

The role of TIMELESS protein in the initiation of DNA replication in human cells

Summary

TIMELESS is a crucial component of the replication fork, known to play a key role in response to replication stress. While *Timeless* is an important part of replication initiation, its exact role in this process is unclear. The goal of this PhD project is to study the role of *Timeless* protein in the initiation of DNA replication in human cells.

Research field:	Chemistry and biotechnology
Supervisor:	Dr. Tatiana Moiseeva
Availability:	This position is available.
Offered by:	School of Science Department of Chemistry and Biotechnology
Application deadline:	Applications are accepted between November 16, 2020 00:00 and December 16, 2020 23:59 (Europe/Zurich)

Description

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DNA replication is one of the major targets of cancer therapies, as cancer cells tend to proliferate faster and are generally more prone to replication stress. Most of the information about DNA replication initiation currently comes from model organisms, such as yeast, but their applicability to human system is limited. Some of the critical steps of replication initiation are very poorly understood in human system. It is important to study replication initiation in human cells in order to be able to exploit the findings in cancer therapies.

Human *TIMELESS*, or *TIM1*, together with its binding partner, *TIPIN*, is a component of the replication fork and it plays an important role in replication fork stability. *TIM1* knockouts are lethal, but knockdown delays S-phase entry, which implies that it may play a role in replication initiation. This project will use short-term knockdown systems and cell cycle synchronizations to elucidate the exact role of *TIM1* in replication initiation.

Methods:

- CRISPR-Cas9 genome editing, cloning, mammalian cell culture, flow cytometry, transfections, siRNA, survival/proliferation assays
- co-immunoprecipitations, pulldowns, western blots

Responsibilities and tasks:

- Plan and perform experiments, analyse data, write scientific papers
- Keep up to date on scientific literature related to the topic of thesis
- Attend PhD classes and fulfil the requirements for homework, evaluations, etc.
- Presentations at conferences, seminars, workshops, etc.
- Write and defend a PhD thesis at the end of the study program

The applicants should fulfill the following requirements:

- We are looking for a highly motivated PhD student with a strong background in molecular or cell biology.
- Previous experience in the field of genome maintenance is preferred but not required.

Desired qualifications:

- M.Sc. in a related discipline
- Strong communication skills (English) that are compatible with doctoral-level requirements, i.e., writing academic papers and giving presentations in English
- Proficiency in two or more of the following methods: mammalian cell culture, protein and DNA gel electrophoresis, western blot, immunoprecipitations or affinity pulldowns, PCR, cloning, site-directed mutagenesis, CRISPR/Cas9 genome editing



- Ability to follow protocols
- Good organizational skills, ability to document and analyze experiments



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