

Genotype to phenotype mapping in *Fusobacterium nucleatum*

Project ID: 3612

Supervisory team

Lead supervisors: Prof Darryl Hill (University of Bristol) & Dr James Robson (University of the West of England; UWE)

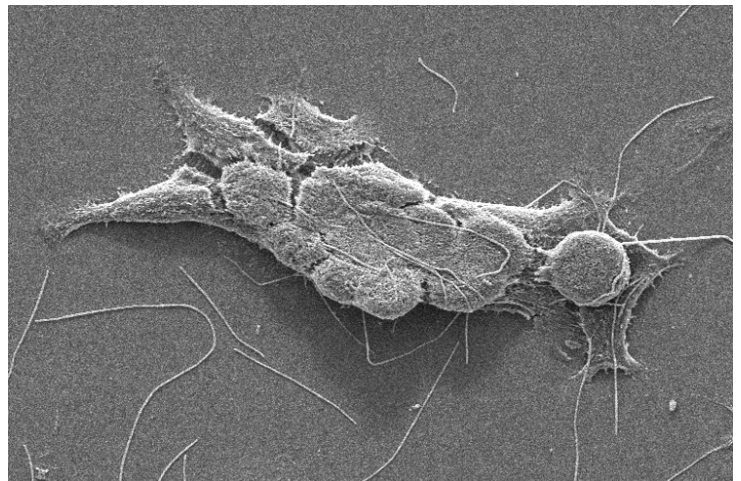
Other supervisors: Prof Mark Szczelkun (University of Bristol) & Dr Robin Thorn (University of the West of England; UWE)

Collaborators: Dr Sarah Maddocks (Cardiff Metropolitan University)

Registered institution: University of the West of England (UWE) & University of Bristol*

Host institutions: University of the West of England (UWE)/University of Bristol

Project description: *Fusobacterium* is an important constituent of the oral microbiota, is frequently isolated from the colonic microbiota and has also been associated with numerous pathologies including periodontitis, sepsis, adverse pregnancy outcomes and cancer. Our understanding of the role of *F. nucleatum* in homeostasis and pathology is confounded by the organism's diverse genome. At least four distinct subspecies exist within *F. nucleatum*, which exhibit significant genomic variation affecting their metabolic pathways, adhesion to host surfaces and other microorganisms, and virulence. Our previous research has explored the genomic diversity within both publicly



available genomes and clinical isolates. Within the *F. nucleatum* pangenome, the presence of key adhesion molecules that facilitate attachment to other microbes and host surfaces e.g. FadA, Fap2, RadD and CbpF is highly variable. Additionally, approximately 50% of the pangenome consists of hypothetical proteins, with no identified structure or function. There is therefore a gap between our understanding of the *F. nucleatum* genotype and phenotype, and therefore in our knowledge of the role of this organism in normal microbiota homeostasis and pathogenesis. This project will seek to explore this gap by analysing the behaviour of a panel of whole genome sequenced *F. nucleatum* isolates in vitro. Several phenotypes shall be explored (i) the ability of *F. nucleatum* isolated to adhere to and form biofilms on biotic surfaces e.g. collagen, mucin, fibrinogen. (ii) interactions between *F. nucleatum* and other cells including other microorganisms and epithelial cell organoids (iii) antimicrobial resistance with the species (iv) the metabolic output of *F. nucleatum*. The phenotypes will be compared with genotypic data to identify the driving genetic factors behind these behaviors to identify whether adhesion gene content and hypothetical protein reservoir can predict key microbial characteristics such as biofilm formation, host cell interaction and tissue tropism. This project will involve a multidisciplinary approach whereby the student will gain skills in microbiology, bioinformatics and human tissue culture. The project will involve the use of cutting-edge techniques including the development of a bespoke anaerobic biofilm culture system, colonic organoid systems and selected ion flow tube mass spectrometry. The project will be in collaboration with clinical partners within the UK Anaerobe Reference Unit and the North Bristol NHS Trust.

Please note: This project is in collaboration with the University of Bristol and the University of the West of England (UWE) and subject to a **joint degree award. Successful applicants will be registered at both these institutions, and graduates will be awarded a joint degree from these two institutions upon successful completion of the PhD programme. Continued on next page.....*

Our aim as the SWBio DTP is to support students from a range of backgrounds and circumstances. Where needed, we will work with you to take into consideration reasonable project adaptations (for example to support caring responsibilities, disabilities, other significant personal circumstances) as well as flexible working and part-time study requests, to enable greater access to a PhD. All our supervisors support us with this aim, so please feel comfortable in discussing further with the listed PhD project supervisor to see what is feasible.