Industrial Microbiology and Biotechnology
MICB 418
Winter Term 2011

Instructor: JOHN SMIT, jsmit@interchange.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 1510

Co-Requisite: BIOL 335 (or MICB 201)

Texts: Through a special arrangement with J.W. Wiley we negotiated 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 official 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.

Vista: I will also post **audio recordings** of all lectures. Tutorial information 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 (mandatory) will be on 10 February 2011. The second midterm will be on 31 March 2011.

Tutorials: Tutorial sessions for review of lecture material will be held on the Thursdays and Fridays (at 2-3 PM) that follow the lectures of the week. They will be held in LSC 1510. They are not mandatory.

These sessions will be run by the course Teaching Assistant: **Sally Lee** (leesally@interchange.ubc.ca). There will be no tutorials in the first week of classes. First tutorials will be on Jan 13 and 14.

MICB418 - Industrial Microbiology and Biotechnology

Topics for 2011 - John Smit

•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
- -Biochemical and microbiological issues in maximizing ethanol production
- -Markets for ethanol and an analysis of economic and environmental issues
- -Future trends

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

-Immobilized bacterial cells for biotransformations – 2 examples
- -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-V 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 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 year 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 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

-Stimulating innate immunity

•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?