Mechanistic Toxicology Syllabus

Course Descriptions: Mechanistic Toxicology looks at how chemicals disrupt homeostasis of cells. The study of mechanism of interactions between foreign chemicals and biological systems, including the physiological, developmental, and genetic consequences of exposure of human beings to environmental contaminants and medications.

Level: M.Sc. in pharmacology and toxicology

Credit Hours: 2 hours

Meeting Times: Wednesday, 9:00-11:00 am

instructor's full names : Prof. Dr. Inam Sameh Arif
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Required Materials:

- Casarett & Doull's Toxicology, The essential of Toxicology, 4th Edition,2021.
- Mechanistic Toxicology, The Molecular Basis of How Chemicals Disrupt Biological Targets, U.A. Boelsterli, CRC Press, Taylor & Francis Group, 2007.
- Toxicology for the Health and Pharmaceutical Sciences Edited Dr. Antonio Peña-Fernández, PhD, SFHEA, CRC Press, Taylor & Francis Group, 2022.
- In addition, we will be using recent articles that will be provided via instructors

Goals: The general goals of this course are:
Students will have an understanding of:

1. Basic principles in toxicology including dose/response, toxic effects, Toxicokinetic (absorption, translocation, biotransformation & excretion).
2. Basic analysis and understanding of the molecular mechanisms associated with the risk of xenobiotics, as drugs, toxics or environmental and food contaminants.
3. How the body adapts to xenobiotics in an attempt to maintain homeostasis

Objectives:
Students will be able to:

1. Describe how toxicants enter the body, are metabolized, distributed and excreted from the body.
2. Describe biological adaptations to cellular stress and types of toxic responses.
3. Discuss organ-selective, species selective, etc. differences in toxic effects.
4. Differentiate between types of cellular transport and their roles in accumulating xenobiotics.

5. Discuss bioactivation and detoxification of Xenobiotics during metabolism and biotransformation.
6. Differentiate between mechanisms resulting in bioactivation vs detoxification.
7. Differentiate between Phase I and Phase II mechanisms.
8. Describe Reactive Oxygen Species and their role in toxicity.
9. Explain the toxicological consequences of oxidative stress.
10. Discuss mechanisms that interfere with antioxidant stress.
11. Describe how mechanisms of oxidative stress affecting signaling, gene regulation and cell injury.
12. Discuss the role of Calcium in maintaining cellular homeostasis and mechanisms of toxicity by disruption of this process.
13. Differentiate between Genotoxic and Non-genotoxic xenobiotics in promoting carcinogenesis.
14. Compare toxic mechanisms of Cell Proliferation vs Tissue Repair
15. Explain normal mitochondrial function and how this could be impaired via xenobiotics.
16. Describe mechanisms within the mitochondria that are susceptible to xenobiotic insult and the effects that result from toxic injury.

Topics Will Include:

- Introduction to Mechanistic Toxicology
- Types of Toxic Responses and cellular adaptations to stress
- Transport Mechanisms and their effect on toxicity
- Biotransformation/Metabolism of Xenobiotics-Toxicokinetics
- Xenobiotic-Induced Oxidative Stress- ROS, Cell Injury, Signaling and Gene Regulation
- Changes in ionic homeostasis: Disruption of Calcium Homeostasis
- Apoptosis and necrosis
- mechanisms of cytotoxicity
- Epigenetic changes
- Xenobiotic Impairment of Cell Proliferation and Tissue Repair-including carcinogenesis
- Xenobiotic-Induced Energy Stress- Damage to Mitochondria
- Mechanisms of cytotoxicity : Studies : toxicogenomicos , transcriptomicos and metabonómicos

Grading: grades will be based on the total of the grades earned on mid-term exam, assignments, discussion boards and a final exam.

*Note the course schedule is subject to change: dates, time, location. The updated information will be available to students.