Industrial Microbiology and Biotechnology

MICB 418 - Winter Term

Instructor: JOHN SMIT**,** jsmit@mail.ubc.ca
Office hours: By appointment - 2509 Life Sciences Centre (822-4417)

Lectures: Tuesday and Thursday at 11:00-12:30 in Life Sciences Centre Room 1510

Co-Requisite: BIOL 335 or MICB 325

Textbook: Through an arrangement with J.W. Wiley we have a reduced bundled price for these two textbooks by Gary Walsh:

1) Biopharmaceuticals: Biochemistry and Biotechnology, 2nd edition
2) Proteins: Biochemistry and Biotechnology, 1st edition

These are the recommended textbooks for the course; I recommend you buy them, BUT lectures are **not** taken directly from them and they should be considered a useful, **but not essential** resource. They are also available on reserve at the Woodward Library.

There are other texts that are helpful but are not required:

- "Microbial Biotechnology" - Fundamentals of Applied Microbiology" 2nd edition, by A.N. Glazer and H. Nikaido, Cambridge University Press. A number of topics covered early in the course are addressed in this text.
- "Introduction to Biotechnology" W.J. Thieman and M.A. Palladino, Pearson/Benjamin Cummings.
- "Basic Biotechnology" 3rd edition, edited by C. Ratledge, B. Kristiansen
- "Bioprocess Engineering. Basic concepts" 2nd edition, M.L. Shuler and F. Kargi, Prentice Hall
- "Biotechnology" 4th edition, John E. Smith, Cambridge University Press
- "Molecular Biotechnology – Principles and Applications of Recombinant DNA", 4th edition, B.R. Glick, J.J. Pasternak, and C.L. Patten, ASM Press.

Connect: I post **audio recordings** of all lectures on the web site (www.connect.ubc.ca). General information, tutorial information and **study aids** will also be there.

Examinations: There will be two midterms during the term and a final exam in April. There will be **two options** available:

1) Take both midterms and the final exam. In this case each midterm will account for 25% of the grade and the final exam for the remaining 50%.
OR:
2) Take only the first midterm and the final exam. In this case the midterm will account for 30% of the grade and the final exam 70%.

The first midterm is **mandatory** and will be mid- February. The second midterm will be in late March.

Tutorials: Tutorial sessions for review of lecture material will be held on the Thursdays (1-2 PM) and Fridays (at 3-4 PM) that follow the lectures of the week. They are not mandatory. These sessions will be run by the course Teaching Assistant

MICB418 - Industrial Microbiology and Biotechnology - Topics

- **Topic 1 - Classical Industrial Microbiology (15 hours of lecture)**

-Beer brewing and Wine-making
  -History and current practices
  -"Secondary" fermentations and their uses in wine making
  -Genetic engineering of yeast strains to address key industry problems

-Industrial ethanol production
  -Methods, sources of feedstocks used
  -Current and potential microorganisms used to produce ethanol
  -Biochemical and microbiological issues in maximizing ethanol production
  -Markets for ethanol and an analysis of economic and environmental issues
  -Future trends and alternatives

-High fructose corn syrup
  -How it is made and where it is used
  -The role of amylases and isomerases

-Immobilized bacterial cells for biotransformations
  -High-fructose corn syrup
  -Acrylamide synthesis – an example of "Green Chemistry"
  -L-aspartic acid from fumarate

-Detergent enzymes -Proteases, cellulases, xylanases, lipases and amylases
  -Why they are used
  -The development of the fermentation industry

-Vitamins and amino acids – addressing the need for chiral-specific synthesis
  -Vitamin C production
  -Amino acids synthesis, with a focus on monosodium glutamate (MSG)
   Aspartame
   Aspartic acid

-Yeast production for the food industry – the transition from a beer-making by-product

-Single cell protein production – for animal and human food
  -Methylotrophus, Spirulina, Candida, Fusarum
  -RNA reduction

-Antibiotic production
  -Classes of antibiotics; when found, mode of action, limitations, current usage, etc
  -Semi-synthetic synthesis issues and evolution of generations of antibiotics with beta-lactams as a focus

- **Topic 2 - Recombinant protein production by microbial systems (11 hours of lecture)**

-General issues regarding cost of goods, proper folding, glycosylation, endotoxin, animal proteins in media, disposal issues, etc.

-Production of Human Insulin as a focus—detailed analysis of the molecular genetic and biochemical process to produce insulin in *E. coli* and Saccharomyces.

-Bacterial expression systems

  -The *E. coli* advantage

-Secretion systems--pros and cons in biotech applications
-Sec dependent pathway, especially for Bacillus, Streptomyces
-Type I-VI secretion mechanisms-- which are suitable for biotech?
-Genetic engineering issues--codon usage, internal translation initiation, folding

-Yeast expression systems
Saccharomyces, *Pichia* and *Hansenula*

-Fungal expression systems
-*Aspergillus*, *Neurospora*, *Trichoderma*

-Cultured Higher order cells-
-Mammalian -CHO cells, and others
-Methods, stability, limits.
-Transient heterologous gene expression.
-Insect cell culture and Baculovirus –infected insect cell culture

•Topic 3 - Scaled-up Fermentation and Downstream Processing (3 hours of lecture)

-Reactor types, methods of aeration, etc.

-Method of operation of fermenters – Batch, fed-batch, semi-continuous, perfusion, etc.

-Single-use fermenters

-Downstream processing – processing steps, chromatography issues, process diagrams

-Protein refold technology

-Focus on insulin - downstream processing after *E. coli* fermentation.

•Topic 4 - Discovery of small human therapeutic molecules (2 hours of lecture)

-Importance to pharmaceutical industry-

-Chemical compound libraries

-Rational Drug Design and the interface with chemical libraries

-Targets for small molecule screening that involve microbes
- Classical targets—e.g., sulfa drugs, bacitracin
- Newer targets, e.g., LPS biosynthesis, fungal wall polymer synthesis, quorum sensing (HSL analogues)

•Topic 5 - Discovery and production of human therapeutic proteins (3 hours of lecture)

-Vaccines – acquired/adaptive immunity
-Assessment of market opportunity
-Targets, immunomodulators, adjuvants
-Anti-cancer vaccines
-Newer subunit vaccines, e.g., Hepatitis B

-Focus on Influenza Vaccines
-Current processes and how they compare to standard vaccine approval processes
-Challenges in dealing with the need for estimating the type and quantity of vaccine

Needed on a yearly basis.
-Challenges in dealing with a pandemic

-What happened during the last years from a biotechnology perspective
-The future of flu vaccines

-Recombinant antibodies for therapy
-Reasons for producing antibodies
-Diagnostic applications
-Therapeutic applications
-Types of full-size antibodies, from mouse monoclonal to fully recombinant and humanized expression
-Types of reduced size antibodies and their uses; scFv, Fab, multimeric scFvs
-Methods of producing antibodies in quantity
-In vitro antibody libraries
-Classical antibody libraries
-Alternative platforms for antibody library preparation
-Library screening methods

•Topic 6 - The Legal and Ethical side of Biotechnology (3 hours of lecture)

-Regulatory Aspects
-GLP and GMP issues in production
-FDA approval process for Chemical and Biological Pharmaceuticals
-Clinical trials- Preclinical, Phase I-III and IV processes
-Generic drugs – how are they handled

-Patenting of Biotechnology
-General scope of what is intellectual property
-What is patentable and the types of patents
-US specific issues
-World-wide patenting – The Patent Cooperation Treaty
-When to patent
-Why patent?

LEARNING OUTCOMES

By the end of the course you can expect:

1) To have a good general understanding about how wine and beer is produced.
2) To be able to articulate in biochemical terms what features of yeasts make them suited to alcoholic beverage fermentation.
3) To be better equipped to apply your background knowledge of chemistry to the biotech industry in useful and practical applications.
4) To have an understanding of the bioethanol industry and be better equipped to judge the suitability of new biofuel technologies.
5) To understand why biological agents are often needed to produce chemicals in the biotechnology industry and to assess when a biological agent (e.g., enzyme) is needed or could offer an economic or practical advantage.
6) For small molecule therapeutics, to have an understanding of what they are, how they are discovered and developed into products, and why they have been the traditional drivers for the pharmaceutical industry.
7) For a given recombinant protein to have some ability to judge which microorganism protein production system(s) is suited to produce the protein for industrial uses.
8) To have an improved ability to determine whether a particular idea or invention is patentable and whether it would important to patent it to successfully bring the concept to the marketplace.
9) To be able to analyze the characteristics of a monoclonal antibody and determine what generation of development it came from, how it was made and the range of uses possible.