View results

Respondent

9 Anonymous

108:38
Time to complete

Project number

1. Project ID (please leave blank, to be completed by the steering committee)

2. Date of Project submission *

04/10/2023

Contact Details

3. Grant Holder/Project Lead Name *

Adele Marston

4. Email Address *

adele.marston@ed.ac.uk

5. Institute *

Cell Biology

6. Do you have funding for this project? *

If you have funding and a grant number select 'yes'. If you are applying for funding select 'no'

- (●) Yes
- ( ) No

7. Funding body *

Wellcome

8. P&M codes *

9999999_9999999

9. Grant end date *

28/02/2026

Project proposal

With the exception of question 16, the information given in this section will be shared with Wellcome.

10. Project Title *

How is crossover recombination suppressed within pericentromeres?

11. Project Background *

Give an overview of the proposed project, include details of the work to be done and how the project advances the field. Max 200 words

Crossover recombination links homologs and is essential for their accurate segregation during meiosis I, but must be suppressed within the region surrounding centromeres (pericentromeres) to avoid chromosome segregation errors, as shown in yeast, flies and humans. Though critical, how correct crossover placement is achieved is not understood. Our observations lead us to the hypothesis that three coupled steps establish pericentromeric crossover suppression: (1) Pericentromeres fold into an isolated structure that prevents homolog engagement, (2) Synaptonemal complex (SC) nucleation from kinetochores enforces crossover suppression within this structure, (3) Sgo1-PP2A phosphatase excludes pro-crossover factors from pericentromeres. We will test this hypothesis and elucidate the mechanism of pericentromeric crossover suppression to answer the long-standing question of how meiotic crossover recombination is spatially regulated.

12. Project Objective *

State the aim(s) of the project. Max 200 words

1. Determine the role of pericentromere structure in crossover suppression
2. Investigate the importance of synaptonemal complex nucleation at kinetochores
3. Understand the mechanism and significance of crossover suppression by Sgo1-PP2A

13. How does the project align with the DRP - HCB? *

State briefly how the project fit with the aims of the DRP-HCB. Please refer to the overall vision and goals of the DRP (link to webpage). Max 200 words

The suppression of crossovers around centromeres is an essential and conserved feature of meiosis and has been known for decades, but its mechanism is unknown. This project will therefore uncover new biology that has been difficult to address previously.
The project will align with all three DRP pipelines as follows:
1. Proteome characterisation. We found that during meiotic prophase, when the outer kinetochore disassembles, a unique set of proteins identify with the kinetochore. We will use the proteome characterisation pipeline to understand which proteins are present at which stage of meiosis and in different mutants. We will identify the modifications present (phosphorylation) and the role of specific kinases.
2. Atom to cell. We aim to understand the structure and organisation of the meiotic prophase kinetochore which fits with the atom to cell pipeline.
3. Rare events. Crossovers near centromeres are rare events in wild type cells and where they occur they are detrimental. We are very interested in using the rare events pipeline to detect these rare crossovers and to understand their impact on chromosome segregation.

14. How will the DRP platform cores help to overcome barriers that you are facing? *

Word Limit 200.

Proteomics - to identify the proteome and phosphoproteome at the meiotic kinetochore in different stages and in different mutant situations.
Microscopy - using a live cell crossover assay. We are also interested in exploring automation of this and using it for high content screening.
Structural Biology - we will take a biochemical and structural biology approach to understand the organisaion of the specialized meiotic kinetochore.
Bioinformatics - we plan to use nanopore sequencing to map crossovers and this will require establishment of new bioinformatic pipelines.

15. What is the status of the project? *

This information will indicate the type of support required.

- ( ) Costing for future grant application - no funding yet.
- ( ) Planning phase - new project, funding in place
- (•) In progress - completion of existing ongoing project

16. Expected project start date *

01/12/2023

17. Expected duration of the project *

until grant end

18. List all the researchers involved in this project *

Only named researchers will be authorised to access the Cores.

Joe bloggs (PhD student)
marie Curie (Postdoc)
Albert Eistein (Postdoc)
Adele Marston (PI)

Use of DRP-HCB Platforms

19. Which Technology Cores will be involved in the project *

Select all that apply. Note that the Microfluidics Core is not yet established. Users will be notified when this core is available.

- [x] Bioinformatics Core
- [x] Microscopy and Microfluidics Core
- [x] Proteomics Core
- [x] Structural Biology Core (including EM)

20. Rank the the cores according to expected usage *

Rank the Cores you will use, leaving those you will not use at the bottom.

1 Proteomics Core

2 Microscopy and Microfluidics Core

3 Structural Biology Core

4 Bioinformatics Core

Confirm Agreement with the DRP-HCB Terms and Conditions

Sign below to confirm that you have read and agree to the DRP-HCB terms and Conditions (link to T&C here), including but not limited to:

- Correct acknowledgement of Technologists
- All projects must be registered with the DRP and only authorised users with a project number will be given access to the cores.
- Reporting on your advancements annually.

21. Name: *

Adele Marston

22. Signature: *

Adele Marston

23. Date: *

4 Oct 2023