

BIOTRANSFORMATION CONSIDERATIONS IN DRUG DESIGN
FALL SEMESTER 2022, 2 CREDITS

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PHONE		
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OFFICE HOURS		M.O. James: call or email. C. Xing: call or email.
PREREQUISITES		Recommended: Organic Chemistry (e.g. CHM 5224), undergraduate Biochemistry (e.g. BCH 4024). Drug Design I and II. If in doubt, seek instructors' approval.
TIME & PLACE OF CLASS		Tuesday and Thursday 2:00-3:00pm or TBA. Lectures and Exams will be held in rooms in the HSC Communicore C1-004
CANVAS WEBSITE		Course materials and announcements will be on the Canvas website associated with this course.

LEARNING OBJECTIVES.

1. To gain knowledge of how enzymes and transporters in the body interact with drug molecules.
2. To predict, from the molecular structure of a drug, the structures of its probable metabolites, including intermediates and final products.
3. To predict the enzymes (including isozymes where known) likely to be involved in the biotransformation of a drug and its primary metabolites.
4. To predict the transporter proteins likely to facilitate elimination of a drug or its metabolite
5. To correctly use the terminology of the field.
6. To critically review evidence from the literature about how certain chemicals can upregulate biotransformation enzymes present in liver and other organs through different cellular mechanisms.
7. To be able to predict the effects of inhibitors of drug biotransformation and describe the mechanisms of inhibition.
8. To understand the role of route of administration on the fate of a drug or the action of a modulator of drug biotransformation, as well as on its transporter-mediated elimination.
9. To learn why some metabolites are chemically reactive, and therefore potentially toxic and to be able to predict the likelihood of formation of a reactive metabolite from a given drug molecule.
10. To understand the principles of the metabolism of endogenous and exogenous chemicals and appreciate the values of associated specific metabolites as biomarkers for disease diagnosis and risk prediction.
11. To appreciate the contribution of genetic polymorphism in drug metabolism, drug toxicity and disease risk.

DESCRIPTION : Explores the importance of considering biotransformation in the process of drug design and discovery. Topics include the major pathways of biotransformation of various functional groups present in drugs and the enzymes involved, including their regulation and factors affecting metabolism and enzyme activity. Other topics are the role of metabolism in drug toxicity and examples from the literature of metabolic activation of drugs and naturally occurring toxic chemicals.

THERE IS NO REQUIRED TEXT: Original journal articles may be assigned, depending on the topic. All reading material is available at the UF library. Reference details for topics are given in lectures, and lecture slides will be posted on Canvas ahead of presentation.

Reference reading material:

Foye's "Principles of Medicinal Chemistry", 8th edition, Roche, V.E. et al., editors. Wolters Kluwer publisher, ISBN-13:978-1-4963-8502-4. Pages 48 to 130.

Cytochrome P450, P. Ortiz de Montellano, ed., 4th edition, Springer 2015 ISBN 978-3-319-12107-9.

LECTURE LIST, with approximate timetable.

Date and classroom	Topic
Aug 25	Introduction
Aug 30	Cytochrome P450: Reactions catalyzed, chemistry and mechanisms, role of NADPH-cytochrome P450 reductase
Sept 01	Cytochrome P450: Multiplicity, nomenclature, pharmacogenetics
Sept 06	Cytochrome P450: Regulation of expression
Sept 08	Cytochrome P450: Modulation by inhibitors and enhancers
Sept 13	No Class
Sept 15	Flavin Monooxygenase/ Aldehyde oxidase
Sept 20	Ester/amide/ epoxide hydrolases
Sept 22	Exam Phase I (6 lectures)
Sept 27	UDP-glucuronosyltransferases and glucosyltransferase (UGTs): reactions
Sept 29	UGTs: enzymology and regulation, inhibition
Oct 04	Glutathione transferases (GSTs)
Oct 06	GSTs and related pathways (cysteine β -lyase)
Oct 11	PAPS-sulfotransferases (SULTs)
Oct 13	SULTs
Oct 18	Acetylation, Amino acid conjugation
Oct 20	Chiral inversion of carboxylic acids; Fatty acid conjugation; Methylation
Oct 25	Transporter proteins
Oct 27	Exam Phase II (9 lectures)
Nov 01	Metabolism, toxicity, disease risks, and genetic polymorphism - general concepts
Nov 03	Metabolic activation of natural product: Pennyroyal oil natural products
Nov 08	Metabolic activation of natural product: Ipomeanines from sweet potatoes
Nov 11	Metabolism of nicotine and tobacco carcinogens: addiction, cancer risks, and associated metabolic and genetic biomarkers
Nov 15	Metabolism of nicotine and tobacco carcinogens: addiction, cancer risks, and associated metabolic and genetic biomarkers
Nov 17	Principles for the development of metabolism-based disease biomarkers
Nov 22	No class
Nov 24	No class: UF holiday Thanksgiving
Nov 29	Student presentations (see accompanying document)
Dec 01	Student presentations

Dec 06	Student presentations
Dec 08	Final Exam

EXAMS AND GRADING:

Format:

The format of the course will involve lectures using combinations of Power Point presentations, chalk-board presentations, overhead projection and handouts to deliver the materials.

Evaluation:

The students will be evaluated in **THREE** exams and the TERM paper, each of which accounts for 25% of the final grade. The exams will involve structure, short or numerical answers. Students will be allowed to inspect their exams to verify their scores but exam will be kept by the faculty for three years. A letter grade will be assigned for the materials covered by each faculty. The final grade will be based on the grades of all the exams, weighed proportionally based on the number of the lectures for each exam.

Grading will be on a point basis with >90 (A), >87 (A-), >83 (B+), >80 (B), >77 (B-), >73 (C+), >70 (C), >67 (C-), >63 (D+), >60 (D), >57 (D-), >53 (E). ***There will be no make-up exams.***

More information on UF grading policy may be found at:

[UF Graduate Catalog](#)

[Grades and Grading Policies](#)

MISCELLANEOUS:

Attendance:

Class attendance is not mandatory. However, the student will be tested on the lecture material and in-class handouts, which, for the most part, are not covered in precisely the same way in any available textbook.

Students Requiring Accommodations

Students with disabilities who experience learning barriers and would like to request academic accommodations should connect with the disability Resource Center. [Click here to get started with the Disability Resource Center](#). It is important for students to share their accommodation letter with their instructor and discuss their access needs, as early as possible in the semester.

Course Evaluation

Students are expected to provide professional and respectful feedback on the quality of instruction in this course by completing course evaluations online via GatorEvals. Guidance on how to give feedback in a professional and respectful manner is available at <https://gatorevals.aa.ufl.edu/students/>. Students will be notified when the evaluation period opens, and can complete evaluations through the email they receive from GatorEvals, in their Canvas course menu under GatorEvals, or via <https://ufl.bluera.com/ufl/>. Summaries of course evaluation results are available to students at <https://gatorevals.aa.ufl.edu/public-results/>.

University Honesty Policy

UF students are bound by The Honor Pledge which states, “We, the members of the University of Florida community, pledge to hold ourselves and our peers to the highest standards of honor and integrity by abiding by the Honor Code. On all work submitted for credit by students at the University of Florida, the following pledge is either required or implied: “On my honor, I have neither given nor received unauthorized aid in doing this assignment.” The Conduct Code specifies a number of behaviors that are in violation of this code and the possible sanctions. [Click here to read the Conduct Code](#). If you have any questions or concerns, please consult with the instructor in this class.

In Class Recording Policy

Students are allowed to record video or audio of class lectures. However, the purposes for which these recordings may be used are strictly controlled. The only allowable purposes are (1) for personal educational use, (2) in connection with a complaint to the university, or (3) as evidence in, or in preparation for, a criminal or civil proceeding. All other purposes are prohibited. Specifically, students may not publish recorded lectures without the written consent of the instructor.

A “class lecture” is an educational presentation intended to inform or teach enrolled students about a particular subject, including any instructor-led discussions that form part of the presentation, and delivered by any instructor hired or appointed by the University, or by a guest instructor, as part of a University of Florida course. A class lecture does not include lab sessions, student presentations, clinical presentations such as patient history, academic exercises involving solely student participation, assessments (quizzes, tests, exams), field trips, private conversations between students in the class or between a student and the faculty or lecturer during a class session.

Publication without permission of the instructor is prohibited. To “publish” means to share, transmit, circulate, distribute, or provide access to a recording, regardless of format or medium, to another person (or persons), including but not limited to another student within the same class section. Additionally, a recording, or transcript of a recording, is considered published if it is posted on or uploaded to, in whole or in part, any media platform, including but not limited to social media, book, magazine, newspaper, leaflet, or third party note/tutoring services. A student who publishes a recording without written consent may be subject to a civil cause of action instituted by a person injured by the publication and/or discipline under UF Regulation 4.040 Student Honor Code and Student Conduct Code.

Campus Resources:

Health and Wellness

U Matter, We Care: If you or someone you know is in distress, please contact umatter@ufl.edu, 352-392-1575, or visit [U Matter, We Care website](#) to refer or report a concern and a team member will reach out to the student in distress.

Counseling and Wellness Center: Visit the [Counseling and Wellness Center website](#) or call 352-392-1575 for information on crisis services as well as non-crisis services.

Student Health Care Center: Call 352-392-1161 for 24/7 information to help you find the care you need, or visit the [Student Health Care Center website](#).

University Police Department: Visit [UF Police Department website](#) or call 352-392-1111 (or 9-1-1 for emergencies).

UF Health Shands Emergency Room / Trauma Center: For immediate medical care call 352-733-0111 or go to the emergency room at 1515 SW Archer Road, Gainesville, FL 32608; Visit the [UF Health Emergency Room and Trauma Center website](#).

GatorWell Health Promotion Services: For prevention services focused on optimal wellbeing, including Wellness Coaching for Academic Success, visit the [GatorWell website](#) or call 352-273-4450.

Academic Resources

E-learning technical support: Contact the [UF Computing Help Desk](#) at 352-392-4357 or via e-mail at helpdesk@ufl.edu.

Career Connections Center: Reitz Union Suite 1300, 352-392-1601. Career assistance and counseling services.

[Library Support](#): Various ways to receive assistance with respect to using the libraries or finding resources.

[Teaching Center](#): Broward Hall, 352-392-2010 or to make an appointment 352- 392-6420. General study skills and tutoring.

[Writing Studio](#): 2215 Turlington Hall, 352-846-1138. Help brainstorming, formatting, and writing papers.

Student Complaints On-Campus: Visit the [Student Honor Code and Student Conduct Code webpage](#) for more information.

On-Line Students Complaints: View the [Distance Learning Student Complaint Process](#).