CAPS 434 Course Syllabus

CAPS 434. Endocrinology and Metabolism in Human Health and Disease (3 credits)

Academic Calendar Description:

Major discoveries and current advancements that are revolutionizing our understanding of thebiology, disease states, and therapeutic approaches for metabolic and reproductive disorders, stress and endocrine disorders including diabetes

Prerequisites

CAPS 305 or CAPS 301.

Corequisites: None

Other Requirements

This course is open to CAPS Majors and Honours students. Other 4th year students with 3 and 4 year cell biology credits may be considered at the discretion of the Course Director

Instructional Schedule: 2 x 90 min sessions each week

Student Expectations

Attend all classes and all exams in person. Read all assigned literature. Prepare any requested materials for presentations in class. Actively contribute to all class discussions.

Course Structure

TWO LECTURE SESSIONS PER WEEK (1.5 HOURS EACH). Each session comprises in-person classes. All classes will be a combination of lecture as well as group discussion in a flipped classroom model. The course is divided into five modules. All relevant literature and lecture materials will be provided on CANVAS prior to the lectures. An exam at midterm and at end of term will be in person and will examine the respective half of the course.

Learning Activities

All learning and reading material will be provided in PDF format on Canvas prior to the start of lectures. This will include all assigned reading and Instructor lecture and instructional material.

Prior to each session, students must have read the provided relevant research articles (examples listed below). The expected level of comprehension will be a broad understanding of the article's main goals, methodologies, observations and conclusions. This should take no longer than 2 hours per article.

Additionally, each student will write one 3-page critique per term, on the assigned research articles and associated lecture content of their choice. Each report will include introductory background and context to the article, its main methodologies and key data, as well as a conclusion that incorporates the contribution of the article to the overall field discussed in the lecture session. For each section, the student should provide a critique as to how well the authors address the overall goals & hypothesis for the work, and these perceived strengths and weaknesses should be supported by rationale. The reports are to be submitted within one week of the session.

Learning Materials

All learning and reading material will be provided in PDF format on Canvas prior to the start oflectures. This will include all assigned reading and instructor lecture material.

The majority of the lecture material will be based on current and seminal literature; the following are examples of the types of articles that will be used in class, including for critique assessments.

Session 4. Herman, Psychoneuroendocrinology. 2022 Mar:137:105641. PMID: 34954409 De Kloet and Holsboer, Nat Rev Neurosci. 2005 Jun;6(6):463-75. PMID: 15891777 Session 9. Leibel et al. N Engl J Med. 1995 Mar 9;332(10):621-8. PMID: 7632212 Session 14. Ashcroft et al. Trends Endocrinol Metab. 2017 May;28(5):377-387. PMID: 28262438 Session 17. Ramzy et al. Physiol Rev. 2022 Jan 1;102(1):155-208. PMID: 34280055 Session 20. Cheung et al. Science. 2000 Dec 8;290(5498):1959-62. PMID: 11110661 Session 22. Keymeulen et al. Nat Biotechnol. 2023 Nov 27. PMID: 38012450 Ramzy et al. Endocr Rev. 2023 Mar 4;44(2):222-253. PMID: 36111962 **Instructor Contacts** James Johnson. <james.d.johnson@ubc.ca>

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Clinical Assistant Professor, Dept. of Obstetrics & Gynaecology

Other Instructional Staff

TAs to be updated annually

Acknowledgement

UBC's Point Grey Campus is located on the traditional, ancestral, and unceded territory of the xwməθkwəỳ əm (Musqueam) people. The land it is situated on has always been a place of learning for the Musqueam people, who for millennia have passed on their culture, history, andtraditions from one generation to the next on this site.

Learning Outcomes

At the successful completion of this course, students will be able to:

Module 1. Endocrine disorders in reproduction, stress and growth

- Apply knowledge of the reproductive system to learn the basic principles of reproductive medicine, including in vitro fertilization and preimplantation genetic testing.
- Recognize the impact of gender affirming care on multiple endocrine systems and healthoutcomes.
- Apply knowledge of hypothalamic-pituitary-adrenal axis organization towards explaining the glucocorticoid-steroid basis for individual differences in responses to homeostatic threat and predisposition to disease.
- Apply knowledge of the growth hormone and IGF-1 pathway to understand the biologyof growth disorders and related pathological sequelae, as well as modern treatment approaches.

Module 2. Type 1 and type 2 diabetes. Genetics and disease mechanisms

- Apply knowledge of gene and protein structure, transcription factors, developmentalbiology and endocrine physiology to predict how rare gene mutations, for example MODY-related mutations, lead to the development of diabetes.
- Generate hypotheses regarding the mechanisms that lead to type 1 diabetes, including genetic and environmental factors, as well as be able to explain features of the autoimmune attack on insulin-producing beta cells in the pancreas that lead to pancreaticbeta-cell death and dysfunction.
- Generate hypotheses regarding the mechanisms that lead to type

2 diabetes, including theroles of various pancreatic beta-cell stresses and pathogenic beta-cell states that contribute to insulin insufficiency in the setting of insulin resistance.

Module 3. Biology and disorders of body weight

- Generate hypotheses regarding the mechanisms by which body weight is regulated andhow genetic alterations contribute to obesity.
- Explain the concept of energy balance.
- Generate hypotheses regarding how endocrine regulation of lipid homeostasis anddysregulation of lipid homeostasis leads to disease.
- Assess the role of preventative and therapeutic nutrition strategies for the treatment of metabolic conditions, including the role of caloric intake and macronutrient compositionin obesity and diabetes.

Module 4. Personalized medicine in endocrine and metabolic disorders

- Provide an overview of precision health approaches for diagnosing and treating rareendocrine disorders, with a focus on diabetes.
- Explain the importance of biological sex as a variable in mammalian endocrinology, and the importance of studies in female animals and in women to address the historical neglect of these populations in biomedical and clinical research.
- Convey how endocrine systems change and are changed throughout the human lifespan, from the in utero environment to old age.

Module 5. Therapeutics

- Explain to concept of biomarkers (cells, DNA, circulating hormones) as measures of disease and cell/system function, types of biomarkers in endocrine disease (e.g. misprocessed peptide hormones, miRNAs), genetic risk score, and the value of biomarkers in disease prediction, diagnosis, and in tracking response to therapy in clinical trials.
- Explain the pre-clinical to clinical drug development pathway by which new and iterativedrugs are developed in the endocrine field, with a focus on diabetes.
- Explain the pre-clinical to clinical drug development pathway by which new and iterativedrugs are developed in the endocrine field, with a specific focus on obesity.
- Assess approaches to in vivo gene therapy for hormone replacement to treat endocrinedisorders.
- Propose genetic engineering strategies to create designer cells for therapeutic purposes.

• Propose cell therapy approaches for hormone replacement to treat endocrine disorders, with a focus on diabetes.

Schedule of Topics

For each week: Assigned literature comprises original research or review articles (maximum 2 per class) that are intended to be 'current', therefore these will be added before the start of eachterm. Prior to each class discussion session, students must have read these research articles.

MODULE 1. ENDOCRINE DISORDERS IN REPRODUCTION,

STRESS AND GROWTHWEEK 1

Session 1: Course introduction and endocrinology refresher

• Students will be able to outline foundational concepts of endocrinology.

Session 2: Reproductive disorder therapies, including in vitro fertilization

• Students will apply knowledge of the reproductive system to learn the basic principles of reproductive medicine, including in vitro fertilization and preimplantation genetic testing.

WEEK 2

Session 3: Gender affirming care

• Students will recognize the impact of gender affirming care on multiple endocrinesystems and health outcomes.

Session 4. Rethinking stress resilience and vulnerability

• Students will be able to apply knowledge of hypothalamic-pituitary-adrenal axisorganization towards explaining the glucocorticoid-steroid basis for individual differences in responses to homeostatic threat and predisposition to disease.

WEEK 3

Session 5: Disorders related to growth hormone/Insulin Growth Factor

• Students will be able to apply knowledge of the growth hormone and IGF-1 pathway to understand the biology of growth disorders and related pathological sequelae, as well asmodern treatment approaches.

MODULE 2. TYPE 1 AND TYPE 2 DIABETES. GENETICS AND DISEASE MECHANISMS

Session 6. Genetics of diabetes: Rare diseases, MODY

• Students will be able to apply knowledge of gene and protein structure, transcription factors, developmental biology and endocrine physiology to predict how rare gene mutations, for example MODY-related mutations, lead to the development of diabetes.

WEEK 4

Session 7. Pathogenesis of type 1 diabetes

• Students will be able to describe the mechanisms that lead to type 1 diabetes, includinggenetic and environmental factors, as well as be able to explain features of the autoimmune attack on insulin-producing beta cells in the pancreas that lead to pancreaticbeta-cell death and dysfunction.

Session 8. Pathogenesis of type 2 diabetes

• Students will be able to describe the mechanisms that lead to type 2 diabetes, including the roles of various pancreatic beta-cell stresses and pathogenic beta-cell states that contribute to insulin insufficiency in the setting of insulin resistance, then compare and contrast the physiological dysregulation in type 1 vs type 2 diabetes.

MODULE 3. BIOLOGY AND

DISORDERS OF BODY WEIGHTWEEK 5

Session 9: Body weight regulation

• Students will be able to describe the mechanisms by which body weight is regulated, howgenetic alterations contribute to obesity, and apply this knowledge to differentiate male and female processes.

Session 10. Lipid homeostasis

• Students will be able to describe how endocrine regulation of lipid homeostasis and dysregulation of lipid homeostasis leads to disease, and will compare and contrast maleand female responses.

WEEK 6

Session 11. Nutrition

• Students will be able to defend the role of preventative and

therapeutic nutrition strategies for the treatment of metabolic conditions, including the role of caloric intakeand macronutrient composition in obesity and diabetes.

Session 12. Active learning in endocrine and metabolic disorders

• Students will be able to demonstrate current concepts and experimental approaches inendocrine disorders.

WEEK 7

Session 13. Mid-term exam (covering material in module 1,2,3)

MODULE 4. PERSONALIZED MEDICINE IN ENDOCRINE AND METABOLICDISORDERS

Session 14. Personalized/Precision medicine

• Students will be able to differentiate between precision health approaches for diagnosing and treating rare endocrine disorders, with a focus on diabetes.

WEEK 8

Session 15. Sex differences and women's health. Hormone replacement/ablation therapy

• Students will be able to examine the importance of biological sex as a variable in mammalian endocrinology, and the importance of studies in female animals and in women to critique the historical neglect of these populations in biomedical and clinicalresearch.

Session 16. From developmental origins of health and disease to aging

• Students will be able to convey how endocrine systems change and are changedthroughout the human lifespan, from the *in utero* environment to old age.

MODULE 5. THERAPEUTICS

WEEK 9

Session 17. Biomarkers

• Students will be able to evaluate the concept of biomarkers (cells, DNA, circulating hormones) as measures of disease and cell/system function, types of biomarkers in endocrine disease (e.g. misprocessed peptide hormones, miRNAs), genetic risk score, and the value of biomarkers indisease prediction, diagnosis, and in tracking response to therapy in clinical trials.

Session 18. Drug development in endocrinology disorders

• Students will be able to distinguish between steps in the preclinical to clinical drug development pathway and how new and iterative drugs are developed in the endocrinefield, with a focus on gut-derived peptides and enzyme inhibitors for diabetes & obesity.

WEEK 10

Session 19. Drug development in metabolic disorders

• Students will be able to distinguish between the steps in the preclinical to clinical drugdevelopment pathway by which new and iterative drugs are developed in the endocrine field, with a specific focus on metabolic diseases, in particular obesity.

Session 20: Gene therapy in endocrinology

• Students will be able to justify approaches to in vivo gene therapy for hormonereplacement to treat endocrine disorders.

WEEK 11

Session 21: Advances in genome engineering of cells for therapies in endocrinology

• Students will be able to defend genetic engineering strategies to create designer cells fortherapeutic purposes.

Session 22. Implant of differentiated stem cells for hormone replacement therapy

• Students will be able to critique cell therapy approaches for hormone replacement to treatendocrine disorders, with a focus on diabetes.

WEEK 12

Session 23 and 24. Active learning in endocrine and metabolic therapies

• Students will be able to compare and contrast current concepts and approaches inpersonalized medicine and therapies in endocrine and metabolic disorders.

WEEK 13

Session 25. Structured Review

Session 26. End of term exam (covering material from module 4,5).

Assessments of Learning

Assessment is in the following form: 1) Assigned literature report of one of the assigned research articles in the context of the field of the associated lecture. 2) Two invigilated in person exams. The midterm exam takes place after module 3 and will assess the content of modules 1, 2, 3. The end of term exam will assess the content of modules 4, 5.

Grading scheme:

| Literature reports | ` | 20% |
|--------------------|----------|-----|
| Midterm exam | | 40% |
| End of term exam | | 40% |

| Category | Outstanding | Meets Standards | Below Required Standards | Inc. * | Score |
|--|--|--|---|-----------|-------|
| Introduction | 5 A clear presentation of the paper's hypothesis A clear, concise and accurate summary of the rationale for the hypothesis | A reasonable summary of the hypothesis and its rationale | Either the hypothesis or its rationale are unclear. | 0 | 5 |
| Methods, Results and Conclusions | 5 • A clear, concise and accurate description of the methodology, results and conclusions. | An incomplete or partially unclear description of the methodology, results or conclusions. | The methods, results or conclusions are unclear. | 0 | 5 |

Grading Rubric for Literature Report (Graded out of 15 and worth 20% of grade)

| Critique of the Selected Paper | 5 • Generated an engaging, thought provoking discussion about the interpretation, strengths and weaknesses of the study | Generated a relevant discussion about the interpretation about the strengths and weaknesses of the study | Generated a limited discussion about the interpretation and strengths and weaknesses of the study | 0 | 5 |
|-----------------------------------|---|--|---|---|---|
| | | | *In | | |

*Inc ompl ete

University Policies

UBC provides resources to support student learning and to maintain healthy lifestyles but recognizes that sometimes crises arise and so there are additional resources to access including those for survivors of sexual violence. UBC values respect for the person and ideas of all members of the academic community. Harassment and discrimination are not tolerated nor is suppression of academic freedom. UBC provides appropriate accommodation for students with disabilities and for religious observances. UBC values academic honesty and students are expected to acknowledge the ideas generated by others and to uphold the highest academic standards in all of their actions. Details of the policies and how to access support areavailable at the Policies and Resources section of the UBC Senate website.

Academic Integrity

The academic enterprise is founded on honesty, civility, and integrity. As members of this enterprise, all students are expected to know, understand, and follow the codes of conduct regarding academic integrity. At the most basic level, this means submitting only original workdone by you and acknowledging all sources of information or ideas and attributing them to others as required. This also means you should not cheat, copy, or mislead others about what isyour work. Violations of academic integrity (i.e., misconduct) lead to the breakdown of the academic enterprise, and therefore serious consequences arise and harsh sanctions are imposed. For example, incidences of plagiarism or cheating may result in a mark of zero on the assignment or exam and more serious consequences may apply if the matter is referred to the President's Advisory Committee on Student Discipline. Careful records are kept in order to monitor and prevent recurrences.

A more detailed description of academic integrity, including the University's policies and procedures, may be found in the <u>Discipline</u> <u>for Academic Misconduct</u> section of the UBCAcademic Calendar.

- No assignment may be submitted to any other instructor of any course for a grade.
- The minimum penalty for plagiarism in any assignment is a zero for the paper; themaximum penalty is a zero for the course.

UBC Grading Standards

Undergraduate Grading Scale

| Percentage (%) | Letter Grade |
|----------------|--------------|
| 90-100 | A+ |
| 85-89 | А |
| 80-84 | A- |
| 76-79 | B+ |
| 72-75 | В |
| 68-71 | В- |
| 64-67 | C+ |
| 60-63 | С |
| 55-59 | C- |
| 50-54 | D |
| 0-49 | F |

Learning Resources

All learning resources will be accessible on CANVAS from the start of each term

Copyright

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