MEDICAL UNIVERSITY OF VIENNA

Molecular mechanisms in cell biology

Thesis Program of the Curriculum of
"Doctor of Philosophy"
N094

Coordination:

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Short description:

The existence of multicellular organisms depends on highly coordinated proliferation, growth, differentiation, and death of cells. Life starts with the proliferation of pluripotent stem cells, which start to differentiate upon initiation of preformed programs or signals from neighboring cells. Cell proliferation is orchestrated by a sequence of biochemical and cell biological events referred to as the cell cycle. Proliferation and differentiation are considered as two alternative possibilities for survival of cells; terminal differentiation usually leads to cells that irreversibly have lost the ability to proliferate. Cell differentiation is due to a selective, cell-specific expression of genes, whose products generate cells with specific phenotypes and functions such as neurons, erythrocytes, muscle cells, germ cells, to name a few. Cell growth is an intrinsic feature of proliferating cells, which have to increase their size prior to cell division. Specialized cells such as oocytes or muscle cells grow during terminal differentiation to an extraordinary size intimately related to their function. Finally, to ensure proper development of the organism and organ architecture, cells have to die in a coordinate fashion (apoptosis).
Defects in the controlled life cycle of cells in man usually result in severe defects or diseases. Uncontrolled cell proliferation, blocked cell differentiation, and/or inhibition of apoptosis often lead to the development of neoplastic cells and tumors. Differentiation defects cause malformations during embryonic development. In addition, pathogens like bacteria and viruses affect cell homeostasis often resulting in cell degeneration and cell death. The understanding of molecular mechanisms of the "normal life cycle" of a cell is a prerequisite to understand aberrations, which cause disease. This program includes projects related to **cell proliferation, growth, differentiation, and death.** In addition, several projects directly relate to diseases caused by intrinsic or induced aberrations of these cellular programs. Due to the broad spectrum of cell systems used (germ cells, muscle cells, neurons, hematopoietic cells, yeast) and topics covered (chromatin structure, signal transduction, transcription factors, protein/protein interaction, extracellular matrices, enzyme biogenesis, virology, molecular modeling) and techniques applied in the different groups, students enrolled in this program will have the opportunity to become familiar with many aspects of cellular and molecular biology. Another advantage of this program is that it is embedded in all the activities of the Vienna Biocenter, which houses not only the Max. F. Perutz Laboratories but also the IMP, the IMBA, and the GMI. The program will be run in conjunction with the international FWF-funded PhD programs at the Vienna Biocenter together with the IMP, IMBA, and GMI. Thus,

students will be able to participate in the lectures and seminars offered by the Biocenter. In addition, the students will have the opportunity to meet world-class scientists who present invited talks at the Biocenter on a weekly basis.

Admission

Students have to fulfill the general criteria defined by the Medical University of Vienna for the admission to the PhD programs. In addition, candidates who have not been recruited via the general procedure at the Vienna Biocenter will be selected by a committee. This selection committee consists of 3 group leaders of this program and will be assembled ad-hoc. All candidates for the program must submit an informal written application including a C.V. and two letters of reference to the coordinator of the program. The applicant will be provided with 2 papers (selection of the papers will be made by the committee). The candidate will select one paper for her/his presentation at the interview.
The interview will last 45 minutes and will be structured in the following manner. For the first 15 minutes the candidate will present the selected paper and will discuss its conclusions. During the second 15 minutes, the candidate will be asked to present her/his Diploma work. For both presentations the candidate will not be allowed to use PowerPoint or overheads, but may use a blackboard or flip chart. The last 15 minutes will be used for a general interview of the candidate.
The final decision about the admission will be made by the committee after the interview, and the candidate will be informed immediately.

Courses:

- **Propedeutics** **6 semester hours**
- **Basic Lectures** **4 semester hours**
- **Thesis Seminars** **8 semester hours**
- **Journal Clubs and Progress reports** **12 semester hours**

Basic Lectures

1. **Molecular mechanisms of normal and pathological cell proliferation**
   2 semester hours, coordinator: Edgar Wawra

2. **Advanced Methods in Molecular Cell Biology**
   2 semester hours, coordinator: Roland Foisner

Thesis Seminars

1. **Molecular Medicine I**
   2 semester hours, coordinator: Wolfgang Schneider

2. **VBC-Lecture Series**
   4 (6) semester hours; 2 (3) out of 4 lecture series have to be chosen

3. **Basic principles in animal handling**
   2 semester hours, Marcela Hermann

The course "Basic principals in animal handling" is mandatory for students who will work with animals during their project and optional for others. If not chosen, 3 instead of 2 lecture series must be taken.

Journal Clubs/Progress Reports

1. **MFPL – Research Seminars I – IV**
   Weekly student seminar together with IMP and IMBA, where each student is obliged to report once a year on her/his project
   1 semester hour, runs every semester for the duration of 3 years which adds up to a total of **6 semester hours**

2. **Journal Club**
   Weekly journal club which is organized by individual groups of the MFPL where students are obliged to present and discuss novel publications.
   1 semester hour, runs every semester for the duration of 3 years which adds up to a total of **6 semester hours**

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Molecular mechanisms of normal and pathological cell proliferation

Seminar, 2semester hours

Coordinator: E. Wawra (edgar.wawra@meduniwien.ac.at, tel: 4277/61707)

Program:

E. Wawra: Bioelements: Function and Toxicity

C. Seiser: The Human Genome

C. Seiser: Chromatin: Structure and Function

E. Wawra: Metabolism of Nucleic Acid Precursors and its Inhibitors

R. Hofbauer: Cell-Cycle

R. Hofbauer: Growth Factors

E. Wintersberger: Transcription Factors

E.Wintersberger: Hereditary Mutations in Transcription Factors

E. Müllner: Regulation of Translation

E. Müllner: Stem-Cells

J. Rotheneder: Oncogenes and Carcinogenesis

J. Rotheneder: Tumor Suppressors and Gene Therapy

E. Ogris: DNA Tumor Viruses

E. Ogris: RNA Tumor Viruses

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Advanced Methods in Molecular Cell Biology

2 semester hours, 3 hours per unit

Coordinator: Roland Foisner, Roland.Foisner@meduniwien.ac.at
Lecturers: Andreas Eger, Josef Gotzmann, Sylvia Vesely

1) Foisner: Light Microscopy
immunofluorescence, epifluorescence, confocal microscopy, live cell imaging, fluorescence recovery after photobleaching, fluorescence resonance energy transfer

2) Vesely: Cell Culture and Protein Expression
primary cell culture, cell lines, differentiation models, gene transfer, eukaryotic and bacterial ectopic gene expression systems

3) Vesely: Protein-Protein Interaction
labeling and purification of proteins, in vitro, in situ and in vivo binding assays (e.g. surface plasmon resonance, Scatchard plots, coimmunoprecipitation, tandem affinity purification, yeast two hybrid)

4) Eger: DNA-Protein Interaction
bandshift assays, footprinting, chromatin-immunoprecipitation, yeast one-hybrid, reporter gene assays

5) Gotzmann: Gene Silencing Part I
methylation CpG islands, histone modifications, RNA-interference, post transcriptional gene silencing (transient, stable)

6) Gotzmann: Gene Silencing Part II
micro RNAs, antisense technologies

7) Gotzmann (and guest speakers): Genomics/Proteomics
microarray technologies, two-dimensional gel analyses, protein identification by matrix-assisted laser desorption ionization mass spectroscopy

8) Foisner: Cell Cycle Analyses
cell culture synchronization methods, analyses of cell cycle stages (fluorescence-activated cell sorting, elutriation, BrdU incorporation, proliferation markers)

9) Eger: Tumor and Metastasis Analyses
organotypic cultures of epithelial cells, xenotransplantation, in vivo imaging of tumor cell invasion, transgenic and knockout tumor models

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Basic principles in animal handling

2 semester hours

Lector: **Marcela Hermann**; Marcela.Hermann@meduniwien.ac.at

Theoretical part, 5 hours

Ethics
Legal basis, laws for animal experimentation
General Biology and Physiology of Laboratory animals
Hygiene
Studies design

Practical part, 25 hours

Handling and housing
Sex determination
Identification
Injections
Blood collection
General anesthesia
General anatomy (mouse, rat, rabbit, chicken, chicken embryo)
SOPs (Standard operation procedures)

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Molecular Medicine

Seminar, 2semester hours

Coordinator: **Wolfgang Schneider**, Wolfgang.Schneider@meduniwien.ac.at

Program:

Nimpf	Methodes in molecular medicine
Schneider	Dominant und recessive Familial Hypercholesterinemias
Kuchler	ABC Transporter in Drug Resistance and Genetic Diseases
Hermann	Deseases associated with defects in genes for apolipoproteins
Weitzer	Stem cells
Ivessa	Quality control in the ER
Strobl	Screening and diagnostik of inherited metabolic disorders
Seiser	Chromatin and disease
Blaas	Rhinovirus - Host Cell Interaction
Hofbauer	Lipid metabolism of and associated gene defects in mitochondria
Ogris	Human cancers of viral etiology: part I
Rotheneder	Human cancers of viral etiology: part II
Barta	RNA Metabolism and gene expression
Seipelt	Methods in gene therapie

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Participating principal investigators

Supervisor´s name	Clinics/Institution	email	Status
BARTA Andrea	Department für Medizinische Biochemie	andrea.barta@meduniwien.ac.at	senior
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WOHLRAB Franz	Department für Medizinische Biochemie	franz.wohlrab@meduniwien.ac.at	senior

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Experimental techniques

Method	Group
Antibodies (monoclonal, polyclonal)	Hermann, Ogris, Warren, Eger
Apolipoprotein analysis	Hermann
Bacterial cultures	alle
Chromatin immunoprecipitation	Seiser, Weitzer, Barta
Cloning	alle
Confocal microscopy	Foisner, Barta, Warren, Fuchs, Ellinger
Cytoplasmic pH and Ca^{++} determination	Fuchs
Electrophoretic mobility shift assay (EMSA)	Rotheneder, Barta
Embryonic stem cells	Weitzer, Seiser
Enzymatic assays	Ogris, Seiser, Ivessa, Warren, Eger, Ellinger
Expression profiling	Müllner, Foisner, Barta, Eger
FACS analysis and sorting	Müllner, Ogris, Weitzer, Rotheneder, Warren, Eger, Chiba
Fluorescent microbead technology	Schneider, Barta
Footprinting	Rotheneder, Barta
FPLC	Skern, Nimpf, Eger
Histochemistry	Foisner, Nimpf, Fuchs, Ellinger
HPLC	Barta
Immunofluorescence microscopy	Alle
Immunoprecipitation	alle
In vitro endosome acidification/virus uncoating	Fuchs
In vitro mutagenesis	Rotheneder, Blaas, Ivessa, Skern, Weitzer, Ogris, Barta, Warren
Live cell imaging	Foisner, Warren, Fuchs, Eger
Ligand blotting	Blaas, Schneider, Nimpf, Hermann, Warren
Lipoprotein preparation	Hermann, Schneider, Nimpf
Metabolic labeling	Hermann, Ivessa, Warren, Fuchs
Mass spectrometry	Chiba
Molecular graphics and structure visualization	Blaas
Northern blotting	alle
PCR	alle
Primary cell culture	Müllner, Nimpf, Schneider, Hermann, Weitzer, Foisner, Fuchs, Eger
Protein expression	alle
Protein expression in baculovirus	Schneider, Skern, Ogris
Protein identification (mass spectrometry)	Barta, Warren
Protein purification	alle
Pull-down assays	Rotheneder, Nimpf, Skern, Ogris, Barta, Ivessa, Warren
Pulse-chase experiments	Hermann, Ogris, Barta, Ivessa, Warren, Fuchs, Eger
Receptor binding	Schneider, Nimpf, Hermann, Fuchs
Reporter assay	Rothender, Weitzer
Retroviral infection	Müllner, Rotheneder, Nimpf, Ogris
Real time PCR	Seiser, Nimpf, Weitzer, Fuchs
RNAi	Seiser, Nimpf, Ogris, Rotheneder, Foisner, Warren, Müllner
RNA transcription and translation	Skern, Barta
Sequencing	alle
Signal transduction analysis	Müllner, Nimpf, Weitzer, Ogris
Southern blotting	alle
Subcellular fractionation	Ivessa, Nimpf, Ogris, Barta, Warren, Fuchs, Eger
Tissue culture	alle

Transfection	alle
Transgenic mice	Foisner, Ogris
Two-dimensional electrophoresis	Ogris, Nimpf, Schneider, Weitzer
Western blotting	alle
Virus growth and purification	Blaas, Fuchs
Virus labeling with fluorophores	Blaas, Fuchs
Yeast two hybrid	Ogris, Nimpf, Barta
Yeast cell culture	Ogris, Barta