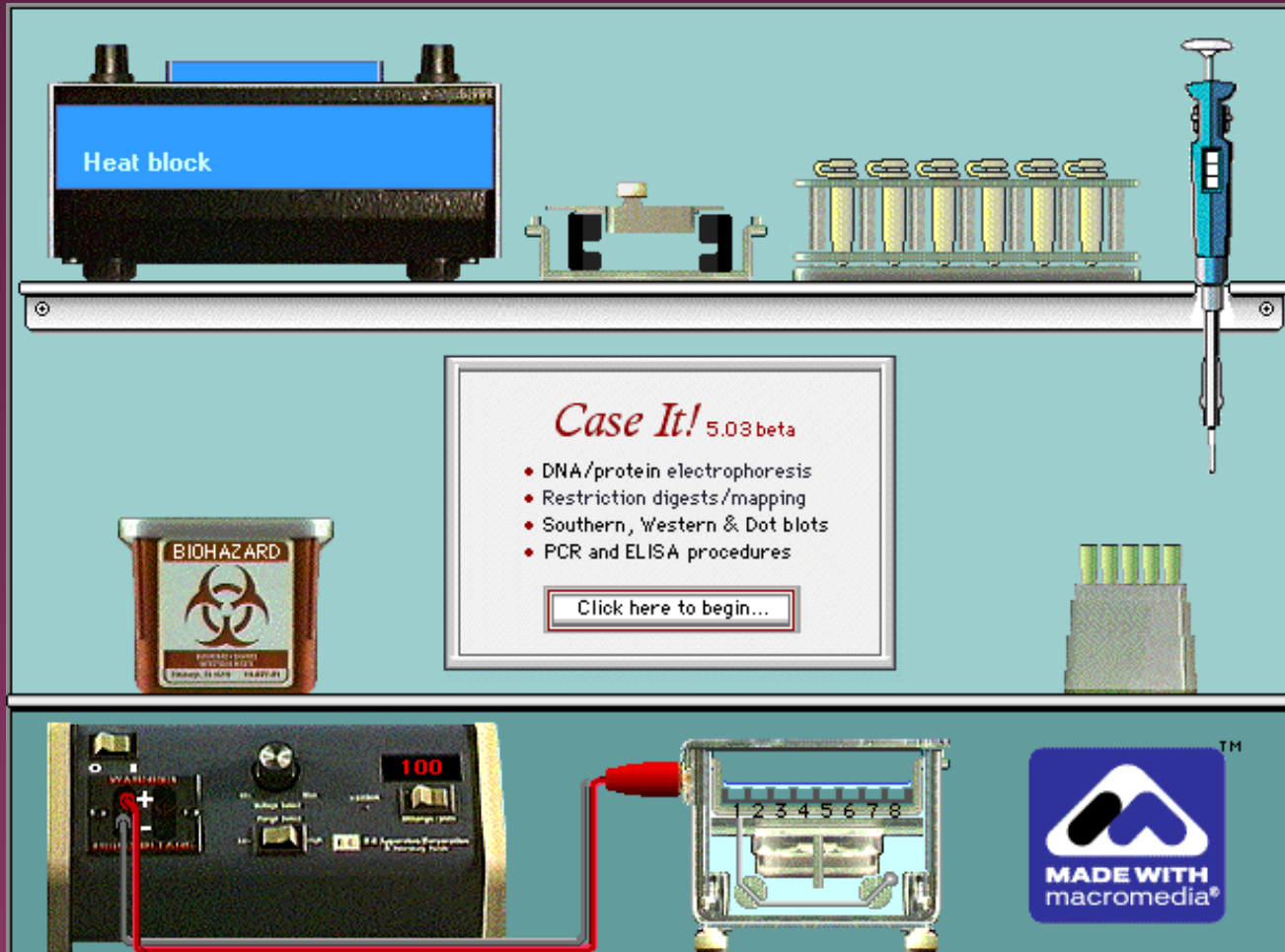# Case It workshop: integrating molecular biology computer simulations and bioinformatics into case-based learning and student research

Mark Bergland and Karen Klyczek University of Wisconsin-River Falls

Coastal Carolina University, April 2012

Case It! Project

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

Workshop overview - morning

- Introduction to Case It! Project

- HIV cases – set in U.S. and Africa
  - Videos, ELISA, Western blot, Bioinformatics

- Honey bee case (developing a new case)
  - Multiplex PCR and tree building
  - Ideas for new cases

- Microarray cases
  - HSV multiplication, gene expression
  - SNP microarray for HIV resistance

Workshop overview - afternoon

- Introduction to Case It! Project

- Huntington's chorea case
  - PCR to detect triplet repeat
  - Sequence alignment and BLAST

- Prostate cancer case
  - Microarray to detect SNPs associated with high blood PSA levels

Case It! Project

URL for <u>Case It! Home Page:</u>

<u>http://caseit.uwrf.edu</u>

- Includes tutorials and download links
- Access to cases descriptions, problem spaces

Contact: mark.s.bergland@uwrf.edu

Supported by the TUES program (formerly CCLI) of the National Science Foundation

Case It! Project

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 and protein electrophoresis
- Restriction enzyme digestion and mapping
- Southern blotting
- Dot blotting
- Polymerase Chain Reaction (single and multiplex)
- ELISA
- Western blotting
- Microarrays (SNP and expression)

➢ Case studies in genetic and infectious diseases and other biology topics

Case It! Simulation
New features in version 6.06

- Bioinformatics tools
  - » Open and save FASTA sequences
  - » Connection to BLAST and other NCBI tools
  - » Integration with MEGA software
    - Alignments
    - Tree building
  - » Other

- Microarray simulation
  - » SNP
  - » Expression

HIV Case studies

Case scenario - video and <u>text</u> (Lisa case), from Case It web site
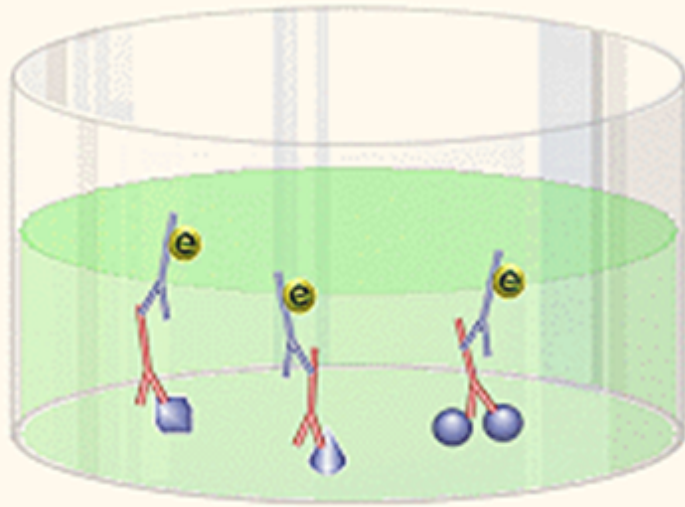
<u>ELISA</u> test - initial screening (new autoload feature)
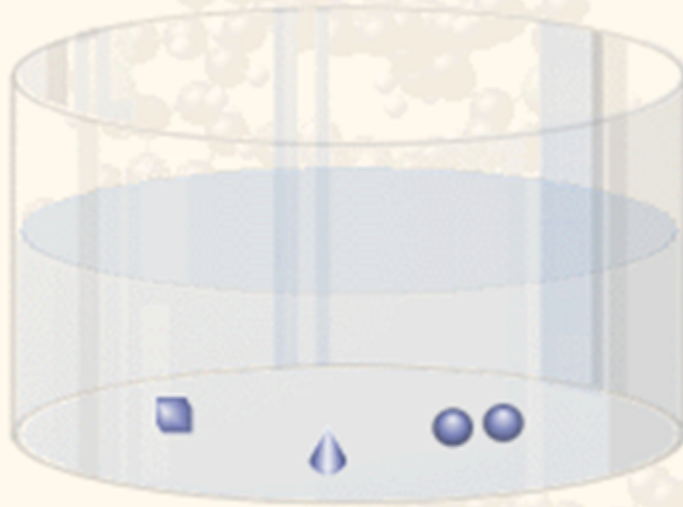
<u>Western blot</u> to follow up ELISA results

<u>PCR</u> to amplify HIV DNA for <u>viral load</u> or sequence analysis

<u>Sequence analysis</u> to determine source of HIV infection

Positive ELISA Test

Negative ELISA Test

■ ▲ ● Partially purified, inactivated HIV antigens pre-coated onto an ELISA plate

Patient serum which contains antibodies. If the patient is HIV+, then this serum will contain antibodies to HIV, and those antibodies will bind to the HIV antigens on the plate.
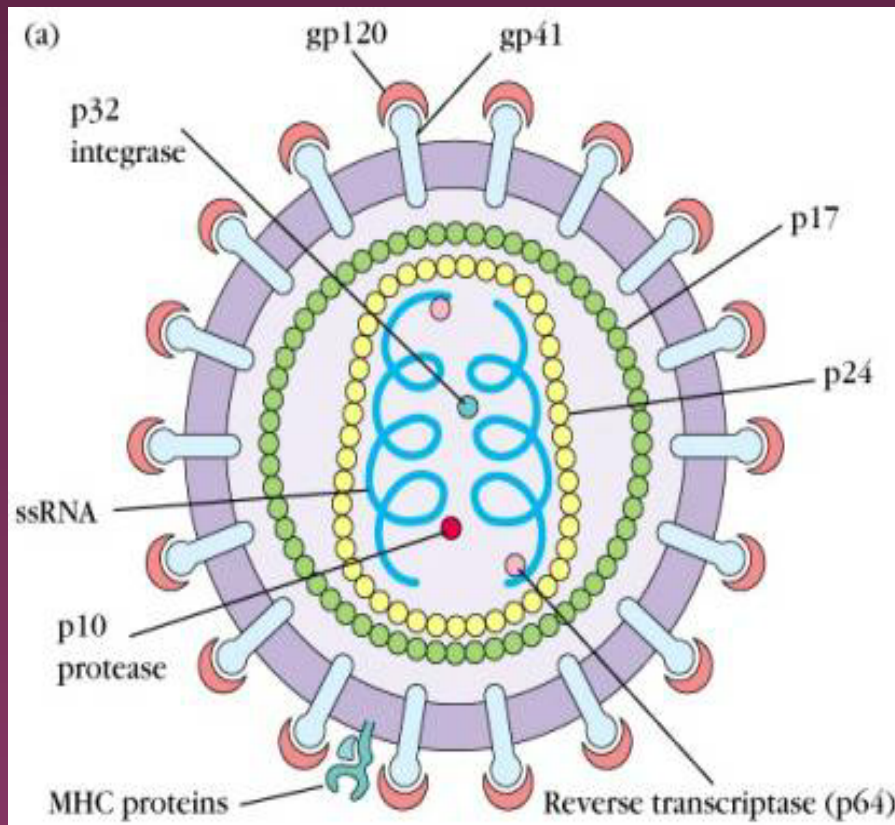
Anti-human immunoglobulin coupled to an enzyme. This is the second antibody, and it binds to human antibodies.

Chromogen or substrate which changes color when cleaved by the enzyme attached to the second antibody.
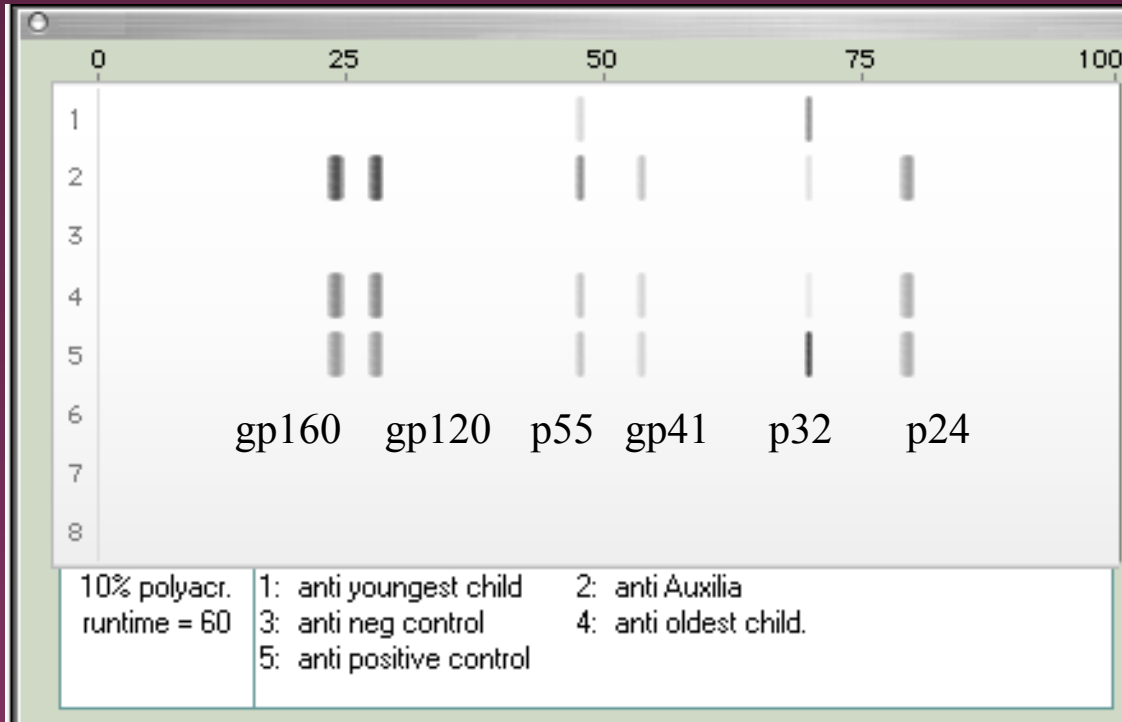
http://www.biology.arizona.edu/

HIV viral proteins

gp160	Precursor of envelope protein (env)
gp120	Outer envelope protein (env)
p55	Precursor of core proteins (gag)
p41	Transmembrane envelope protein (env)
p32	Integrase (pol)
p24	Inner core protein (gag)

Western Blot
Band pattern interpretation

Band interpretation:

|	
No bands	Negative
Bands for two of these three proteins: gp120, gp41, p24	Positive
Any other band pattern	Indeter-minate

HIV resistance case

- Kenyan sex workers resistant to HIV infection despite repeated exposures

- <u>Microarray</u> analysis used to identify SNPs associated with HIV resistance

Breast cancer case

- Woman diagnosed with breast cancer, without prior risk factors

- <u>Microarray</u> analysis used to determine expression of genes linked to potential for aggressive growth and invasiveness of tumor

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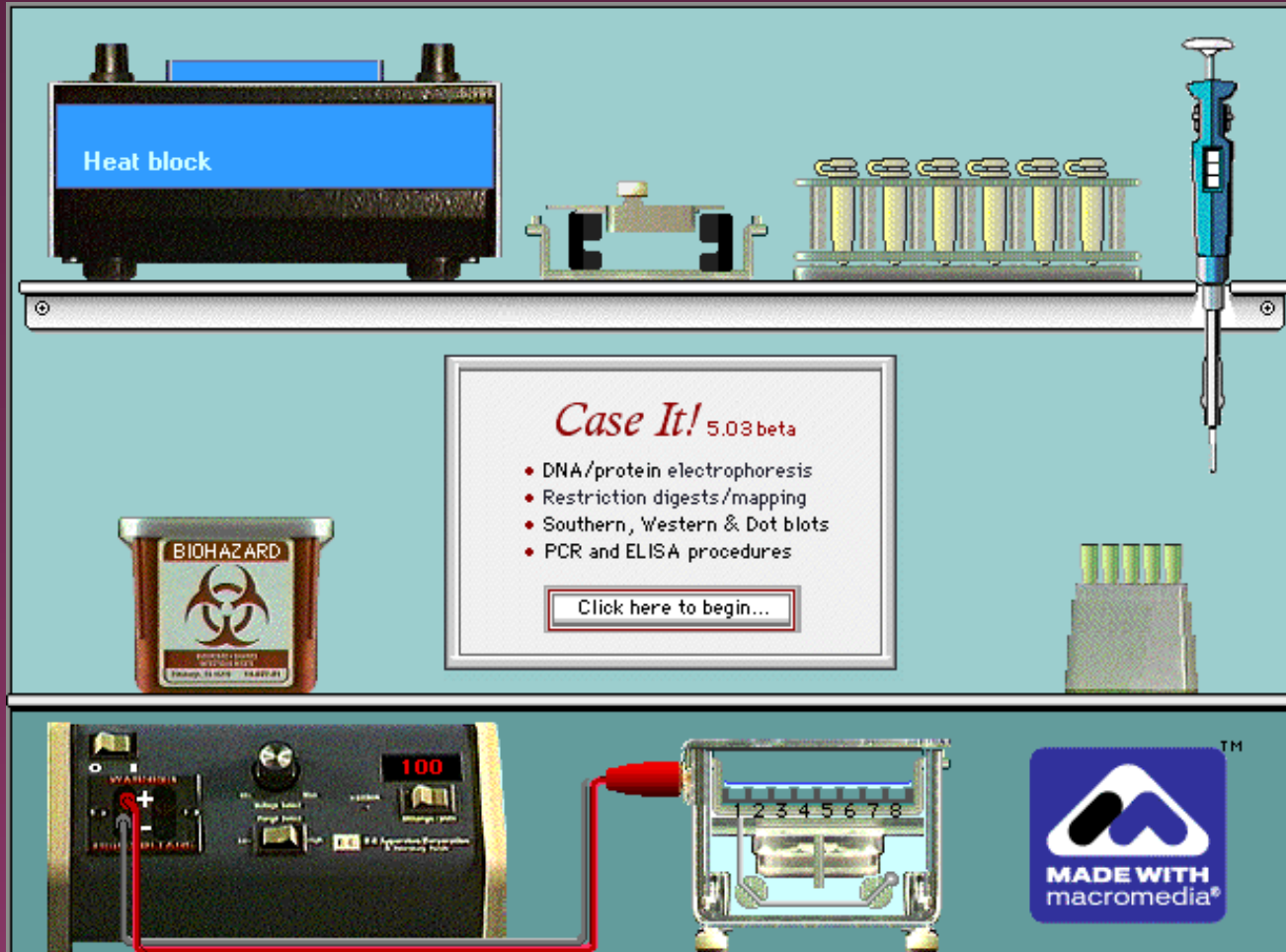
Coastal Carolina University, February 2012

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  - » SNP
  - » Expression

Huntingon's disease case

Case scenario - from Case It web site

Restriction enzyme digestion and Southern blot

PCR and gel electrophoresis

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

Prostate cancer case

- PSA blood test, link to prostate cancer being questioned

- SNPs associated with naturally high blood PSA levels detected by <u>microarray</u>

  ➤ Should biopsy be done based on high PSA test result?