NORGES IDRETTSHØGSKOLE

MAL SENSORVEILEDNING

Sensorveiledning utarbeides av den/de som lager oppgavesettet til den aktuelle eksamen og utarbeides samtidig med eksamensoppgaven.
Sensorveiledningene skal være tilgjengelige for studentene etter at karakterer er fastsatt, jf. UH-loven § 5-3 (3) - https://lovdata.no/lov/2005-04-01-15/§5-3.

Emnekode	THP-301
Emnenavn	Cell Biology
Studieår semester	Fall 2022
Studiepoeng	10
Emneansvarlig	Adam Sharples
Eksamenstype	4 Hour Home Exam

Malen tilpasses eksamenstype/vurderingsform.
Dokumenter som skal være tilgjengelig for sensor

☐ Eksamensoppgave (dersom den ikke følger i WISEflow)
☐ Emneplan eller fagplan
☐ Informasjon som er gitt til studentene om den konkrete eksamen

Læringsutbytte

Hvilke læringsutbyttebeskrivelser er eksamensoppgaven knyttet til?

- Know how exercise creates extracellular signals outside cells that lead to activation of receptors/channels and subsequent intracellular signalling, gene expression and changes in protein levels within cells.
- Understand the molecular adaptation to resistance exercise.
- Understand the molecular adaptation to endurance exercise.
- Understand the epigenetics of resistance and endurance exercise.

Pensum/fagstoff:

Henvis til de mest aktuelle delene av pensum/fagstoff knyttet til eksamensoppgaven.

See the course schedule. Finners at www.nih.no, Or go to link:

Introduction

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The course gives the students an overview on cellular and molecular biology related to the function of DNA, RNA and protein, regulation of gene expression, and intracellular signaling systems involved in molecular exercise physiology.

Learning outcomes

The students should be able to:

- know how exercise creates extracellular signals outside cells that lead to activation of receptors/channels and subsequent intracellular signalling, gene expression and changes in protein levels within cells.
- understand the molecular adaptation to resistance exercise.
- understand the molecular adaptation to endurance exercise.
- Understand genetics of muscle mass, strength and endurance performance.
- understand the epigenetics of resistance and endurance exercise.
- understand the cell and molecular biology of adaptation to skeletal muscle / exercise with performance enhancing drugs.
- understand laboratory methods for assessing intracellular signalling, gene expression and protein levels in skeletal muscle after exercise.

Learning styles and activities

The course consists of lectures, student presentations and one laboratory course (followed by a written lab report – see below).

Assessment

- 4 hours individual exam (school). Graded A-F.
    - Recourses/materials which may be used in the exam: Dictionary
- Laboratory report is assessed on a pass/ fail basis.

Tasks submitted via Wiseflow will be run through plagiarism control.

Core material

1 BOOK:
Sharples, A. P. James P. Morton, J. P. & Henning Wackerhage, H. (2022). *Molecular exercise physiology: An introduction* (2nd ed.). Routledge.
*** You will find the book in the Library, here:** ORIA
**** This book is also available online:** Click here to download.
***** NB! To open electronic books off campus, you must use the following VPN connection:** Click here to download.

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Undervisning

Forelesningsplan og/eller timeplan følger vedlagt. Hvis det er aktuelt, kan man her kommentere vektleggingen av ulike deler av pensum i undervisningen, hvilke undervisningsmetoder som er brukt, og evt. annen informasjon om gjennomføringen av undervisningen/emnet som er relevant for å kunne vurdere besvarelsene på en best mulig måte. Ved selvstendige oppgaver, har studentene fått veiledning underveis?

Session 1 (Week 34) Wednesday 24th Aug, 12.30 – 16.15: Learning Outcome: Know how exercise is sensed by cells and leads to activation of subsequent intracellular signalling, gene expression and changes in protein levels. AND: Understand basic laboratory methods for assessing intracellular signalling, gene expression and protein levels in skeletal muscle after exercise.

Session 2 (Week 36) Wednesday 7th Sept, 12.30 – 16.15: Learning Outcome: Understand the molecular response/adaptation to resistance exercise.

Session 3 (Week 37) Wednesday 14th Sept, 12.30 – 16.15: Student presentations on session 2's topics.

Session 4 (Week 38) Wednesday 21st Sept, 12.30 – 16.15: Learning Outcome: Understand the molecular response/adaptation to endurance exercise.

Session 5 (Week 39) Wednesday 28th Sept, 12.30 – 16.15: Student Presentations on session 4's topic.

Session 6 (Week 40) Wednesday 5th Oct, 12.30 – 16.15: Learning Outcome: Understand genetics of muscle mass, strength and endurance performance.

Session 7 (Week 41) Wednesday 12th Oct, 12.30 – 16.15: Student presentations session 6's topics. Student presentations on session 6's topics.

Session 8 (Week 42) Wednesday 19th Oct, 12.30 – 16.15: Learning Outcome: Understand the epigenetics of resistance and endurance exercise.

Session 9 (Week 43) Wednesday 26th Oct, 12.30 – 16.15: Student presentations on session 8's topics. (*Prof. Adam Sharples*)

Session 10 (Week 44) Wednesday 2nd Nov, 12.30 – 16.15: Learning Outcome: Understand the cell and molecular biology of adaptation to exercise & doping/anabolic steroids

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Session 11/12 (Week 45 / 46) **Laboratory sessions** (to derive data for lab report). There are 2 available sessions: **Wednesday 9th Nov, 10.15 – 16.15 OR Wednesday 16th Nov, 10.15 – 16.15** (**IMPORTANT:** You will be required to only attend **ONE** of these sessions- which date you will attend will be confirmed closer to the time). Lab session entitled: 'Gene expression analysis of skeletal muscle after exercise.' All students will have data for lab report released by Thur 17th Nov **(Lab report deadline: Thursday 1st Dec)**

Session 13 (Week 47): Student Lab Report writing (no physical session).

Session 14 (Week 48) Wednesday 30th Nov, 12.30 – 16.15
Revision for Exam with Course leader (Prof. Adam Sharples).

Session 15 (Week 49): Student-self exam revision (no physical session).

EXAM (Week 49) Friday 9th Dec 10.00 – 14.00.

Fasit/Løsningsforslag/ Vurderingskriterier

Ved konkrete svaralternativ, definer hva kandidaten må ha med i svaret sitt for å svare på hver oppgave, f.eks. i form av fasit, eller moment fra pensum i disiplinbaserte eksamener/muntlige eksamener. Ved individuelt utformede oppgaver, definer punkt/moment oppgaven bør inneholde. Hvilke forventninger er det til et A-svar, et godt gjennomsnittlig svar (altså C-svar) og et E-svar? Ved karakterskala bestått/ikke bestått, hva må være med for å bestå eksamen?

*There are **4 main questions** from 4 of the main topics covered in the Cell Biology Course. Each question contains 2-3 sub-questions (for example a, b and / or c).*

Each main question is worth 25 marks (25 marks x 4 questions = 100 Marks in Total).

Exam is graded A-F.

*You should spend approximately **1 hour on each main question** (4 hours in total).*

Any resources ARE allowed to be used in the HOME exam.

All exams will be subject to plagiarism checks.

Answers in ENGLISH.

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Question 1

Topic- What is Cellular / Molecular Exercise Physiology?

a) Provide a short definition for: What is 'molecular exercise physiology'? (2 marks)

Molecular exercise physiology is, 'the study of the underlying regulatory mechanisms that underpin physiological adaptation to exercise.'

b) What is gene transcription (also termed mRNA or gene-expression)? In your answer, briefly describe the process of gene transcription. (6 marks)

Gene transcription is the process of increasing or decreasing the amount of mRNA of a given gene. Transcription occurs after changes in intracellular signalling lead to activation or deactivation (typically via phosphorylation/dephosphorylation) of proteins called transcription factors. These are proteins that move from the cytoplasm into the nucleus and together with other transcriptional co-factors bind to promoter regions of a gene to initiate the transcription process via recruitment of the enzyme, RNA polymerase. RNA polymerise synthesises the mRNA based on following the DNA template. Students can also describe the processing of mRNA in more biochemical detail which will achieve marks instead of or as well as the above.

a) Define each step in the 'signal transduction hypothesis' for the molecular responses to acute exercise. In your answer, describe and explain the exercise 'signal' through to changes in the amount of protein produced by the cell. Refer to at least one example for each step (17 marks).

Main importance for this question is understanding molecules are catagorized in which response. So that categories of: 1) exercise signal, 2) molecular sensor, 3) intracellular signal, 4) transcription factors, 5) gene transcription, 6) protein translation and or biological outcome are specified. Examples of relevant pathways student may use to demonstrate knowledge of these categories include: 1) signal- energy changes (ATP/NADH) as a result of aerobic exercise, 2) Sensor- AMPK, 3) downstream intracellular signalling e.g. p53 or others 4) including activity of transcription factors/co-factors e.g. PCG1-alpha, 5) turning on gene expression of nuclear metabolic genes (ERRa, PPAR, VEGFA, NRF1/2) that affect 6) mitochondrial genes/proteins (TFAM) evoking mitochondrial biogenesis, angiogenesis and increased oxidative capacity.
Other examples are muscle contraction after aerobic exercise- calcium/CAMKII/calmodulin signalling, p38 MAPK, NFAT, slow myosin gene gene/protein expression. Or a resistance exercise example- Mechanical tension / mTOR / p70s6k increased protein synthesis, anabolism, hypertrophy. Any other relevant pathway as an example is permitted, however students should characterise them approximately in categories 1-6 above (note mTOR pathway results in increases in initiation and elongation of mRNA into proteins in the ribosome (protein synthesis) so not necessarily- categories 4) transcription factors and 5) gene transcription apply to this specific example, which is also acceptable.

Question 2

Topic- Cellular / Molecular Regulators of Resistance Exercise and Hypertrophy

a) List the names of the main molecular pathways involved in 'positively' and 'negatively' effecting muscle mass. (4 marks)

Positive- Tension- Akt-mTOR / p70s6k/ 4EBP-1 (students may include more relevant signalling molecules in the same pathway which is also permitted). Including IGF-I instead of mechanical tension as input into Akt/mTOR is also acceptable.
Negative -Myostatin/activin pathway and/ or the ubiquitin proteosome pathways. Students may include more relevant signalling molecules in the same pathways which is also permitted)

b) Describe how satellite cells contribute to skeletal muscle repair. In your answer, you can describe what a satellite cell is, where it's located in skeletal muscle tissue and how the satellite cell undergoes the cycle of myogenesis to contribute to repair of muscle. (7 marks)

Description of satellite cell should include they are an adult muscle stem cell, their location is the periphery of the fibres underneath the sarcolemma. Upon mechanical loading they undergo the process activation, proliferation, fusion/differentiation to the existing fibres. If they can describe the molecular regulators of these processes e.g. MRF5, myod, myogenin, myomaker, MYHC's they can achieve an additional mark if they miss a mark earlier. However, the molecular regulation description is not required for full marks.

c) Describe the mTOR pathway and how it activates protein synthesis after resistance exercise via its downstream signalling. In your answer, briefly explain the 'upstream' signals that can activate mTOR. Then discuss how mTOR 'senses' mechanical load and how it is thought to convert this mechanical signal into a molecular signal. You should use examples from the research literature, using human resistance exercise studies and/or rodent models (e.g., synergistic ablation) to support your answer. (14 marks)

Students can describe the mTOR complex and upstream input such as growth factors and amino acids. Additional mark for explaining the regulation of amino acids vs. growth factors. Students should then detail about how tension is thought to be sensed by mTOR by mechanosensors such as FAK or TSC1/2 or ERK. How this activates downstream signalling involved in protein synthesis e.g., mTOR/P70s6K or ERK/p90RSK and eIF proteins are activated and how this initiates mRNA initiation and elongation into the ribosome increasing protein synthesis. Literature cited could note the requirement/lack of requirement for upstream IGF-I /IGF-IR/Pi3K/Akt input in activation of downstream mTOR/P70s6K or ERK/p90RSK, protein synthesis and hypertrophy. Any relevant examples of changes /increases in mTOR signalling in human muscle e.g., Baar/Esser p70S6K & overload in animals, Drummond papers using rapamycin in humans to block mTOR with/without exercise are relevant. Higher level marks could be given to role of exercise intensity or optimal resistance exercise regime to evoke most advantageous signalling responses.

Question 3

Topic – Cellular / Molecular Regulators of Endurance Exercise

a) After a bout of endurance/aerobic exercise list the main molecular 'sensor' for each of these exercise 'signals': 1) Calcium, 2) ADP/AMP levels, 3) ROS and/or NAD/NADH levels. (3 marks)

Answers: CAMKII, AMPK and SIRT1

b) Define autophagy and mitophagy, and briefly describe how these processes might support mitochondrial quantity and reticulum quality after exercise (7 marks).

Students should define the general process of autophagy & mitophagy. Explain that these processes support an increase in mitochondrial quantity and quality. Additional marks will be given for describing how these processes have been shown to improve mitochondrial quantity and quality after exercise (and perhaps reference to a key original paper).

c) Describe the time-course of molecular responses through to physiological adaption following endurance exercise and training. For example, describe the main molecular signal(s) & sensors for endurance exercise. In your answer you should include the role of the so called 'master' regulator of endurance adaptation, PGC1-alpha, and associated metabolic/mitochondrial genes. You should also discuss how PGC1-alpha alters nuclear and mitochondrial gene expression after exercise and how these changes cause adaptation to mitochondria and ultimately endurance performance. You should use original research articles to support your answer, for example, how exercise intensity and other exercise parameters may affect the above molecular pathways (15 marks).

First few seconds- calcium flux, ATP turnover, redox and reductions in muscle glycogen. Minutes- activation of protein kinases such as CAMKII, AMPK, p38 MAPK, SIRT1. Hours, mRNA expression of transcription factors (PGC-1α, PPAR, NRF) Mitochondrial TF's (Tfam, p53), Substrate metabolism (PDK4, Hexokinase), Angiogenesis (VEGF) mRNA and protein expression, increase in rates of mtDNA. Days - mitochondrial protein synthesis, citrate synthase activity. Weeks- total protein of multi-subunit respiratory complexes, quality and size of mitochondria. Students should draw on at least two empirical articles that perhaps characterise the molecular response to acute aerobic exercise (perhaps highlighting differences in exercise intensity) and aerobic training studies demonstrating adaptation to mitochondria.

Question 4

Topic - Epigenetics of Exercise

a) What is epigenetics? Define epigenetics, and list some of the main epigenetic modifications. Finally, briefly describe how the epigenetic modification of DNA methylation regulates gene expression. (5 marks)

Epigenetics 'above' genetics are modifications to our genetic material caused by environmental interactions and not alterations in genetic code itself. Histone modifications (acetylation etc), DNA methylation, miRNAs as main modifications to list. DNA methylation is a biochemical modification to DNA that incorporates a methyl group typically into CpG sites. Increased DNA methylation (hypermethylation), generally in promoter or enhancer regions, blocks transcription factor binding and inhibits/reduces gene expression. Alternatively, reduced (hypomethylation) allows transcription factor binding and gene expression increases. This is a generic explanation and one that is expected. However, the students may include more detail on the biochemical processing of DNA methylation that will also gain them marks.

b) Describe what is currently known about how DNA methylation may be involved in regulating the response and adaptation to resistance exercise. For example, what does resistance exercise do to DNA methylation across the entire genome, what overarching

molecular pathways demonstrate altered DNA methylation following acute exercise or chronic resistance training. (7 Marks)

Students should comment on the studies in acute or chronic resistance exercise/training and the data suggesting there is predominantly hypomethylation after exercise (include information of studies, study design and detail the direction of change in methylation and in which molecular pathways in both aerobic and resistance exercise). Highlighting the changes in key pathways.

c) Skeletal muscle has been proposed to possess an epigenetic memory of earlier exercise. In this context, define what muscle memory is. Describe and discuss studies that have demonstrated epigenetic muscle memory in the literature and discuss potential future implications for the research into epigenetic muscle memory (13 marks).

Students should briefly describe/define what muscle 'memory' is in the context of adaptation to skeletal muscle. They should summarise the main studies in this area. The study design, the overarching methods, results and conclusions. Interpretation of these studies and the level of interpretation will be key in achieving higher marks. The ability to integrate findings from more than one study will also be considered. Also, importantly highlighting how these studies support the theory for the role of epigenetics in muscle memory. Also, the implications for research / applied practice in this field. Students can refer to 'cell memory' via nuclear accretion to support their answer but should focus on epigenetic memory. Although if they manage to discuss recent papers looking at nuclear retention and epigenetic profiles then this would be advantageous.

Veiledende mal for innhold

- **Overordnede kriterier for vurdering**: Læringsutbyttebeskrivelser og/eller vurderingskriterier satt for den enkelte eksamen (f.eks. praktisk eksamen/muntlig eksamen, bachelor-/masteroppgaver og andre større oppgaver)
- **Generelle karakterbeskrivelser for UH-sektoren** (6. august 2004), https://www.uhr.no/_f/p1/i4bfb251a-5e7c-4e34-916b-85478c61a800/karaktersystemet_generelle_kvalitative_beskrivelser.pdf, eller beskrivelse av krav til **bestått/ikke bestått karakter** (avhengig av karakteruttrykk for den enkelte eksamen)
- **Relevant pensum for oppgavesettet**. Ved konkrete spørsmål oppgis pensumreferanse til det enkelte spørsmål
- **Forventninger til besvarelse**. Ved eksamener med flere konkrete spørsmål beskrives forventninger til hva som gir full uttelling på det enkelte spørsmål, evt. hva som forventes for bestått besvarelse. Spørsmålsstillingen vil avgjøre hvor konkret sensorveiledningen kan utformes. Hvis det brukes poenggiving som hjelpemiddel i vurderingen, beskrives i grove trekk hvordan poengene fordeles.
- **Bruk av faglig skjønn – helhetlig vurdering** bør presiseres, opp mot generelle karakteruttrykk og/eller vurderingskriterier for den aktuelle eksamenen
- **Andre forhold av betydning for vurdering.** (F.eks. hvis oppgaver skal vektes ulikt, hvis noe av pensum er mindre vektlagt enn andre deler, evt. plagiatkontroll m.m.)