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## **Long-term stability of DNA methylation in transmissible cancers**

PhD project opportunity

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The Transmissible Cancer Group at the University of Cambridge has a vacancy for a PhD student to study DNA methylation in the context of transmissible cancers.

DNA methylation is an epigenetic modification which controls gene expression and heterochromatin formation in mammalian cells [1]. Dysregulation of DNA methylation is associated with aberrant gene expression, transposable element mobilisation and genome instability. DNA methylation changes are often observed in cancer, and can be causally involved in cancer by driving adaptive changes in gene expression. However, the stability of the DNA methylation landscape in cancer is variable, and the processes that regulate this are not completely understood.

In this project, we will use transmissible cancers to investigate the long-term stability of DNA methylation in mammalian cells. Transmissible cancers are unusual diseases which occur when cancer cells themselves become infectious agents and spread through populations [2]. Among mammals, transmissible cancers are known in only two species: dogs (a transmissible genital cancer that spreads between animals by the transfer of cancer cells during mating), and Tasmanian devils (two transmissible facial cancers spread by biting). The transmissible cancer in dogs is ancient, having first arisen in a dog that lived several thousand years ago [3]; the two Tasmanian devil cancers are of more recent origin, though, having arisen in the last decades [4]. The longevity of these cancers provides an opportunity to investigate the

stability of DNA methylation over the long term, and to understand the causes and consequences of this.

In this project, we will sequence the methylome of dozens of tumours from dog and Tasmanian devil transmissible cancers. We will use knowledge of these tumours' phylogenetic relationships [3, 4] to screen for sites which stably alter their methylation state, and use matched RNA sequencing data to understand how this impacts gene expression. By screening many tumours across the phylogenetic tree, we will assess if methylation changes may be under selection in these cancers. We will investigate how global changes in methylation patterns associate with genome instability, and screen for causative mutations. This project will provide unique insight into how gene expression programmes are maintained and eroded over long time-periods, and the significance of this in the context of cancer. The project will, for the most part, involve computational analysis of genomic data, but there may also be opportunities for field work with dogs and Tasmanian devils.

For further information about the project please contact Prof Elizabeth Murchison, [epm27@cam.ac.uk](mailto:epm27@cam.ac.uk). Successful candidates will be put forward for PhD scholarships. The project would be expected to start in October 2026.

#### References:

- [1] Nishiyama and Nakanishi 2021: [10.1016/j.tig.2021.05.002](https://doi.org/10.1016/j.tig.2021.05.002)
- [2] Murchison 2009: [10.1038/onc.2009.350](https://doi.org/10.1038/onc.2009.350)
- [3] Gori et al 2025: [10.1073/pnas.2424634122](https://doi.org/10.1073/pnas.2424634122)
- [4] Stammnitz et al 2023: [10.1126/science.abq6453](https://doi.org/10.1126/science.abq6453)