Decision Support for Antibiotic Prescription

Dr. Guy Tsafnat,

University of New South Wales, Centre for Health Informatics, UNSW

Line R. Sanden and Ninna Kæseler

Dept. of Health Science & Technology, Aalborg University, Denmark
The ABR Problem

- Some bacteria are resistant to some antibiotics
- Antibiotic resistance spreads (horizontal transfer) and aggregates ➔
  - More multi-resistant infections
  - Mobile Genetic Elements
- Nosocomial (hospital acquired) infections
- Estimated (AU)$2.5B per year in Australia
- **According to WHO, ABR is one of top three global health issues**
Gene Cassettes

conserved sequence cassette cassette cassette conserved sequence

conserved sequence cassette cassette cassette cassette conserved sequence
Transposition

Insertion Sequence

transposase

Inverted Repeats

Transposon

Integron

Composite Transposon
The Challenge

• Most effective therapy for patient
• Minimal ecological impact
• Simple and quick pathology
Current Practice

- “given patient symptoms, what is best practice?”
- Guidelines (pink book\(^1\))
- Computed Guideline Support (Shahar et al.)
  - Not yet applied to AB
- Adaptive heuristic models based on any of: symptoms, patient records, pathology, risk
- Delayed pathology (2+ days)

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Current Pathology

- Measures the chromosome
  - Species
  - Strand
  - Morphology
  - Symptoms
- Should measure Plasmids
  - Multi-resistance regions
- Requires culturing (2 days)
Computational Support

- First developed 1976 (MYCIN)
  - shown some improvement in practice
- Modern systems:
  - Same model:
    - Clinician enters symptoms
    - Gets recommendations
  - Cost/benefit recommendation
    - Ecological impact
    - Risks to patient
    - Likely outcomes
  - Questionable adoption
  - No pathology
A new DSS Model for AB prescription

• Target the question:
  – “given a patient scenario and an environmental context, what is best action?”

• “Context” here means molecular data in the environment of the patient
  – Temporal
  – Monitored and adjusted

• Complements heuristics from existing systems
Approach

• Catalogue of molecular resistances
  – Mobile Genetic Elements
  – Species independent
  – Co-occurrences

• Specialised catalog per environment
  – Device, ward, hospital, city, country
  – Migration from other environments
  – Emergence from new sequences
genetic expert system

test design system

local genetic history

tissue sample

prescriber

rapid genetic testing

within hours

test interpretation

evidence presentation
Rapid Testing System

• A system that quickly checks for genes of interest without culturing
• Easily adjustable to new genes, tests
• Most likely PCR (2 under development)
Why PCR?

• PCR is a method for asking DNA yes/no questions for presence of sequence of interest
• Currently (likely always will be) cheaper than sequencing
• Cost per probe can be optimised further
  • [Hejlesen et al., DNA-Based Bayesian Inference and Analysis of Bacterial Antibiotic Resistance, Scandinavian Health Informatics 2009]
  – Extra probes can be used for monitoring
Offline set selection

- 2 structures
  1. 4 R genes: A, B, C, D
  2. 3 R genes: B, E, F
  3. 3 R genes: A, D, F

- C → B
- A → C
- B → C
- AB → C

\[ p = \frac{O(A,B)}{O(A)} \]
Post-test results extrapolation
Results Interpretation - Example

Offline selected probes (5/270):
aadB1a  aacA4  dfrB17  blaVIM-1  dfrA1
Rapid test returns
  x     x     x
Interpretation adds
blaOXA-10  dfrB1  dfrB2  aadB
Rapid genetic testing

prescriber

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genoic expert system

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local genetic history

new sequence request

Delphi-like expert system

evidence presentation

test interpretation
Thank You …

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