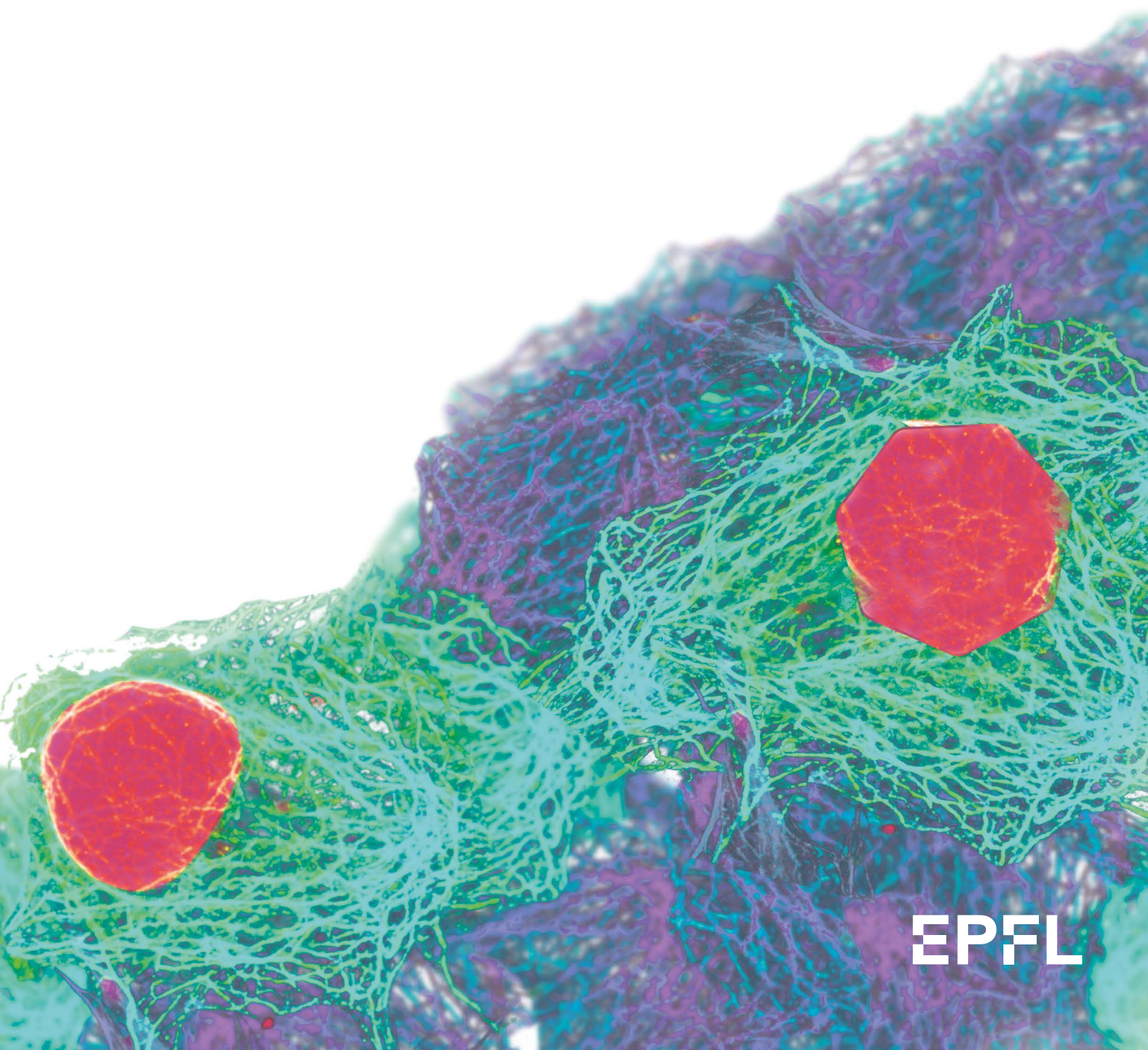


DOCTORAL
SCHOOL

MOLECULAR LIFE SCIENCES



EPFL

Cancer, infectious diseases and metabolic syndromes are the most prevalent life-threatening disorders. This program trains the next generation of scientists in basic and translational research to elucidate the underlying molecular mechanisms and to develop innovative therapeutic strategies.

Research topics include:



“Innate immune sensing of cytosolic chromatin fragments through cGAS promotes senescence” *Nature Cell Biology* (2017) 19(9):1061-1070

Cyclic GMP-AMP synthase (cGAS) is an enzyme that initiates antiviral responses through the recognition of DNA derived from pathogens. This event results in interferon and NF- κ B signaling dependent on the receptor stimulator of interferon genes (STING).

Selene Glück and collaborators found that during senescence cGAS binds to aberrant self-DNA in form of cytosolic chromatin fragments, thereby activating STING and triggering the induction of several senescence associated secretory phenotype (SASP) factors. This cGAS-STING dependent SASP can reinforce and relay the senescence response.

Senescence is a multistep program that is initiated upon various genotoxic stresses and is associated with a stable cell cycle arrest.

These findings suggest that cGAS-STING signaling has an important regulatory role in senescence and thus might be involved in several senescence-related diseases.

Selene Glück

“Single Live Cell Monitoring of Protein Turnover Reveals Intercellular Variability and Cell-Cycle Dependence of Degradation Rates” *Molecular Cell* (2018) 71(6):1079-1091

Cells need to reliably control their proteome composition in order to maintain homeostasis and regulate growth. In cycling cells, protein levels need to be precisely doubled throughout one cell cycle. How this doubling is achieved and how synthesis and degradation interplay to control global protein homeostasis remains unclear.

Andrea Alber and colleagues developed 2 live imaging strategies in order to monitor protein synthesis and degradation in single mouse embryonic stem cells. They discovered a substantial cell cycle dependence in protein synthesis rates and a stabilization of proteins around cell division. In addition, global protein degradation rates were highly variable between single cells and correlated with protein synthesis rates. This suggest that cells with similar protein levels might differ considerably in their turnover rates.

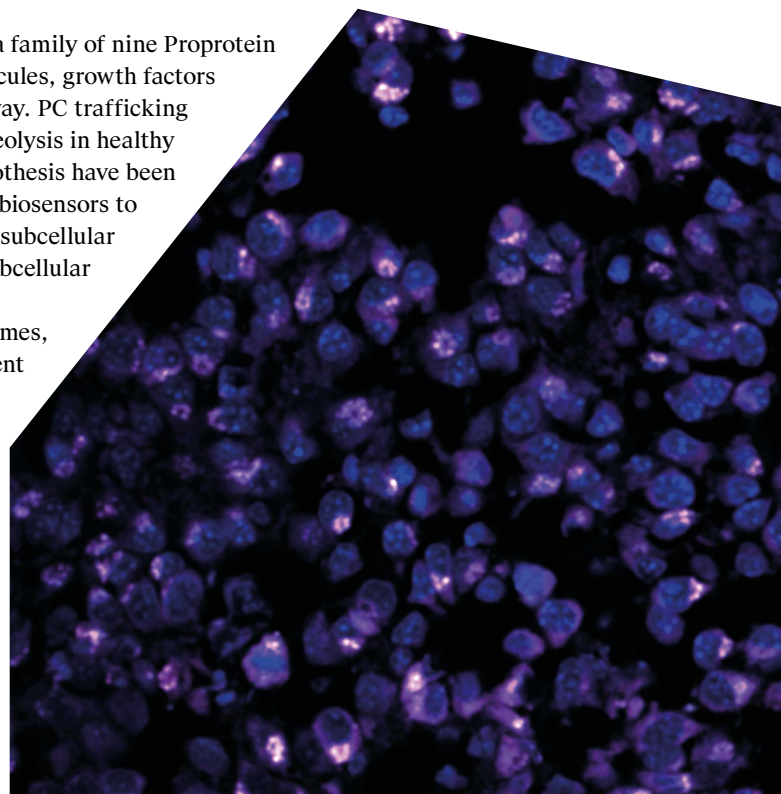
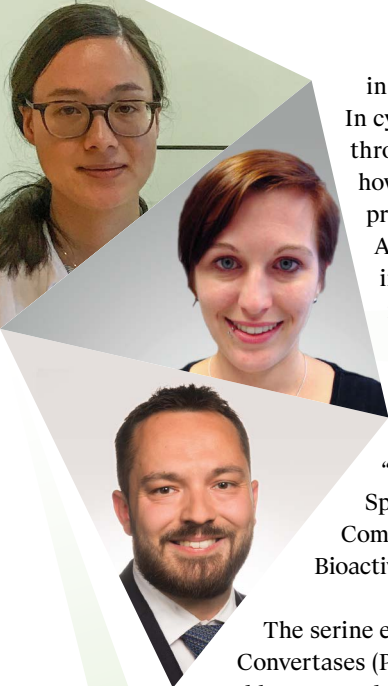
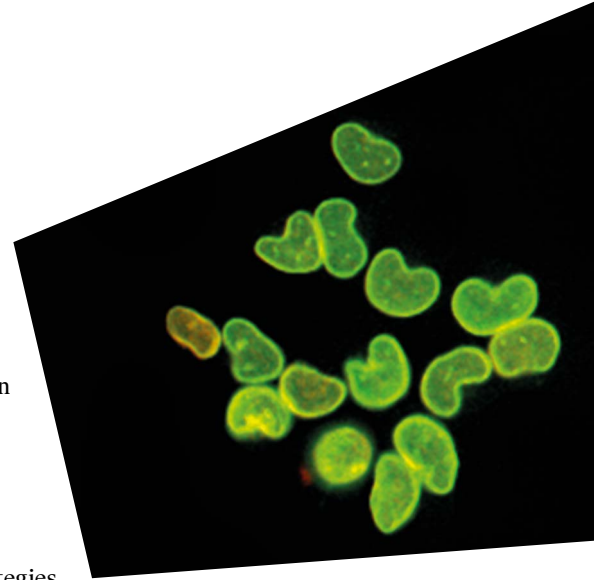
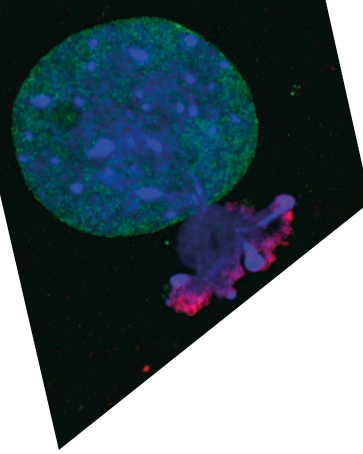
Andrea Alber

“Compartment-Specific Biosensors Reveal a Complementary Subcellular Distribution of Bioactive Furin and PC7” *Cell Rep.* (2018) 22:2176-2189

The serine endoproteases Furin and PC7 belong to a family of nine Proprotein Convertases (PCs) that activate various adhesion molecules, growth factors and hormones during their transit in the secretory pathway. PC trafficking may regulate which substrates are accessible for endoproteolysis in healthy and cancerous tissues, but tools to directly test this hypothesis have been lacking. Pierpaolo Ginefra and collaborators developed biosensors to map and quantify individual PC activities in different subcellular compartments. Their work shows that differential subcellular distribution regulates PC substrate specificities.

While Furin activity was most enriched in endosomes, PC7 was active in a distinct exocytic compartment resistant to a pan-PC inhibitor. These findings are important to inform future strategies how Furin and PC7 may be targeted pharmacologically to preferentially block the processing of unique or shared substrates, respectively.

Pierpaolo Ginefra



How to apply

There are two yearly application deadlines:

April 15th and November 1st

You will first have to fill in the online application form including your personal details, official transcripts of diplomas and your academic background, as well as your statement of objectives and the contact details of three referees.

The program's committee will evaluate and make a decision on your application, taking into account the research interests and potential thesis directors you indicate.

Some applicants will be selected and invited for interviews at EPFL for three days. During this time, they will meet group leaders with open positions, present their master's project and visit the institute, as well as Lausanne. At the end of the three days interview, some of the students will be accepted in the program and invited to pursue a PhD with their chosen thesis director.

Overview of the program

The duration of PhD studies is usually of 4 years or less. Students will obtain a doctoral degree from EPFL (Swiss Federal Institute of Technology).

During their PhD studies, students will participate in teaching (contact hours, preparation, corrections of exams, supervision of bachelor student projects, currently a total of approximately 300 hours during the entire PhD).

Students will be followed by a PhD committee that offers guidance. A mentor will ensure that the student has settled satisfactorily into the lab and the program.

Graduate students complete their education by attending practical and theoretical courses, as well as seminars.

Students are required to accumulate 12 ECTS credits during their doctoral studies.

Starting salary: 51'900 CHF

Why choose the EDMS doctoral program?

- Access to a large portfolio of laboratories in both basic and applied life sciences.
- Access to state-of-art technology platforms and core facilities.
- International environment.
- Education « à la carte » in a European leading university.
- Experience in teaching at the university level.
- Access to all EPFL courses and events including seminars, courses, training and industrial network.
- Conviviality: participation to the student retreat and other get-together activities.
- Alumni PhD students have access to Swiss fellowships.
- Life in a beautiful environment, Lausanne.

List of host laboratories:

Interschool Institute of Bioengineering - IBI

<http://bioengineering.epfl.ch/>

Swiss Institute for Experimental Cancer Research - ISREC

<http://isrec.epfl.ch/>

Global Health Institute - GHI

<http://ghi.epfl.ch/>

Nestlé Institute of Health Sciences - NIHS

<http://www.nestleinstitutehealthsciences.com/>

Contact:

Further information and contacts can be found at:

go.epfl.ch/phd-edms