THREE IDEAS PRESENTATION:

BOOSTING THE BODY

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THE THREE IDEAS

1. BACTERIAL INFECTIONS
2. PRIONS
3. VIRAL INFECTIONS

Introduction

- Increasing defenses of the body !
- The three broad categories of infectious agents: Bacteria, Prions and Viruses
- We chose these topics because regardless of the infecting agent, we want to treat the body to overcome the disease in the early stages

BACTERIAL INFECTION

Bacteria are everywhere !

Some good and some bad !

The bad ones cause widespread diseases !

Bacteria cause endemic, epidemic and pandemic infectious diseases !

Find the cure to one = Finding possible cures to others !

Tackling Bacteria: Why it will help

- Many of the sicknesses we get today are still bacteria related.
- The Centers for Disease Control and Prevention lists over 20 bacteria related diseases that are still major concerns.
- Diseases like meningitis and pneumonia still kill people.
- By making the body more able to fight off bacterial infections, we would be helping to eradicate a major health concern.

Things We Can Target

- **Flagella**
  - Long, thin filaments on the cell surface that enable bacteria to move.
- **Spores**
  - Dormant form that enable bacteria to survive when environmental conditions are difficult.
- **Capsules**
  - Helps prevent white blood cells from ingesting these encapsulated bacteria.
- **Biofilm**
  - A secreted substance that helps them attach to other bacteria, cells, or objects.
- **Outer Membrane**
  - Gram-negative bacteria have an outer membrane that protects them against certain antibiotics. When this membrane is breached, it releases endotoxins.
- **Antibiotic Resistance**
  - Genes that encode for drug resistance can be passed to later generations or even other species of bacteria

Streptococcus

- Gram positive bacteria
  - High amount of peptidoglycan in the cell wall
  - Lack the outer membrane seen around gram negative bacteria
- Occur in chains
- Nonmotile
- Nonsporeforming
- Adhesins
- Hyaluronic acid capsule
- M Proteins

Image removed due to copyright restrictions.

Structure of gram positive and gram negative bacterial cell walls.

http://www.sigmaaldrich.com/etc/medialib/life-science/biochemicals/migrationbiochemicals1/Bacterial_Cell_Lysis.Par.0001.Image.569.gif

Streptococcus

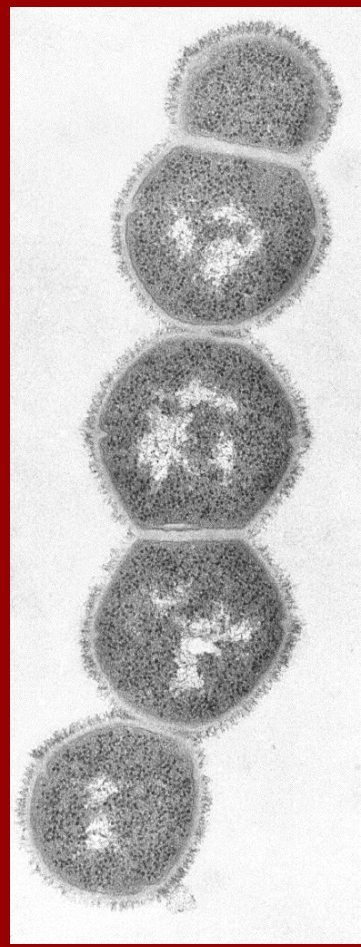
- Expresses streptolysin-s on its surface
  - Which kills the white blood cell through necrosis, a death in which the cell swells and eventually bursts
  - Cause lytic granules (lysosomes) of the white blood cell to be emptied into the WBC's cytoplasm instead of on the bacteria

- Streptococcus pyogenes (Class A) causes strep throat, rheumatic fever
- Streptococcus agalactiae (Class B) causes bacterial pneumonia, meningitis

Images of Streptococcus pyogenes removed due to copyright restrictions.
See http://www.textbookofbacteriology.net/streptococcus.html

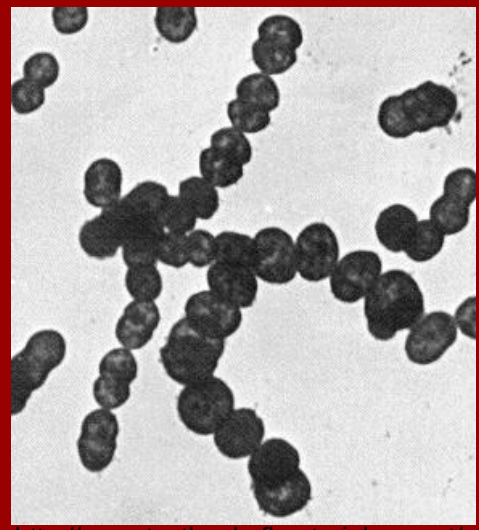
How to set up the bodies defenses

- Attack adhesins
- Make antibodies more sensitive to the factors on the surface of the bacteria
  - Better identify the M proteins
- Defeat the hyaluronic acid capsule
  - Unfortunately looks like host connective tissue cells
- Eliminate the production of streptolysin-s by the bacteria



Competition

- Skin, phagocytes, antibodies
- Antibiotics
  - Penicillin is still effective when diagnosis is early; however, body not given the chance to develop persistent antibodies
  - No effective vaccine
    - M protein vaccines
      - Risk of autoimmunity
- Increase polysaccharides
  - Many different types of polysaccharides
  - Normally not much of a response



http://www.textbookofbacteriology.net/streptococcus_4.html

Knowns and unknowns

- Penicillin still effective
- Antibiotic resistance
- A few M proteins
- How unique are the proteins and carbohydrates that we are identifying?
  - Similarity to human cells or beneficial bacteria?

Impact

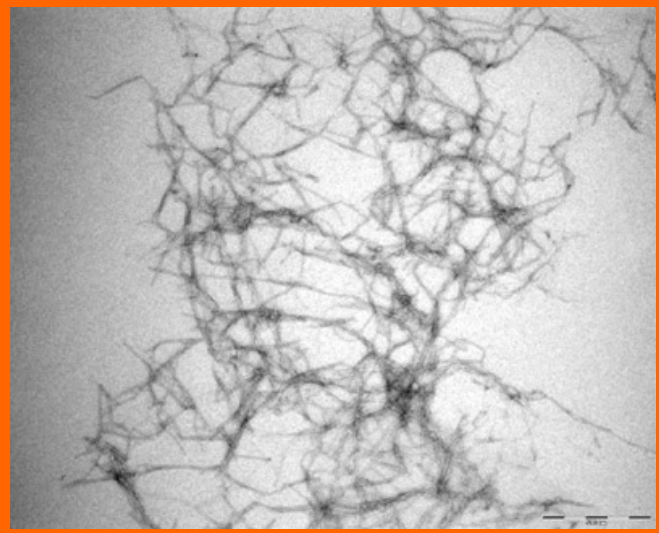
- If we can effectively tackle Streptococcus, this would help eliminate the common cases of strep throat seen in the school systems.
- Fewer deaths due to pneumonia and meningitis.
- Possibly transfer treatment ideas to defeat other bacteria.

PRIONS

Proteins are everywhere !

Some good and some bad !

The bad ones cause bad diseases !



Courtesy of JA del Rio. Used with permission.

Find the cure to prions diseases = Safer and happier eating of beef !

http://www.irbbarcelona.org/files/Image/PrP106_126_big.jpg

Prions?

- What is a Prion?
- Researchers, not 100% sure
  - Misfolded protein
  - Virus
  - Heavy Metal
  - Combination of many factors and cofactors
- Disease in mammals: BSE and Creutzfeld-Jakob disease
- Affect Neural tissue (spongy)

Transmission and Structure

- For BSE, which when ingested causes Creutzfeld-Jakob, normal protein is PrP^{C} and mutant is PrP^{SC} (Very stable)
- Mutant replaces a-helices with b-sheets in secondary structure which facilitate amyloid fibers (lead to holes/spongy tissue)
- Transmitted mainly through ingestion of affected tissue, but also genetically inherited

Image removed due to copyright restrictions.

Prion structures: normal conformer and rogue conformer (speculative).

http://www.bioquest.org/bedrock/problem_spaces/prion/assets/prion_structure.jpg

Importance

- Prion infectious diseases currently affect 1 in 1 million people between the ages of 30-45 and 3 in 1 million under the age of 30
- While this is not a great amount, there currently is no cure
- Prion infection is always fatal

Impact

- If fully successful, can eat without fear of infection
- Though affected population is not widespread, a solution will relieve fears of infection from a fatal, untreatable disease

Photo removed due to copyright restrictions.
Deep-fried Cow Brain Sandwich.
http://blogs.law.harvard.edu/dowbrigade/2004/01/20/deep-fried-cow-brain-sandwich/

Competition

- Recently developed vaccine, only tested in mice, prevents them from developing neural plaques
- Altering genome of cows/livestock so they don't carry protein PrP^C

Photo courtesy of CameliaTWU on Flickr.

Knowns

- Prions are mainly misfolded proteins
  - Though some evidence points to cofactors, etc.
- Affect structure of brain/neural tissue (create plaques, spongy tissue)
- Currently untreatable
  - Resistant to protease, heat, radiation
- Main method of transmission: ingestion

Unknowns

- Researchers THINK:
  - Prions might mutate other healthy proteins to become mutant proteins
  - Prions might not be proteins
    - Viruses
    - Heavy Metal Poisoning
    - Combination of many factors
- The 3D structure of PrP^{SC}

Possible Solutions

- Disable the replication of proteins, mutant protein transforms healthy protein
- Disable the aggregation of mutant proteins by blocking the end of the amyloid fiber so no free proteins can attach
- Reduce or destroy tertiary structure of mutant protein

VIRUS INFECTIONS

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Some good and some bad !

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HEPATITIS C VIRUS

Image removed due to copyright restrictions.
Hepatitis C virus structure.
See http://www.rkm.com.au/VIRUS/HCV/Hepatitis-C-Virus-Group.html

What is Hepatitis?

- Hepatitis is an inflammation of the liver.
- Caused by viruses.
- The most important types of viral hepatitis are hepatitis A, hepatitis B, and hepatitis C. Newly discovered forms of viral hepatitis also include hepatitis D, E, and G.

What is Hepatitis C?

- Hepatitis C, a disease causing cirrhosis of the liver brought by the attack of an RNA virus, HCV.
- In mid-1995 the hepatitis C virus was seen for the first time.
- The virus is a linear single-strand RNA virus 40-50 nanometers in size. It is covered with a lipid envelope and is encased with glycoprotein peplomers or "spikes".
- This virus brings about the cirrhosis of the liver : where normal liver cells are damaged and replaced by scar tissue, decreasing the amount of normal liver tissue

Probable outcome of contact with HCV

If 100 people contract HCV at the same time

- Between 80 to 85 people have chronic hepatitis C infection
  - Around 20 people will never develop any liver damage
  - Between 60 to 65 people will develop some level of liver damage (after an average of 15 years)
    - Between 20 to 25 people will develop cirrhosis of the liver (after about 20 years)
      - Between 5 to 10 of those people with cirrhosis will experience liver failure or cancer (after 25 to 30 years)
- 15 to 20 people get rid of the virus within 2 to 3 months (but carry antibodies for some time)

McInnis, Vikki. "What is HCV?" Hepatits C Information Center. 8 Aug. 2002. 8 Mar. 2009 <http://www.hepatitis-central.com/hcv/whatis/whatishcv.html>.

Importance of the problem

- The liver is the most important organ of our body.
- It is our bodies filter system.
- It not only helps remover toxins, drugs and waste material, but also helps produce bile, essential to the digestion of fats.
- BUT : the liver infected, HCV, can cause mild problems like jaundice, nausea, fever, diarrhea or more serious illness such as cancer.

Importance of the problem contd.

- The World Health Organization considers Hepatitis C an epidemic.
- Because a patient living with Hepatitis C can be infected for decades before being discovered, it is often called the "silent" epidemic.
- Hepatitis C is the most common blood-borne infection in the United States. It affects at least 4 million people in the U.S. and 175 million people worldwide.
- It is the leading cause for liver cancer !

Current treatment

- Combination therapy with pegylated interferon and ribavirin is the treatment of choice resulting in sustained response rates of 40%-80%.
- Interferon monotherapy is generally reserved for patients in whom ribavirin is contraindicated.
- Ribavirin, when used alone, does not work.
- Interferon, reduces the amount of liver enzymes to normal limits. With liver enzymes at the optimum amount, the normal liver cells function better.
- Ribavirin may suppress viral replication, but does not appear to eradicate the virus. Hence, the liver enzymes drop with the viral load remaining the same.

Problems of the current treatment

- Most persons have flu-like symptoms (fever, chills, headache, muscle and joint aches, fast heart rate) early in treatment. Later side effects may include tiredness, hair loss, low blood count, trouble with thinking, moodiness, and depression.
- Severe side effects include thyroid disease, depression with suicidal and homicidal thoughts, seizures, acute heart or kidney failure, eye and lung problems, hearing loss, and blood infection.
- Although rare, deaths have occurred due to liver failure or blood infection, mostly in persons with cirrhosis.
- An important side effect of interferon is worsening of liver disease with treatment, which can be severe and even fatal, because once the interferon has been removed from the body the liver enzymes once again increase in production

Reasons behind the problem : The Unknowns

- Six subtypes of hep C, plus variations, all of which respond to treatments differently.
- Exactly how the virus attacks the cells of the liver and what it does to the cells
- General methods to kill viruses inside the human body
- How to prevent the virus from multiplying within the body

The known's

- It is known that HCV replicates by hijacking the nucleotides of its host cell. It is the liver cells that still have available nucleotides in sufficient supplies even after the cells have stopped dividing.
- Studies have shown that if the nucleotides in the cells are replaced by nucleosides the HCV are inhibited from replication.

Tang-Nelson study at FSU, 2006.

First Possible solution !

- KILLING THE VIRUS BEFORE IT ATTACKS MULTIPLE CELLS
- Viruses have protein capsids.
- Increase the production of Hydrogen Peroxide in the peroxisomes of cells, and shut off its conversion to water.
- Direct it to the proteinaceous capsid of the virus and destroy it, releasing the RNA / DNA into the blood stream.
- By increasing the production of exo-nucleases, the RNA and DNA could be destroyed.

Other Possible Solutions !

- 2. PREVENTING THE REPLICATION OF VIRUSES: Reengineer the DNA of the host cell so as to prevent the replication of viruses, by converting the existing nucleotides to nucleosides.
- 3. HELP HEALTHY CELLS FROM VIRUS ATTACKS: Reengineer the DNA of the liver cells so as to produce more interferon faster than the virus can replicate.
- 4. HELP HEALTHY PEOPLE FROM THE INFECTION: Discovering a vaccine against HCV.

Impact of solution

- Thus, coming up with a solution to help Hepatitis C patients, would help people from around the world.
- Since there is no current vaccine against Hepatitis C, creating an efficient vaccine may even lead to the eradication of this disease.
- Moreover, since it is a virus infection, a cure to this disease may even lead to a generic cure to all viral infections.

SUMMARY

- Infectious agents, either bacteria, prions or viruses, bring about prolonged degradation of our body.
- If these agents can be stopped at the early stages of their attack by boosting our human bodies, then a number of humans around the world can be saved from a lifetime of illness.
- Take a look at the handouts !!!

SURVEY !

Could you please take a moment to look at the handouts we passed around and fill out the survey sheet !

Thank you !!!

BIBLIOGRAPHY

- http://ghr.nlm.nih.gov/condition=priondisease
- "What is Hepatitis?" What is Hepatitis ? <http://www.hepcprimer.com/what.html>.
- American Academy of Pediatrics (2006). Hepatitis C. In LK Pickering, ed., Red Book: 2006 Report of the Committee on Infectious Diseases, 27th ed., pp. 355–359. Elk Grove, IL: American Academy of Pediatrics.
- McInnis, Vikki. "What is HCV?" Hepatits C Information Center. 8 Aug. 2002. 8 Mar. 2009 <http://www.hepatitis-central.com/hcv/whatis/whatishcv.html>.
- http://www.sciencedaily.com/releases/2009/02/090223221427.htm
- http://www.merck.com/mmhe/sec17/ch190/ch190a.html
- http://www.textbookofbacteriology.net/streptococcus.html
- http://www.sciencedaily.com/releases/2007/05/070503135420.htm
- http://www.washingtonpost.com/wp-dyn/content/article/2006/12/31/AR2006123100672.html

20.020 Introduction to Biological Engineering Design
Spring 2009