PhD position: The structural organization of telomeric expression site chromatin

Application: Please send curriculum vitae, a brief statement of research interests (one-page max), and contact information for three references to Igor Cestari (igor.cestari@mcgill.ca).

The Cestari Lab
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Description: A Ph.D. position is available for a highly motivated individual interested in chromatin organization and transcriptional control mechanisms. The project involves chromatin conformation capture, RNA-seq and ChIP-seq using Illumina and nanopore sequencing to determine the 3D organization of the telomeric chromatin in the trypanosome pathogen. The project also entails investigating proteins involved in chromatin organization and transcription control of telomeric genes essential for pathogen immune evasion. The candidate will acquire knowledge in molecular biology, bioinformatics, analysis of large/complex datasets, skills in genetics including gene knockouts using CRISPR/Cas9, and pathogen biology.

Requirements: MSc. degree or previous laboratory experience in molecular and cellular biology (or related disciplines); knowledge or interest in bioinformatics (Linux/R); good communication skills; highly motivated.

Timeline: Start in Fall 2021/Winter 2022; check program application deadlines:
https://www.mcgill.ca/parasitology/graduatestudies

Project summary: Antigenic variation is the mechanism by which pathogens change their surface coat to evade host immune recognition during infection. In *Trypanosoma brucei*, antigenic variation entails the expression of a single Variant Surface Glycoprotein (VSG) gene at a time from a repertoire of over 2,500 VSG genes and the periodic change in the VSG gene expressed. The active VSG gene is transcribed from one of the 20 telomeric expression sites (ESs), and VSG switching occurs by transcriptional or recombination mechanisms. We found that the control of VSG gene expression entails a phosphoinositide-regulated Telomeric ES Complex (TESC). The TESC associates with sequences flanking the VSG gene, namely 70 bp and telomeric repeats, and the knockdown or mutation of some TESC proteins results in transcription of all VSG genes simultaneously. Our model indicates that the TESC functions in the control of telomeric gene silencing. The silencing involves TESC proteins' association with ES chromatin to regulate its structural organization and VSG gene transcriptional status. In this project, we will use chromatin conformation capture to determine the 3D organization of ES chromatin. We will express mutant TESC proteins to activate silent ESs and investigate the TESC role in the ES structural organization and spatial distribution in the nucleus. Our data will provide insights into how the TESC regulates the ES chromatin organization and compartmentalization and its function in VSG gene transcription.

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References: Cestari, 2020, PLOS Pathogens; Cestari et al. 2019, Mol Cell Biol; Cestari and Stuart, 2015, PNAS; Cestari et al., 2016, Cell Chem Biol.