

Career Connection: Eric Brown & Antibiotics

Teacher Resource

Course: Grade 12 University Biology

Ontario Curriculum Expectations

- Scientific Investigation Skills and Career Exploration
A2.1 identify and describe a variety of careers related to the field of science under study (scientific journalist, fisheries and wildlife officer, physician, infectious disease researcher, geneticist) and the education and training necessary for these careers
A2.2 describe the contributions of scientists, including Canadians (e.g. Evelyn Roden Nelson, Maude Menten, Albert Juan Agugyo, Kimberley J. Fernie, Michael Archer), to the fields under study
- Understanding Basic Concepts
B3.2 describe the structure of important biochemical compounds, including carbohydrates, proteins, lipids, and nucleic acids, and explain their function within cells

Background

In this activity students will explore the work of Prof. Eric Brown, Department of Biochemistry and Biomedical Sciences at McMaster University. Prof. Brown is a member of the GlycoNet. A brief biography will be reviewed and a video outlining his work will serve as the basis of this activity.

Activity Length: approximately 50 min

Last update: April, 2020

Prof. Eric Brown is a member of GlycoNet. To understand his work and his colleagues, use the following video to answer the questions.

Watch the GlycoNet Story: <https://www.youtube.com/watch?v=CQGEGloqTpQ>

1. Define glycomics
 - the study of sugars or carbohydrates in living cells.
2. Why are carbohydrates important?
 - they are important food sources,
 - important components of all cells
 - carbohydrates are important in communication between cells
 - they are important in cell invasion by viruses and other infections, and understanding how this works can help us prevent infections
3. What is GlycoNet?
 - A new Canada wide research network
 - Combining 20 research institutions to work in glycomics
4. According to Prof. Stephen Withers... Canada has many well recognized researchers in glycomics. What type of scientists work in this field?
 - microbiologists, chemists, biochemists
5. What are the benefits of having this network of researchers?
 - They are better able to collaborate with their work
 - They can contribute to each other's research and have better overall results
 - Share resources
6. GlycoNet brings together a variety of researchers. What are their research initiatives?
 - Antimicrobials
 - Rare genetic diseases
 - Diabetes and obesity
 - Rare genetic diseases of carbohydrate metabolism
 - Therapeutic proteins and vaccines

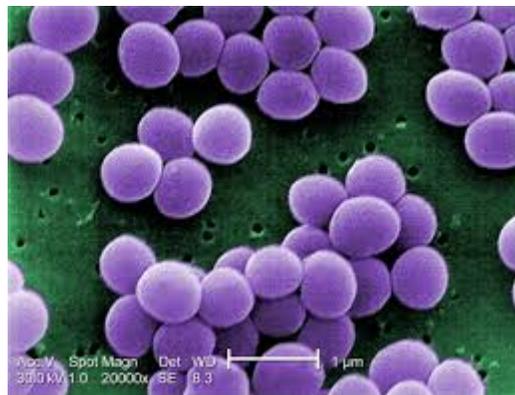
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Prof. Brown suspects his interest in science may have sparked when he was in grade 1 and he dressed up for Hallowe'en as a mad scientist winning the costume contest at his school in Dundas Ontario. He was interested in science in school and decided to pursue a degree in Food Science at the University of Guelph. Choosing a co-op option for this degree enabled him to get a wide range of experiences and pay for his own education. During one of his placements his interest in fundamental research was ignited



when studying the folding of proteins. This experience drew him towards more theoretical research. He received his M.Sc. and PhD. at the University of Guelph with a focus on biological chemistry. He then completed a post-doctoral program at the prestigious Harvard Medical School. Prof. Brown then spent several years working in the pharmaceutical industry in Boston prior to coming to McMaster University to continue his research. He is very active in his research and appreciates the atmosphere in his position at McMaster that still allows him to follow his curiosity. He has also started initiatives to combine biomedical discoveries and business studies at McMaster. He has won numerous awards and is currently the Canada Research Chair in Microbial Chemical Biology. He has a very active laboratory; mentoring many undergraduate and graduate students.

Outside the laboratory he has many interests. He is an avid sailor; a pastime he shares with his family. According to Prof. Brown he has a dormant golf game and still regularly plays hockey.



MRSA-Methicillin-resistant
Staphylococcus aureus

For more information on his laboratory, his graduate students, and his research projects see <http://www.brownlab.ca/>

Last update: April, 2020

We will use the following video to investigate Prof. Brown's pioneering work.

Taking on superbugs with new insights into uncharted biology:

<https://www.youtube.com/watch?v=jIAU4ZAhmSU>

1. Where do we find *Staphylococcus aureus*?

- in and on our bodies
- in healthy people

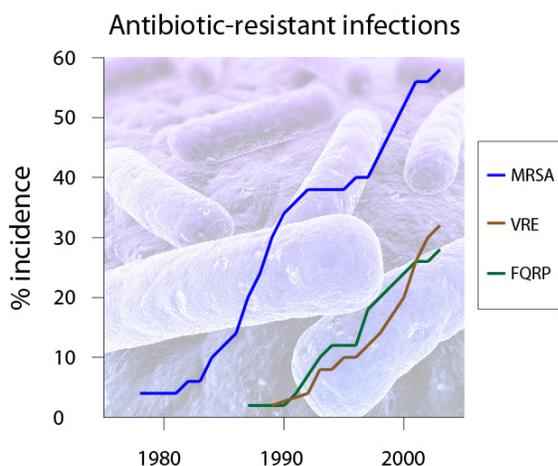
2. What does *Staphylococcus aureus* cause?

- pimples, boils, respiratory diseases like pneumonia, dangerous blood-borne infections

3. When does *Staphylococcus aureus* become known as MRSA

- When it is resistant to methicillin

4. Professor Brown uses the following data



Source: Centers for Disease Control and Prevention

Source:

<http://www.futuretimeline.net/subject/biology-medicine.htm>

Fill in the blanks

Over the past twenty years the incidence of MRSA has increased from zero to 50%. VRE (a vancomycin-resistant) and a FQRP (fluoroquinolone-resistant) bacteria show similar increases.

5. What attitudes were seen when antibiotics were first seen?

- People viewed antibiotics with great optimism, these drugs were seen as very beneficial and saving many lives
- According to Prof. Brown "antibiotics changed our world"

6. Large amounts of penicillin were required in World War II. How did this need get met?

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- Several pharmaceutical companies came together to meet this need.
7. What was the “golden age of antibiotics”?
- A two-decade time period antibiotic discovery beginning in the 1940s
8. What was the attitude towards antibiotics in the 1960s?
- That these will no longer be necessary as the bacterial and viral infections will be eradicated by 2000
9. What was the state of antibiotic research in the 1980s?
- Many pharmaceutical laboratories and stopped investigating antibiotics
10. What does Prof. Brown cite as one of the most important factors in inappropriate antibiotic use?
- Antibiotic use in animal husbandry (the care and breeding of animals for commercial use)
11. What is drug resistance in bacteria? Provide three mechanisms.
- The plasmid containing antibiotic-resistant genes gives rise the antibiotic efflux pump to push antibiotic out of the cell, and the bacteria remains unharmed
 - An antibiotic degrading enzyme can be produced that can destroy antibiotics inside the bacteria cell
 - An antibiotic-altering enzyme can change the antibiotic by adding a component making it ineffective
12. Is this resistance limited to only one bacteria cell?
- No. Plasmids containing DNA resistance can be shared so genes that cause resistance can be share among many cells
13. What are some solutions to antibiotic drug resistance?
- More responsible use of existing antibiotics. Only prescribe when a bacterial infection exists, reduce agricultural and animal use
 - New understanding, new strategies and new drugs
 - Reversing resistance

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14. What is new about Prof. Brown's research on drug combinations? Give the name of this type drug combination.

- Commonly more than one antibiotic is given in combination. Prof. Brown is suggesting that mixing antibiotic and non-antibiotic drugs will result in reversing resistance. This is known as syncretic combinations.

15. What does Prof. Brown mean when he says drugs have "cryptic activities"? Provide an example.

- A drug has a known use but other uses are also discovered e.g. Aspirin has long been used for pain relief but can be beneficial to heart health

16. Prof. Brown's team tried to kill a multi resistant form of bacteria known as *Pseudomonas aeruginosa* and MRSA. Describe his research- include a brief description of the successful combinations.

- He and his team took low dose of tetracycline (a known antibiotic) and combined it with about 1,000 known non-antibiotic drugs
- They checked one pair of these combinations at a time to see if there was a combination that reversed the resistance. They found six promising combinations
- These combinations are: tetracycline and
 - Imodium (used to treat diarrhea)
 - Mitomycin C (used to treat cancer)
 - Chloroxine (used to treat dandruff)
 - Benserazide (use to treat Parkinson's disease)
 - Tegaserod (used to treat irritable bowel)
 - Vitamin C
- In studying MRSA he and his team used cefuroxime (a penicillin type antibiotic) in combination with 2,000 non-antibiotic drugs
 - Ticlopidine (antihypertensive –reduces high blood pressure)

17. Why did the research team choose wax worms as the animal model?

- Large numbers of worms can be tested in a short amount of time
- The immune system of these worms is similar to that of humans

18. Wax worms were exposed to MRSA and tested under a variety of conditions:

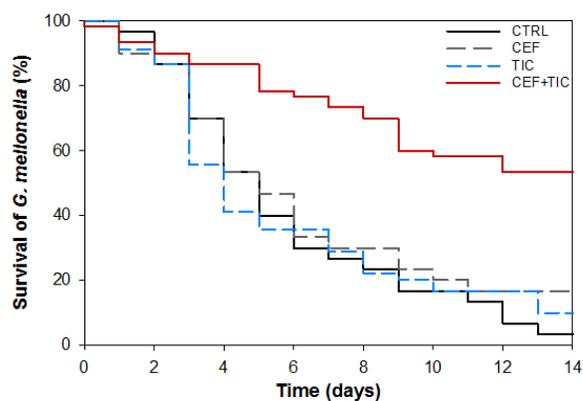
- an antibiotic cefuroxime(CEF)
- a drug of interest ticlopidine (TIC)
- a combination of cefuroxime and ticlopidine (CEF + TIC)

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- a control –without any drugs(CTRL)

Summarize the results of the cefuroxime and ticlopidine in wax worms.

Cefuroxime and ticlopidine are synergistic *in vivo*



Farha, M.A. Leung, A., Sewell, E.W., D'Elia, M.A., Allison, S.E., Ejim, L., Pereira, P.M., Pinho, M.G., Wright G.D. and Brown, E.D. 2013. *ACS Chemical Biology*, 8:226.

- by day 14 almost all wax worms in the control group were dead
- by day 14 under 20% survival was seen for TIC only and CEF only
- by day 14 about 60% survival was seen for the combination of CEF and TIC was seen. This demonstrated that the combined effect of CEF and TIC shows promise in reversing the resistance seen in MRSA

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