

EuReCa International PhD Program

PhD thesis project

2021 Call for application

A multidisciplinary approach to determine the 3-dimensional organization of centromeres in mitosis

General information

Call	2021
Reference	2021-04-DRINNENBERG
Keyword(s)	Centromere; Evolution; Genome organization; Condensin; Microscopy

Director(s) and team

Thesis director(s)	Ines Drinnenberg
Research team	Evolution of Centromeres and Chromosome Segregation
Research department	UMR3664 – Nuclear Dynamics

Description of the PhD thesis project

Please visit: <https://drinnenberg-lab.com>

The centromere is a specialized chromosomal region required for correct chromosome inheritance over cell division. For this, centromere and their associated protein complexes, the kinetochore must bi-orient allowing sister chromatids to attach to spindle microtubules emanating from opposite poles. On condensed mitotic chromosomes centromere- and kinetochore-associated proteins appear on the polar surface of chromosomes implying that precise spatial conformation of chromosomal DNA underlies this peripheral clustering. The peripheral clustering of centromere and kinetochore components is seen across eukaryotes but driven to the extreme in organisms with holocentric chromosomes, where kinetochores assemble chromosome-wide (in contrast to monocentric chromosomes (with restricted kinetochore attachments)). Holocentric organisms thus offer a powerful system to understand this conserved and essential mitotic organization of centromeres.

Here, we propose to get insights into this question using the holocentric organism *Bombyx mori* as model, for which we have recently mapped centromeres along their chromosomes (Senaratne et al, Current Biology 2020).

Using cell biological approaches, we aim to evaluate factors including condensin, cohesion and kinetochore components to test for their importance for peripheral centromere clustering. Using genomics (Hi-C, Hi-ChIP) and fluorescence in situ hybridization (FISH) analyses combined with superresolution microscopy in collaboration with AbbeLight, we aim to precisely quantify and map interactions between centromere regions. Those data will also be used for biophysical modeling approaches to reconstruct the spatial conformation of chromosomes.

This project will provide fundamental insights into the mechanism underlying centromere organization to establish its correct chromatin topology to enable faithful segregation of chromosomes.

International, interdisciplinary & intersectoral aspects of the project

This project combines a range of techniques from molecular and cellular biology (IF and FISH), imaging (Abbelight technology), genomics (HiChIP), bioinformatics (analyses of genomic datasets) and physics (spatial reconstruction).

Abbelight is an international company, which develops next generation microscope technologies to analyze molecular structures with high precision.

The candidate will be in close contact with their technical support team to quantify chromatin interactions. The student will also be in close contact with Prof. Kerry Bloom's lab (University of North Carolina), an expert in the field of centromere models, to perform the biophysical modeling of centromere organization.

Recent publications

1. Senaratne AP, Muller H, Freyer KA, Kawamoto M and **Drinnenberg IA**. Formation of the CenH3-deficient holocentromere in Lepidoptera avoids active chromatin. (2020), *Current Biology*, Oct 23:S0960-9822(20)31448-2.
2. Cortes-Silva N, Ulmer J, Kiuchi T, Hsieh E, Cornilleau G, Ladid I, Dingli F, Loew D, Katsuma S and **Drinnenberg IA**, CenH3-independent kinetochore assembly in Lepidoptera requires CCAN including CENP-T. (2020) *Current Biology*, Feb 24;30(4):561-572
3. **Drinnenberg IA**, Berger F, Elsässer SJ, Andersen PR, Ausió J, Bickmore WA, Blackwell AR, Erwin DH, Gahan JM, Gaut BS, Harvey ZH, Henikoff S, Kao JY, Kurdistani SK, Lemos B, Levine MT, Luger K, Malik HS, Martín-Durán JM, Peichel CL, Renfree MB, Rutowicz K, Sarkies P, Schmitz RJ, Technau U, Thornton JW, Warnecke T, Wolfe KH. (2019) *EvoChromo: towards a synthesis of chromatin biology and evolution*. *Development*. vol. 146 no. 19, dev178962
4. Muller H, Gil J Jr, **Drinnenberg IA**. The Impact of Centromeres on Spatial Genome Architecture (2019) *Trends in Genetics*. Aug; 35(8):565-578.
5. **Drinnenberg IA**, DeYoung D, Henikoff S, and Malik HS. (2014) Recurrent loss of CenH3 is associated with independent transitions to holocentricity in insects. *eLife* Featured on the eLife homepage

Expected profile of the candidate

The applicant should be enthusiastic and show a solid capacity for independent and creative thinking.

He/She should also have a strong desire to do multidisciplinary research in genomics, and cellular molecular biology.

Programming skills and expertise in working in computational environments are a plus, but are not compulsory.