Keeping gene expression in check: eliciting the role of transcription in the maintenance of genome integrity

From 2012-11-01 to 2018-10-31, closed project

Project details

| Total cost: | EUR 1 500 000 |
| EU contribution: | EUR 1 500 000 |
| Coordinated in: | Greece |
| Topic(s): | ERC-SG-LS1 - ERC Starting Grant - Molecular and Structural Biology and Biochemistry |
| Call for proposal: | ERC-2012-StG_20111109 | See other projects for this call |
| Funding scheme: | ERC-SG - ERC Starting Grant |

Objective

Genomic integrity is essential for accurate gene expression and epigenetic inheritance. On the other hand, a prolonged transcriptional arrest can challenge genome stability, contributing to genetic and epigenetic defects and the mechanisms of ageing and disease.

Here we aim to identify the molecular mechanisms that couple transcriptional arrest to chromatin alteration and repair. We wish to explore the idea that transcription suppresses cellular toxicity and preserves genetic and epigenetic inheritance.

Towards these goals our work will be focused on:

1. Deciphering the molecular events impinging on the manner cells respond when the progress of a transcribing RNA polymerase II is blocked.
2. Exploring a novel, so far unanticipated function of key players of the transcription-associated repair pathways, such as the Cockayne Syndrome (CS) proteins, not related to repair.
3. Understanding the role of transcription in chemotherapeutic-driven toxicity.
4. Investigating novel post-translational modifications of CS and determining their function.

These objectives will be addressed using advanced proteomics and genome wide technologies in combination with biochemical and cellular techniques in normal human cells and a large battery of patient-derived cell lines. Our rational is that better understanding of CS function will help reach our ultimate goal, which is to identify the regulatory cascades involved in the interplay between genomic stability and transcription. The novel key idea put forward in this proposal is that active transcription itself directly contributes to genome integrity. While the role of DNA damage-driven transcription blockage in promoting repair is well established, the protective role of active transcription in genome stability is entirely unexplored.

If successful, the proposed studies may help reveal the underlying causes of related disorders and explain their clinical features.
Mid-Term Report Summary - TRANSARREST (Keeping gene expression in check: eliciting the role of transcription in the maintenance of genome integrity.)

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Beneficiaries

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Subjects

Biotechnology - Life Sciences