**University of Leicester**

**BBSRC MIBTP Studentship Project 2024-5 entry.**

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| **Project Reference** |  |

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| **First Supervisor** | Dr James Higgins |
| **School/Department** | Genetics and Genome Biology |
| **Email** | [JH555@leicester.ac.uk](mailto:JH555@leicester.ac.uk)  <https://le.ac.uk/people/james-higgins> |

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| **Second Supervisor** | Dr David Guttery |
| **School/Department** | Genetics and Genome Biology |
| **Email** | [dsg6@leicester.ac.uk](mailto:dsg6@leicester.ac.uk) |

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| **Additional Supervisor** |  |

**Section 2 – *Project Information***

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| **Project Title** | Enhancing meiotic recombination in wheat by modulating RECQ helicases |
| **Project Summary** | |
| Wheat accounts for 20% of the calories and protein consumed by humans and is the largest crop in the UK, but yields have plateaued and are susceptible to decline due to extreme weather conditions. Wheat breeding is a numbers game; the more crosses generated, the greater the chance of generating useful trait combinations. However, breeding is dependent on the frequency and distribution of crossovers (CO) that are few in number (1-3 per chromosome pair) and skewed towards the chromosome ends, so even with a large number of crosses, desired combinations may not be attained. CO initiation sites are not limited by location or number, but only ~2% mature into COs, suggesting potential within the system to increase recombination.  In humans, mutations in the RECQ genes, Bloom’s syndrome helicase (BLM) and Werner’s helicase (WRN) are associated with premature ageing and early onset of cancer. RECQs are conserved throughout eukaryotes and repair DNA by homologous recombination. In *Arabidopsis thaliana*, the BLM orthologues (*RECQ4a/RECQ4b*) function redundantly as anti-recombinases during meiosis1. Arabidopsis does not contain a WRN ortholog, but we have identified one in wheat (RECQ7), that is a pro-CO factor2. RECQ4 is an anti-CO factor, so the two proteins may function antagonistically in processing DNA recombination intermediates. In wheat we have isolated knockout mutants of RECQ4 and RECQ7 as well as generating RECQ7 overexpression lines that require analysis for altered recombination patterns. We will use state-of-the-art super-resolution fluorescence microscopy in conjunction with immunolocalisation and a panel of antibodies developed in the lab that target specific proteins in the CO pathway. Using this approach we will be able to determine the spatio-temporal dynamics of recombination protein loading on meiotic chromosomes. Molecular markers will also be utilised to monitor recombination frequency.  There are three outstanding questions that will be investigated in this PhD project:  Q1. How does RECQ7 function as a pro-recombinase in homologous DNA repair?  Q2. Does RECQ4 act as an anti-recombinase during meiosis in wheat?  Q3. Can we determine an antagonistic mechanism of action between RECQ4 and RECQ7 in wheat?  Techniques that will be undertaken during the project  Super-resolution structured illumination microscopy, immunolocalization, fluorescence in situ hybridisation, PCR, cloning, DNA sequencing. | |
| **References** | |
| 1. Séguéla-Arnaud M, Crismani W, Larchevêque C, Mazel J, Froger N, Choinard S, Lemhemdi A, Macaisne N, Van Leene J, Gevaert K, De Jaeger G, Chelysheva L, Mercier R. (2015) [Multiple mechanisms limit meiotic crossovers: TOP3α and two BLM homologs antagonize crossovers in parallel to FANCM.](https://pubmed.ncbi.nlm.nih.gov/25825745/) *PNAS*;112(15):4713-8.  2. Gardiner LJ, Wingen LU, Bailey P, Joynson R, Brabbs T, Wright J, Higgins JD, Hall N, Griffiths S, Clavijo BJ, Hall A. (2019) [Analysis of the recombination landscape of hexaploid bread wheat reveals genes controlling recombination and gene conversion frequency.](https://pubmed.ncbi.nlm.nih.gov/30982471/) *Genome Biology* 20(1):69. | |

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