly explains that the oncologist recommended running a lab test that uses a microarray to measure the expression of specific genes. The pattern of gene expression can predict how quickly the tumor cells will grow and whether they will respond to various treatments. Sarah is meeting with the oncologist to review the results, and she has asked Molly to go with her.



# Microarray method

## General Overview of cDNA Microarray Process





# Breast cancer microarray

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Genes associated with increased cell proliferation (or rapid growth) in breast cancer tumors:

- Ki-67, STK15, Survivin, Cyclin B1, MYLB2

Genes associated with increased tumor cell invasion:

- Stomelysin 3, Cathepsin L2

Genes associated with proliferation in response to estrogen:

- SCUBE2, PGR, ERBB2

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# HIV Case studies

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Case scenario - video and text (Anna case ), from Case It web site

ELISA test - initial screening (new autoloader feature)

Western blot to follow up ELISA results

PCR to amplify HIV DNA for viral load or sequence analysis

Sequence analysis to determine source of HIV infection

# Case It! Project

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## Additional Collaborators

- Mary Lundeberg, Biology Department, University of Wisconsin-River Falls
- Chi-Cheng Lin, Computer Science Department, Winona State University
- Arlin Toro, Biology Department, Inter American University of Puerto Rico-San German campus
- Rafael Tosado, Medical Technology Program, Inter American University of Puerto Rico-Metropolitan Campus
- C. Dinitra White, Biology Department, North Carolina A&T State University