NORGES IDRETTSHØGSKOLE

SENSORVEILEDNING- THP 301

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 2023
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 and explain 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, explain and discuss the molecular adaptation to resistance exercise.
- Understand, explain and discuss the molecular adaptation to endurance exercise.
- Understand, explain and discuss 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:

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Introduction

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 and explain 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, explain and discuss the molecular adaptation to resistance exercise.
- Understand, explain and discuss the molecular adaptation to endurance exercise.
- Understand, explain and discuss genetics of muscle mass, strength and endurance performance.
- Understand, explain and discuss the epigenetics of resistance and endurance exercise.
- Understand, explain and discuss 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 and and perform gene expression methods in skeletal muscle after exercise

These learning outcomes are subject to minor changes, such as specific topics within cell and molecular biology of sport and 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 HOME exam. Graded A-F.

Recourses/materials which may be used in the exam:
Any available resources are allowed to be used in the HOME exam.
All exams will be subject to plagiarism checks.
Answers in ENGLISH.

- Laboratory report is assessed on a pass/ fail basis.

Tasks submitted via Wiseflow will be run through plagiarism control.

Core material

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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.

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 23rd August, 12.30 – 16.15: Introduction to course (Prof. Adam Sharples). Then Learning Outcome: Know-how and explain 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. AND: Understand basic laboratory methods for assessing intracellular signalling, gene expression and protein levels in skeletal muscle after exercise.

NO SESSION WEEK 35

Session 2 (Week 36) Wednesday 6th Sept, 12.30 – 16.15: Learning Outcome: Understand, explain and discuss the molecular adaptation to resistance exercise.

Session 3 (Week 37) Wednesday 13th Sept, 12.30 – 16.15: Student presentations on session 2's topics.

Session 4 (Week 38) Wednesday 20th Sept, 12.30 – 16.15: Learning Outcome: Understand, explain and discuss the molecular adaptation to endurance exercise.

Session 5 (Week 39) Wednesday 27th Sept, 12.30 – 16.15: Student Presentations on session 4's topic

Session 6 (Week 40) Wednesday 4th Oct, 12.30 – 16.15: Learning Outcome: Understand, explain and discuss the epigenetics of resistance and endurance exercise.

Session 7 (Week 41) Wednesday 11th Oct, 12.30 – 16.15: Student presentations session

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6's topics. Student presentations on session 6's topics

Session 8 (Week 42) Wednesday 18th Oct, 12.30 – 16.15:
Learning Outcome: Understand, explain and discuss genetics of muscle mass and strength.

Session 9 (Week 43) Wednesday 25th Oct, 12.30 – 16.15: Student presentations on session 8's topics. **Attendance important- information regarding laboratory practical sessions and important information on the format of the exam.**

Session 10 (Week 44) Wednesday 1st Nov, 12.30 – 16.15 in Aud Innsikt: Learning Outcome: Understand, explain and discuss the cell and molecular biology of adaptation to skeletal muscle / exercise with performance enhancing drugs (focus on anabolic steroids) NOTE- there are NO student presentations for this topic.

Session 11/12 (Week 45 / 46) Laboratory sessions (to derive data for lab report). There are 2 available sessions: **Wednesday 8th Nov, 10.15 – 16.15 OR Wednesday 15th Nov, 10.15 – 16.15.** Learning outcome - Perform gene expression methods in skeletal muscle after exercise.

(**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 16th Nov **(Lab report deadline: Thursday 30th NOV)**

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

Session 14 (Week 48) Wednesday 29th Nov, 12.30 – 16.15
Revision for Exam with Course leader.

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

EXAM (Week 50): Wed 13th 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?

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*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.

Kommentert [AS1]: I now think that students can now answer in English or Norwegian?

Question 1

Topic- What is Cellular / Molecular Exercise Physiology? And the 'signal transduction theory' of exercise adaptation?

a) Provide a short definition for: What is 'molecular exercise physiology'? (3 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 explain what process the term gene transcription is describing. (5 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.

c) Explain, in order, if possible, the stages involved in the overarching molecular response to exercise. From the exercise 'signal' through to changes in the amount of protein produced by the cell. Refer to at least 1 main example for each stage. One example of an exercise 'signal' would be an increase in calcium in the muscle. Therefore, in your answer you may want to explain what causes an increase in this type of exercise 'signal', what are the molecular 'sensors' that detect a change in this signal, and what are the ensuing extracellular/intracellular responses leading to alterations in gene transcription and protein levels. Note- You can use any example of an exercise signal (i.e,. you do not have to use calcium). (17 marks)

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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- Molecular Regulation of Adaptation to Resistance Exercise (and Hypertrophy)

a) List the main molecular pathway or cellular processes involved in 'positively' effecting muscle mass. (3 marks)

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.

b) List the main pathway/pathways involved in 'negatively' effecting muscle mass. (2 marks)

Myostatin/activin pathway and/ or the ubiquitin proteosome pathways. Students may include more relevant signalling molecules in the same pathways which is also permitted).

c) Describe the mTOR pathway and how it activates protein synthesis via its downstream signalling. In your answer then go onto discuss how mTOR 'senses' mechanical load and how it is thought to convert this mechanical signal (e.g. after resistance exercise in humans or mechanical overload in animal models) 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. (20 marks)

Students should 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 –Molecular Regulation of Endurance Exercise Adaptation

a) What are the aerobic exercise 'signals' that activate the molecular 'sensors': CAMKII, AMPK and SIRT1? (3 marks)

Calcium for sensor CAMKII, changes in energy ADP/AMP for sensor AMPK, ROS/free radicals affects NAD/NADH for the sensor SIRT1.

b) Briefly outline the timeline of endurance exercise adaptation in terms of cell/molecular signalling through to physiological and phenotypic changes. For example, describe the main molecular signal(s) & sensors for endurance exercise. Then what happens to the 'master' regulator PGC1-alpha and associated metabolic/mitochondrial genes. Finally, discuss how PGC1-alpha alters gene expression and how these changes cause adaptation to mitochondria and ultimately endurance performance. You need to use examples from at least 2 original research articles to support your answer referring to exercise intensity and how this may affect the above molecular pathways (22 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. They can also mention information discussed in the lectures/presentations on autophagy/mitophagy and mitochondrial protein quality control following exercise training.

Question 4

Topic - Epigenetics of Resistance and Aerobic Exercise (and muscle memory)

a) What is DNA methylation? Describe the process of DNA methylation, and how DNA methylation regulates gene expression. (3 marks)

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.

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b) Describe what is currently known about how DNA methylation may be involved in regulating the response and adaptation to aerobic exercise. For example, what does aerobic exercise do to DNA methylation across the entire genome, what overarching molecular pathways demonstrate altered DNA methylation following acute aerobic exercise or chronic exercise training. Note- you can also use examples from diseased/aged/patient groups as well as those in healthy adults. (10 Marks)

Students should comment on the studies in acute or chronic aerobic training and the data suggesting there is predominantly hypomethylation in metabolic pathways (include information of studies, study design and detail the direction of change in methylation and in which cellular molecular pathways). Highlighting the changes in methylation with changes in exercise intensity and including information about the literature in this area would provide additional marks. Studies including exercise in type-II diabetics, obese individuals investigating genome wide methylation are relevant as there aren't many in healthy young adults.

c) Describe what is currently known about how DNA methylation may be involved in regulating the response and adaptation to resistance exercise. Discuss what is meant by muscle possessing an **epigenetic 'memory'** referring to original research studies in your answer. Note- you do not need to discuss cell memory or myonuclei retention in your answer as this is not an epigenetic modification. (12 Marks)

Students should briefly describe/define what muscle 'memory' in the context of adaptation to skeletal muscle. Particularly with respect to epigenetic muscle memory. 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.

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

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- **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.)