03-713 Data Integration Practicum

Introduction – 3/19/13

Course Introduction

Objective:

Build data integration pipeline (new software + incorporation of existing software)

That solves the given biological problem (described in a few slides)

Very team-oriented class (we will assign teams today or tomorrow)

Very self-directed; simulates a more real-world bioinformatics analysis scenario.

Survey!

Survey about past experience – will be used to assemble teams by the instructors.

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Everyone introduce themselves:

say what program they're in

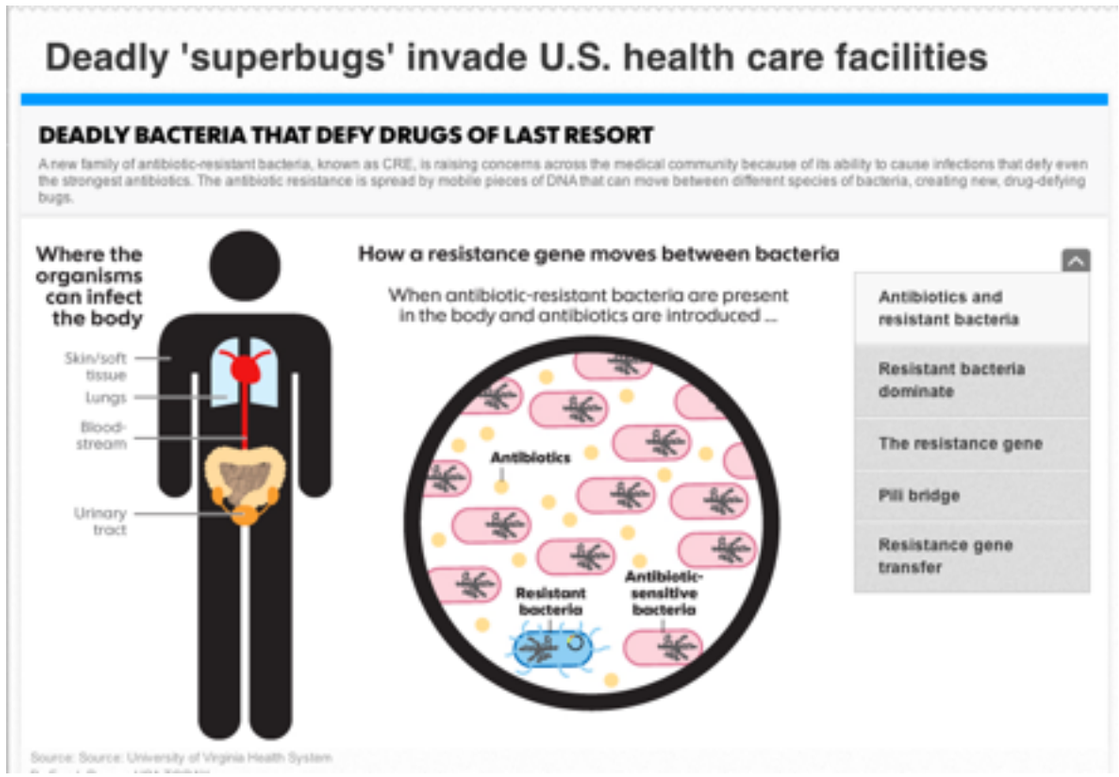
why they're interested in the course

CS or Bio?

what they hope to do after they graduate?

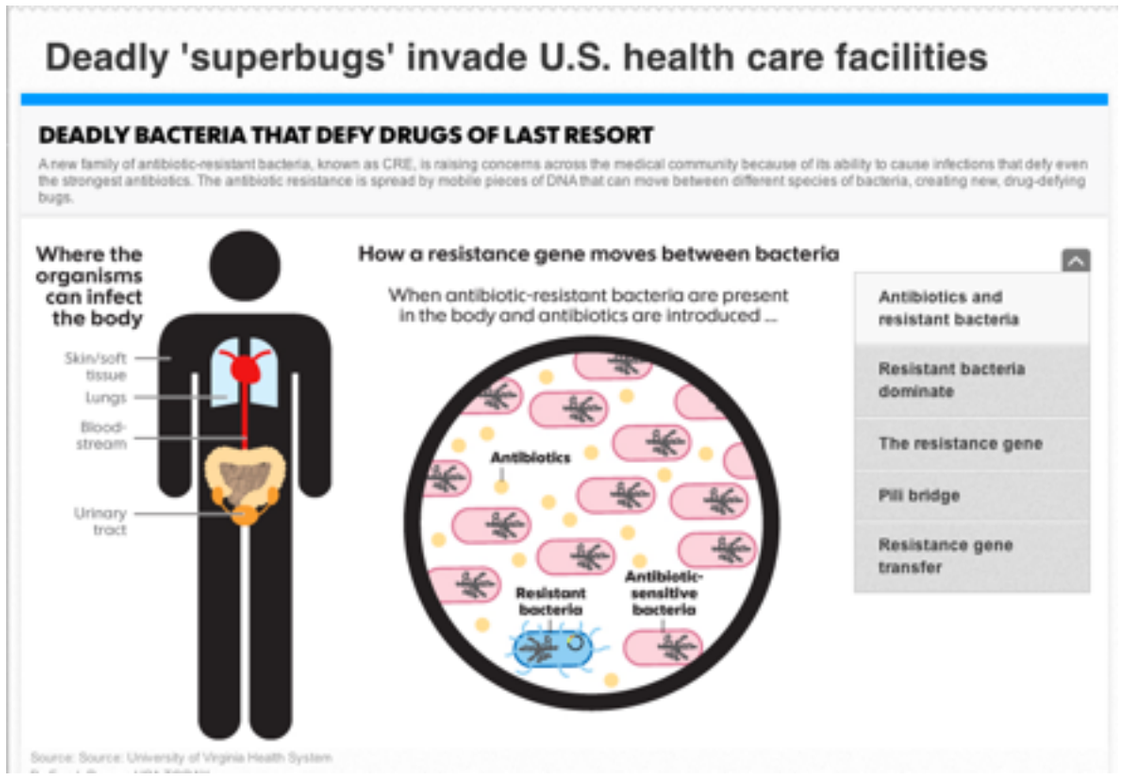
Superbugs!

Superbugs!



http://www.usatoday.com/story/news/nation/2012/11/29/bacteria-deadly-hospital-infection/1727667/

Superbugs!



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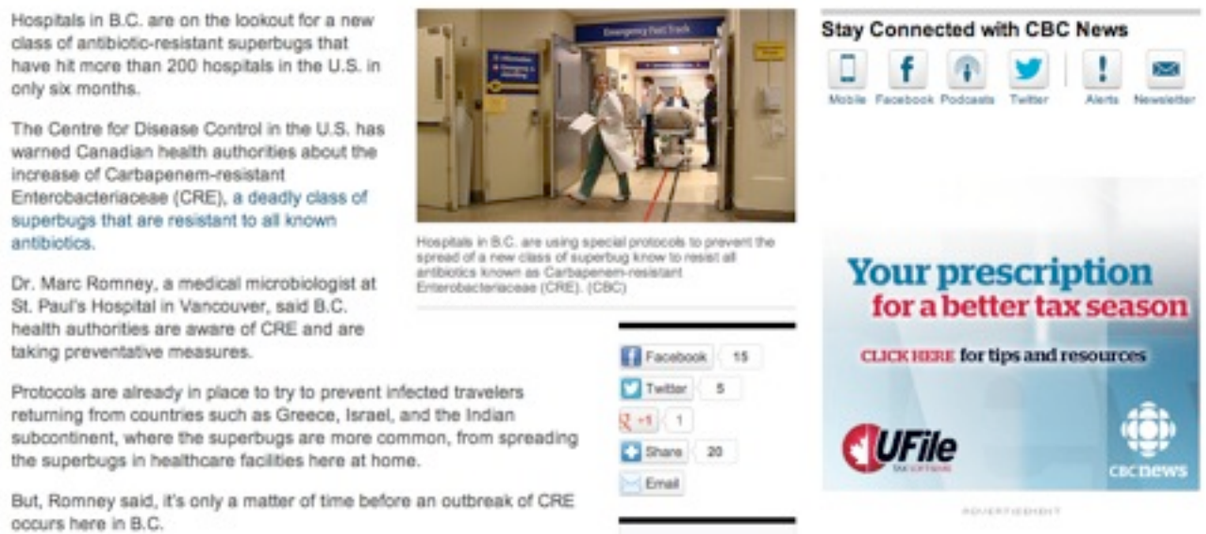


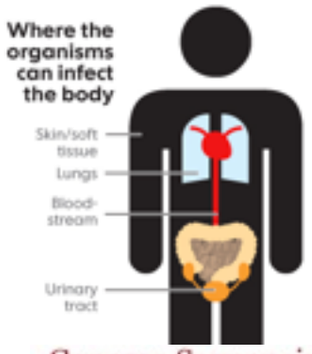
http://www.cbc.ca/news/health/story/2013/03/13/bc-superbug-cre.html

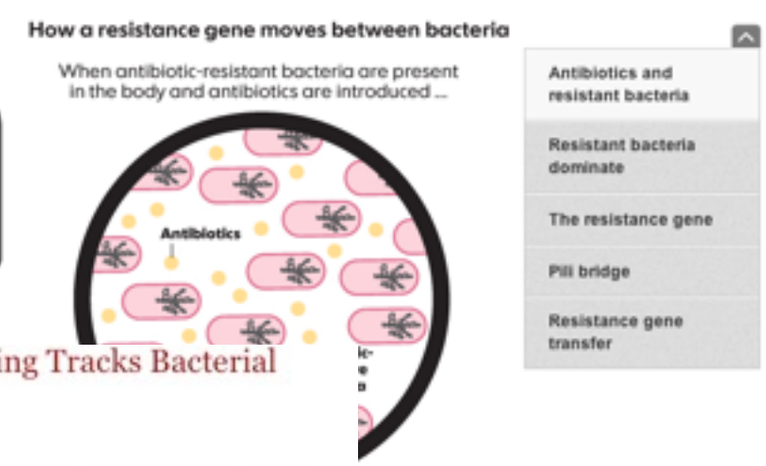
Superbugs!

Deadly 'superbugs' invade U.S. health care facilities

DEADLY BACTERIA THAT DEFY DRUGS OF LAST RESORT

A new family of antibiotic-resistant bacteria, known as CRE, is raising concerns across the medical community because of its ability to cause infections that defy even the strongest antibiotics. The antibiotic resistance is spread by mobile pieces of DNA that can move between different species of bacteria, creating new, drug-defying bugs.





Genome Sequencing Tracks Bacterial Outbreak

Last year, a deadly outbreak of antibiotic-resistant bacteria kept NIH's Clinical Center in a state of high alert. NIH staff used genome sequencing to track the microbes' spread, an approach that can be used to help control similar outbreaks in the future.

http://www.cbc.ca/news/health/story/2013/03/13/bc-superbug-cre.html

B.C. hospitals on watch for new CRE superbugs

New class of antibiotic-resistant superbugs could make routine treatments dangerous again

By Meera Dalal CBC News Posted: Mar 14, 2013 12:07 AM ET | Last Updated: Mar 14, 2013 2:02 PM ET

Hospitals in B.C. are on the lookout for a new class of antibiotic-resistant superbugs that have hit more than 200 hospitals in the U.S. in only six months.

The Centre for Disease Control in the U.S. has warned Canadian health authorities about the increase of Carbapenem-resistant Enterobacteriaceae (CRE), a deadly class of superbugs that are resistant to all known antibiotics.

Hospitals in B.C. are using special protocols to prevent the spread of a new class of superbug know to resist all antibiotics known as Carbapenem-resistant Enterobacteriaceae (CRE). (CBC)

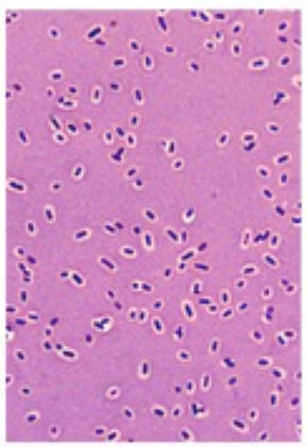
Dr. Marc Romney, a medical microbiologist at St. Paul's Hospital in Vancouver, said B.C. health authorities are aware of CRE and are taking preventative measures.

Protocols are already in place to try to prevent infected travelers returning from countries such as Greece, Israel, and the Indian subcontinent, where the superbugs are more common, from spreading the superbugs in healthcare facilities here at home.

But, Romney said, it's only a matter of time before an outbreak of CRE occurs here in B.C.

http://www.nih.gov/researchmatters/september2012/09102012outbreak.htm

In June 2011, a severely ill 43-year-old woman was transferred from a hospital in New York to the NIH Clinical Center, a 243-bed research hospital on the NIH campus in Bethesda, Maryland. The medical staff knew she was infected with bacteria that were resistant to multiple antibiotics, so she was put in isolation immediately. Additional precautions were taken to keep the bacteria away from other patients.



Klebsiella pneumoniae. Image by Spike Walker, Wellcome Images. All rights reserved by Wellcome Images.

After a month in the hospital, the woman was discharged and never came in contact with another patient. But a few weeks after she left, the same kind of infection was found in 2 other patients. Infections were discovered over the next 4 months at the rate of about 1 a week. *Klebsiella pneumoniae*, the bacteria responsible for the outbreak, is a growing threat in health care facilities, primarily affecting patients with compromised immune systems.

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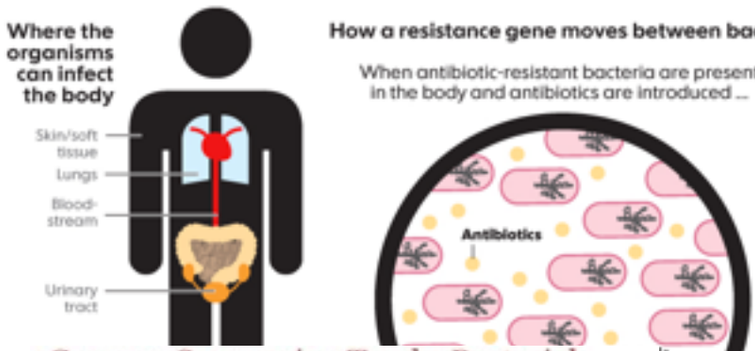

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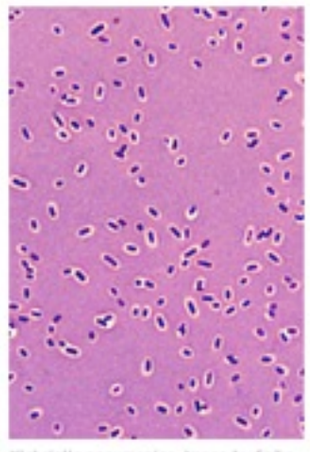

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NIH superbug claims 7th victim

By Brian Vastag and Lena H. Sun, September 14, 2012

A deadly, drug-resistant superbug outbreak that began last summer at the National Institutes of Health Clinical Center claimed its seventh victim Sept. 7, when a seriously ill boy from Minnesota succumbed to a bloodstream infection, officials said Friday.

The boy was the 19th patient at the research hospital to contract an antibiotic-resistant strain of the bacterium *Klebsiella pneumoniae* that arrived in August 2011 with a New York woman who needed a lung transplant. But his case marked the first new infection of this superbug at NIH since January — a worrisome signal that the bug persists inside the huge brick-and-glass federal facility in Bethesda.

"It's heartbreaking," said John Gallin, the physician-researcher who directs the clinical center. "What happened this summer was a very unfortunate case. All of these cases are hugely sad cases."

The boy arrived in Bethesda in April after complications arose from a bone marrow transplant he received last year. His underlying condition — a severe genetic defect that crippled his immune system — increased his risk of acquiring the superbug, as did the steroids and other drugs the boy was given to combat complications from the transplant.

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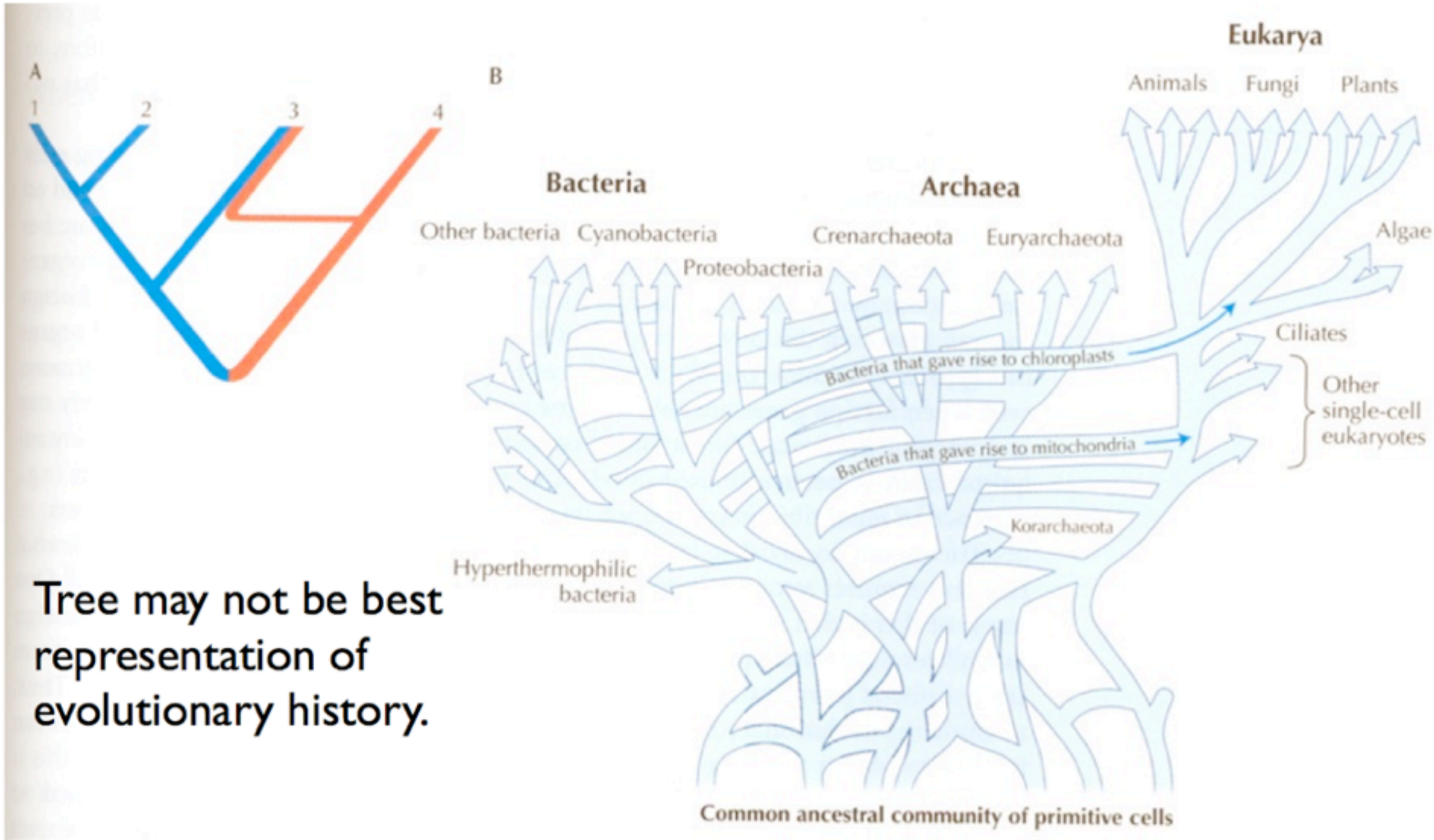
http://articles.washingtonpost.com/2012-09-14/national/35497552_1_superbug-infection-nih

Horizontal Gene Transfer



Tree may not be best representation of evolutionary history.

DNA uptake; retroviruses

Barton et al.

Project Description – Data

You will have access to:

1. A collection of partially assembled, whole-genome sequences of 10 *S. pneumoniae* strains.

   These are clinical isolates from patients with otitis media (throat swabs)

   Collected by Luisa Hiller (CMU) & collaborators at local hospitals

2. The sequencing reads used to create those partial assemblies.

Goal:

You should create a software pipeline that performs the following analyses:

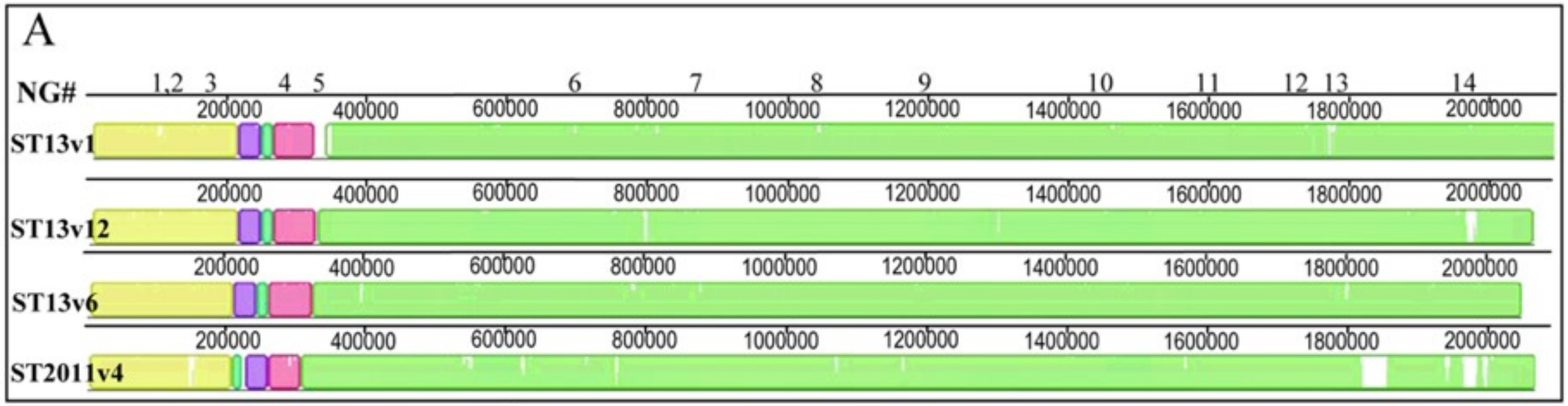
1. **Identify regions that differ across the strains.**

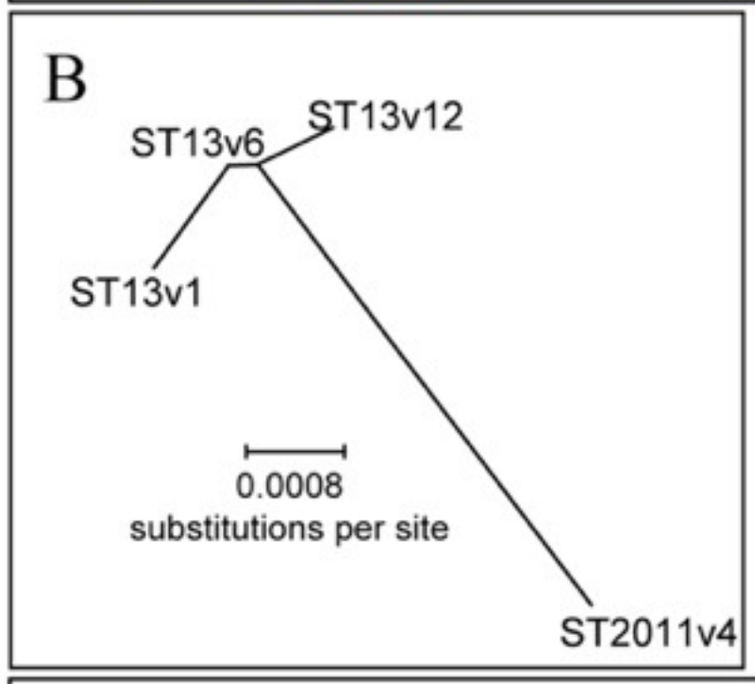
2. **Build a phylogenetic tree using the core whole genome sequence, and excluding any regions that have undergone horizontal gene transfer.**

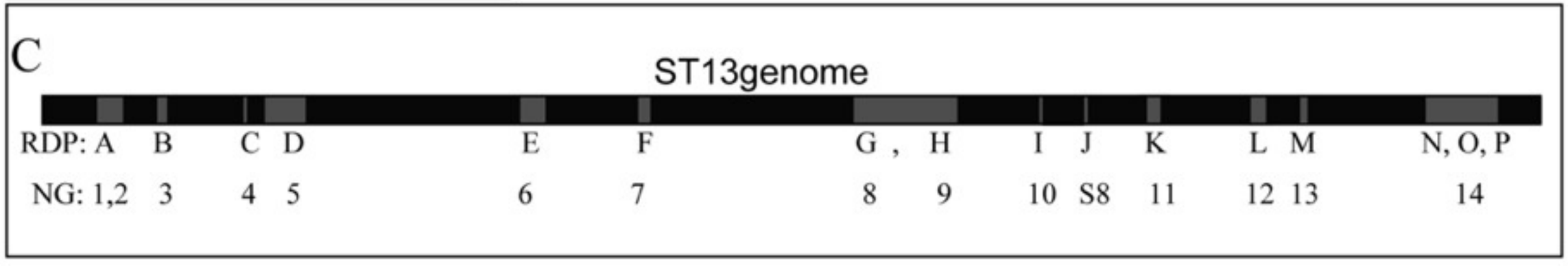
3. **Build phylogenetic trees for each one of the regions that have undergone horizontal gene transfer.**

4. **Annotate the genes within the horizontally transferred regions & other major differences between the strains.**

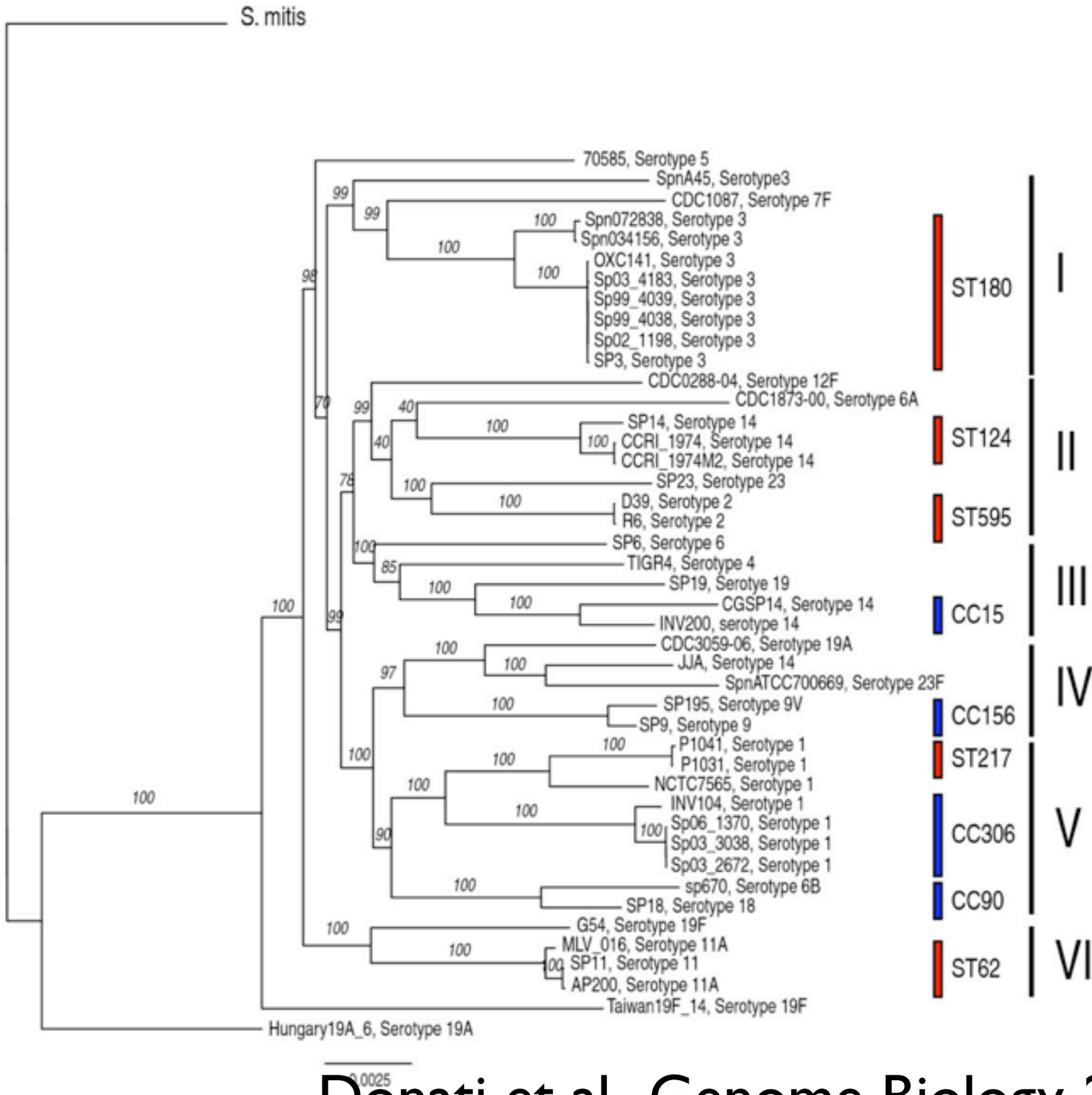
Example (Hiller et al., 2010)







Phylogeny of core genome



Donati et al., Genome Biology, 2010

Reading Assignment 1

Read:

Hiller NL, Ahmed A, Powell E, Martin DP, Eutsey R, et al. (2010) Generation of Genic Diversity among *Streptococcus pneumoniae* Strains via Horizontal Gene Transfer during a Chronic Polyclonal Pediatric Infection. PLoS Pathog 6(9): e1001108. doi:10.1371/journal.ppat.1001108

Hiller NL, Eutsey RA, Powell E, Earl JP, Janto B, et al. (2011) Differences in Genotype and Virulence among Four Multidrug-Resistant *Streptococcus pneumoniae* Isolates Belonging to the PMEN1 Clone. PLoS ONE 6(12): e28850. doi:10.1371/journal.pone.0028850

Plan for Semester

First week: understanding the problem & brainstorming

April 1: Design document due

April 16: Mini demo in class

April 29: Deliver software & user manual to instructors and **other team**

April 30 through final exam: use and evaluate other team's solution and also improve your solution.

Final exam time: presentation & peer evaluations

First Deliverable

Research Phase: produce a report with the following sections (at least 2 pages, longer is better):

1. A brief statement of the problem in your own words.
2. A list of relevant papers and software and a 1 sentence description of why they might be relevant.
3. A list of questions that you have about the problem that you have not be able to find the answer to. These questions should be ones that you have seriously tried to answer.
4. An assignment of the following roles on the next slide to team members

Team Roles

The roles you should assign in the first progress report are:

1. **program manager** – responsible for ensuring the design make sense

2. **technical lead** – responsible for ensuring the implementation is done property

3. **lead technical writer** – ultimately responsible for the write-ups that the team produces

4. **Q&A lead** – responsible for testing and evaluating the implementation

5. **communications lead** – responsible for final presentation, communicating with users, instructors, scheduling meetings of the team, scheduling meetings with instructors and clients

Important!

- All team members should be involved in all the aspects on the previous slide!
- The “leads” are just the people who should take responsibility for organizing their particular aspect.
- It is not ok to say “oh the lead technical writer will write up the report”