**University of Leicester**

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

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| **Project Reference** |  |

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| **Additional Supervisor** |  |

**Section 2 – *Project Information***

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| **Project Title** | Unlocking the Secrets of Genome Regulation through cryo-EM |
| **Project Summary** | |
| Are you an ambitious spirit, ready to make breakthrough discoveries at the frontier of epigenetics? Dive deep into the fascinating world of eukaryotic genomes with us!  **Here is what awaits you:**  **A Deep Dive into Chromatin**: Become an expert on the intricate structure of chromatin and its effector complexes. These vital components steer transcription, genome maintenance, repair, and replication.  **Zoom in on Histone Ubiquitination**: This project is your chance to unravel the mysteries surrounding histone ubiquitination. Histone proteins coat the genomes of eukaryotic organisms, serving as a signalling platform vital for genome regulation and protection. Through the study of "writer", "eraser", and "reader" proteins, you'll explore the mechanisms that shape chromatin, the very structure of life’s program.  **Hands-on Techniques and Real-World Experience**: Dive into techniques spanning biochemistry, structural biology, genome analysis, and cell biology. Explore the structure and function of the H2B ubiquitin ligase complex, gaining invaluable experience in the lab and sharpening your skills to uncover the core of biological processes.  **Be at the Forefront of a Thrilling Field**: This is more than just a project; it's a golden intellectual opportunity. Immerse yourself in a rapid-paced, competitive field that promises both challenges and rewards.  **International Collaboration and Cutting-Edge Tools**: You won't be on this journey alone! This initiative is part of a global collaborative push, tapping into our prowess in high-resolution structural analysis. You'll have the chance to use advanced tools like cryo-EM, offering a front-row seat to visualize the sophisticated machinery driving ubiquitination.  **Creating a Lasting Impact**: By establishing structure-function relationships and integrating structural insights with biochemistry and genetic analysis, we're striving to unearth principles that steer eukaryotic genome regulation. Ultimately, this knowledge paves the way for therapeutic innovations.  Apply now and shape the future of science!  **Techniques that will be undertaken during the project**  Cryo-EM, Alphafold II modelling, cloning, protein expression and purification from insect cells and bacteria, enzymatic assays, biophysical techniques. *S. pombe* genetics, Chromatin Immunoprecipitation (ChIP-seq), RT-qPCR | |
| **References** | |
| Bailey, L.T., Northall, S.J., and Schalch, T. (2021). Breakers and amplifiers in chromatin circuitry: acetylation and ubiquitination control the heterochromatin machinery. Current Opinion in Structural Biology 71, 156–163.  Oya, E., Nakagawa, R., Yoshimura, Y., Tanaka, M., Nishibuchi, G., Machida, S., Shirai, A., Ekwall, K., Kurumizaka, H., Tagami, H., et al. (2019). H3K14 ubiquitylation promotes H3K9 methylation for heterochromatin assembly. EMBO Reports 20, e48111.  Shan, C.-M., Kim, J.-K., Wang, J., Bao, K., Sun, Y., Chen, H., Yue, J.-X., Stirpe, A., Zhang, Z., Lu, C., et al. (2021). The histone H3K9M mutation synergizes with H3K14 ubiquitylation to selectively sequester histone H3K9 methyltransferase Clr4 at heterochromatin. Cell Reports 35, 109137.  Stirpe, A., Guidotti, N., Northall, S., Kilic, S., Hainard, A., Vadas, O., Fierz, B., and Schalch, T. (2020). SUV39 SET domains mediate crosstalk of heterochromatic histone marks. BioRxiv 2020.06.30.177071. | |

**To apply please refer to**

[**https://le.ac.uk/study/research-degrees/funded-opportunities/bbsrc-mibtp**](https://le.ac.uk/study/research-degrees/funded-opportunities/bbsrc-mibtp)