



**Medical
Research
Council**



**GW4
BioMed2**
Doctoral Training Partnership

GW4 BioMed2 MRC Doctoral Training Partnership

**Project: 'The Contribution of Mitochondrial Dysfunction to
Alzheimer's disease'**

Lead Supervisor: Dr Gaynor Williams



October 24 - Application Pack

Contents

About the GW4 BioMed2 MRC DTP	3
Project Information	4
Eligibility Requirements	6
Funding	6
How to Apply	7
The Application Process	7
Recruitment Timetable	8
Selection Criteria.....	9
Contact Us	9
Application Form Template.....	10

About the GW4 BioMed MRC DTP

Many thanks for your interest in the GW4 BioMed2 MRC DTP.

The GW4 BioMed2 MRC Doctoral Training Partnership is a collaboration between Bath, Bristol, Cardiff, and Exeter Universities and is funded by the Medical Research Council.

From its launch in 2016, our partnership aims to develop the next generation of medical researchers by offering over 200 studentships over 9 years to both medical and non-medical students across three strategic research themes.

- Infection, Immunity, Antimicrobial Resistance and Repair
- Neuroscience and Mental Health
- Population Health Sciences

Students have access to the combined research strengths, training expertise and resources of the four research-intensive universities with opportunities to participate in interdisciplinarity. Many of the PhD projects supported by the DTP are co-supervised across at least two of the partner universities, allowing students to join existing and emerging research partnerships.

Our portfolio of PhD projects reflects the collective strengths of the DTP: quantitative skills (including mathematical modelling), using data for discovery, in vivo skills, and interdisciplinary training and approaches, including physics, engineering chemistry and health economics. The DTP places a strong emphasis on developing these cross-cutting skills and funds excellent projects that sit outside the strategic themes where they focus on one or more of the skills priorities.

Students in the GW4 BioMed2 MRC DTP have access to a broad range of training opportunities across all four universities. In addition we provide bespoke training specific to students within the DTP, that spans the three strands of our training programme including research skills, professional and career development skills and opportunities to broaden horizons. Events throughout the programme will develop researcher communities across the partnerships.

Each BioMed2 studentship provides funding for 4 years, which includes a 3-month initial preparation period and a 3-month placement.



Project Information

Project Details	
Project Code	MRC24NMHCa Smith
Title	The Contribution of Mitochondrial Dysfunction to Alzheimer's disease
Research Theme	Neuroscience and Mental Health
Summary	Alzheimer's disease (AD) is associated with increased oxidative stress and mitochondrial dysfunction in the brain. The Redox system that helps detoxify neurons is decreased in AD patients and likely contributes to symptoms and neurodegeneration. The PhD student will manipulate Redox and mitochondrial regulating genes in Drosophila and iPSC neuron models of AD to find new potential therapeutic targets.
Description	<p>Alzheimer's Disease (AD) likely manifests through a combination of genetic inheritance and environmental factors. Currently, the biggest risk factor for developing AD is age. Neurons are terminally differentiated and must be maintained throughout our entire lifetimes. However, during ageing levels of oxidative stress, in the form of reactive oxygen species (ROS) accumulate, which leads to oxidation of proteins/lipids, induces DNA damage and may eventually trigger neurodegeneration. Mitochondria are also compromised and produce less ATP. Antioxidant mechanisms which usually protect neurons are decreased with age, and decreased to an even greater extent in the AD patient brain. We have recently found that the AD risk gene WWOX is key regulator of metabolism, redox and mitochondrial health and that metabolism shifts are associated with amyloid beta (AB) protein aggregation and anticipate that other risk gene will be involved in metabolic regulation.</p> <p>Dysregulation of the metabolism and redox is largely understudied in the context of age-dependent neurodegeneration. The focus of this PhD studentship is to determine the mechanism of how redox and metabolism changes manifest in a number of AD models. Aim 1) Deciphering the molecular mechanism of redox and metabolism changes in AD. We will investigate 20 genes related to redox and metabolism pathways that may be contributing to neurodegenerative phenotypes in an AB Drosophila model of AD, chosen from a recent RNA-sequencing experiment. Transgenic RNAi expressing lines against uncovered genes will be driven specifically in neurons for knockdown and genetically encoded fluorescent genetic reporter technology used to measure ROS and mitochondrial dysfunction. To complement this the PhD student will further analyze lifespan, basic behaviour, memory and sleep (through co-supervision with JH) in gene knockdown models. We will also determine if altering redox homeostasis or metabolism plays a role in AB aggregation in the brains of the flies. *Student input - The select enzymes will be chosen from our previous RNA Seq data sets collected on AD models. The student can steer the project here to focus on different metabolic pathways that they find interesting e.g b-oxidation or glycolysis etc. Aim 2) Metabolomic and Lipidomic changes associated with several AD Drosophila models</p> <p style="text-align: right;">Cont.</p>



Description	<p>The student will then have specific 'big data' training for metabolomic and lipid profiling as brain samples from models are sent for mass spectrometry (UK DRI at Imperial). This analysis will be to generate novel yet complementary OMIC data sets to the previous RNA sequencing experiments to determine the molecular outcome of enzymatic changes that we find the AB and risk gene models. *Student input - metabolite and lipid changes will need to be verified through the use of lipid reporters or ELISA and the student will steer the project to find and optimise specific assays for the most promising candidates. Aim 3) Measure mitochondrial dysfunction associated AD risk genes. We will use existing iPSCs resources within the UK DRI to assay mitochondrial dysfunction (metabolism and ROS) associated with AD risk gene knock out or knockdown. The student will learn to differentiate these lines into cortical neurons and perform several relevant assays to measure metabolic and mitochondrial dysfunction (achieved under the co-supervision of NCR). Importantly the vast majority of genes in the redox and metabolism pathways are highly conserved between Drosophila and humans and candidate enzymes and metabolites investigated in previous years will further be examined in iPSC lines. *student input -i) Choosing the most relevant cellular model based off Drosophila in vivo findings ii) There are plenty of analysis methods and tools available for in vitro work and the student will be encouraged to develop different techniques and methodologies to measure cell specific changes.</p>
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Supervisory Team	
Lead Supervisor	
Name	Dr Gaynor Ann Smith
Affiliation	Cardiff
College/Faculty	The College of Biomedical and Life Sciences
Department/School	School of Medicine
Email Address	SmithGA@cf.ac.uk
Co-Supervisor 1	
Name	Dr James Hodge
Affiliation	Bristol
College/Faculty	Life Sciences
Department/School	School of Physiology, Pharmacology & Neuroscience
Co-Supervisor 2	
Name	Dr Natalie Connor-Robson
Affiliation	Cardiff
College/Faculty	The College of Biomedical and Life Sciences
Department/School	School of Medicine
Co-Supervisor 3	
Name	Professor Julie Williams
Affiliation	Cardiff
College/Faculty	The College of Biomedical and Life Sciences
Department/School	School of Medicine



Eligibility Requirements

- This studentship is open to applications from candidates who would be classified as either a home or international students.
- All studentships are competitively awarded.
- Applicants must have obtained, or be about to obtain, a UK degree, or the equivalent qualification gained outside the UK, in an appropriate area of medical sciences.
- The DTP also welcomes students from non-medical backgrounds, especially in areas of computing, mathematics, and the physical sciences.
- Academic qualifications are considered alongside any significant relevant non-academic experience.
- If English is not your first language, you will need to meet the English language requirements of the university that will host your PhD by the start of the programme, Please refer to the Cardiff university website [here](#) for further information on this.

Funding

A GW4 BioMed2 MRC DTP studentship includes full tuition fees for both home and international students, a stipend at the minimum UKRI rate, a Research & Training Support Grant (RTSG) valued between £2-5k per year and a £300 annual travel and conference grant based on a 4-year, full-time studentship.

International students are not required to pay the difference between home and international level fees, however they will be responsible for costs associated with relocating to Cardiff, including visa fees, NHS surcharges/relevant health insurances and accommodation costs.

Part time study may also be available and funding arrangements will be adjusted pro-rata for part-time studentships. Throughout the duration of the studentship, there will be opportunities to apply to the Flexible Funding Supplement for additional support to engage in high-cost training opportunities.



How to Apply

Before completing an application, candidates are advised to review the 'candidate support webinar' presentation on the DTP's website [here](#). This provides additional information on our studentships, hints and tips on completing the application form and answers frequently asked questions. While this applies to our main recruitment round, the application process for this project is the same.

To apply for an offer of funding for this PhD project, please complete the online application for by following this link.

<https://cardiff.onlinesurveys.ac.uk/gw4-biomed2-mrc-dtp-student-application-form-oct-202425-2>

We are open to applications from Tuesday 2nd April 2024. The closing date for applications is **Wednesday, 1st May at 5pm**. We are unable to accept applications after this deadline.

To assist, we have included a template of the application form at the end of this application pack to help you in planning your answers before you complete the online form.

Applications submitted by CV are not accepted and supporting documentation is not required unless you are shortlisted to attend an interview.

The Application Process

To begin a GW4 BioMed2 MRC DTP studentship, applicants must secure an **offer of funding** from the DTP by completing the form linked above. If successful, you will need to obtain an offer to study from Cardiff University.

Stage 1: Applying to the DTP for an Offer of Funding

- **Submit your application** using the online form linked above before 5pm on Wednesday, 1st May 2024.
- **Student shortlisting** is conducted in a blind review of applications by a theme-specific panel. Up to 4 top candidates will be invited to interview.
- **Candidates invited to interview** will be informed by email and provided with further instructions. All candidates will be informed of the outcome of this stage.
- **Informal, virtual meetings** will be arranged by the shortlisted candidates with the lead supervisor, Dr Gaynor Smith, before the formal interview. These should take place between Friday 24th May and Monday 3rd June 2024.
- **Formal interviews** will take place virtually, by the same theme-specific panel including representatives from each GW4 institution on Wednesday 5th June 2024.
- **Student selection** occurs after the formal interviews. The highest ranked candidate will be informed by the end of the day on Wednesday 5th June 2024.



- A **clearing period** will follow until the place has been offered and accepted. For this reason, it is not possible to provide immediate interview results to shortlisted applicants.
- Candidates **must** be able to start their PhD on 1st October 2023. Unfortunately, this cannot be deferred or delayed due to funding arrangements.

Recruitment Timetable

GW4 BIOMED2 MRC DTP ADDITIONAL RECRUITMENT CALL		
KEY DATES (2024-25 Intake)		
Date	Time	Deadline
Tuesday 2 nd April		Projects advertised for student applications
Wednesday 1 st May	By 5pm	Student application deadline
Friday 3 rd May – Friday 17 th May		Applications to IIR panel for shortlisting
Friday 24 th May	Time tbc	Student shortlisting panel
Friday 24 th May	By 5pm	DTP notifies candidates and Supervisor of interview shortlist
Monday 3 rd June	By midday	Supervisor interviews all candidates
Monday 3 rd June	By midday	Candidates sends references and transcripts to the DTP
Wednesday 5 th June	am	DTP interviews
Wednesday 5 th June	pm	Student shortlisting panel
Wednesday 5 th June	By 5pm	Offer made
Thursday 6 th June – Friday 19 th July		Clearing period
Friday 1 st October 2024		Official funding start date



Selection Criteria

Online applications to the DTP will be evaluated against the following criteria:

- **Proven academic quality:** normally evidenced by an excellent performance to first degree and/or Master's level but may also be demonstrated by an equivalent, high quality provision of evidence related to professional practice
- **Research potential:** evidenced through examples of achievement within academia/research related projects and outside of academia, evidencing relevant skills.
- **Personal motivation and commitment:** evidenced through supporting statement of understanding, motivation and suitability for their the project and by their wider enthusiasm, interest and commitment to the MRC DTP programme.
- **Non-biomedical disciplines:** In line with supporting interdisciplinary and quantitative skills, special consideration will be given by the interview panels to non-biomedical applicants. Such candidates should not feel the selection criteria are biased towards biomedical applicants as their unique skills will be taken into account.

Candidates selected to interview will be evaluated against the following criteria:

- **Critical thinking** assessed via discussion of a student-selected piece of data.
- **Fit with the project:** The interview panel will evaluate the candidate's aptitude and understanding of the key issues in the project, supported by feedback from informal meetings with the potential lead supervisor.
- **Personal commitment and motivation**

Contact Us

We wish you the very best of luck with your application to the GW4 BioMed2 MRC DTP Should you have any questions on the application process, please do not hesitate to contact the DTP Hub at GW4BioMed@cardiff.ac.uk.

GW4 BioMed2 MRC DTP: Student Application Form (Oct 2024/25)

Showing 0 of 0 responses

Showing **all** responses

Showing **all** questions

1 Title

No responses

2 First Name:

No responses

3 Preferred Name:

No responses

4 Last Name:

No responses

5 Email Address:

No responses

6 Phone Number:

No responses

7 Correspondence address (including postcode):

No responses

8 Please select the nationality classification that best describes your situation.

UK National (meeting the residency requirement)		0
Pre-settled status - less than 3 years		0
Pre-settled status - more than 3 years		0
UK settled status		0
Indefinite leave to remain or enter		0
International citizen		0
Other		0

9 If you need to provide additional clarification to your response above, or have selected 'other' please provide further information here.

No responses

10 Do you plan to study full-time (4 years) or part-time (50% minimum attendance)?

Full-time		0
Part-time		0

Academic Quality - Please list all awards, including your undergraduate (first) degree

11 Select the description for your first degree. Note: If you hold a non-UK degree please indicate its equivalent UK degree classification. For a conversion table please refer to our website.

BA		0
BSc		0
BEEd		0
BEng		0
LLB		0
MA		0
MSc		0
MEd		0
LLM		0
MBA		0
MRes		0
MPhil		0
MSci (intergrated)		0
PhD		0
MBBS/MBChB		0

11.a Select the classification of this qualification or expected classification based on current average grades.

1st		0
2:1		0
2:2		0
3rd		0
Pass		0
Merit		0
Distinction		0

11.b Provide the name of the institution that awarded this degree, eg, University of Sheffield

No responses

11.c Provide the subject of this degree (eg, Animal Behaviour, Psychology, Mathematics)

No responses

11.d In what year was this degree awarded (YYYY)? If yet to be awarded please state 'pending'.

No responses

12 Select the description for your second degree. If you do not hold another degree please answer 'not applicable'. Note: If you hold a non-UK degree please indicate its equivalent UK degree classification. For a conversion table please refer to our website. If you do not hold a second degree, please select not applicable,

BA		0
BSc		0
BEEd		0
BEng		0
LLB		0
MA		0
MSc		0
MEd		0
LLM		0
MBA		0
MRes		0
MPhil		0
MSci (intergrated)		0
PhD		0
MBBS/MBChB		0
Not applicable		0

12.a Select the classification of this qualification or expected classification based on current average grades.

1st		0
2:1		0
2:2		0
3rd		0
Pass		0
Merit		0
Distinction		0

12.b Provide the name of the institution that awarded this degree, eg, University of Sheffield

No responses

12.c Provide the subject of this degree (eg, Animal Behaviour, Psychology, Mathematics)

No responses

12.d In what year was this degree awarded (YYYY)? If yet to be awarded please state 'pending'.

No responses

13 Select the description for your third degree. If you do not hold another degree please answer 'not applicable'. Note: If you hold a non-UK degree please indicate its equivalent UK degree classification. For a conversion table please refer to our website. If you do not hold a third degree, please select not applicable.

BA		0
BSc		0
BEd		0
BEng		0
LLB		0
MA		0
MSc		0
MEd		0
LLM		0
MBA		0
MRes		0
MPhil		0
MSci (intergrated)		0
PhD		0
MBBS/MBChB		0
Not applicable		0

13.a Select the classification of this qualification or expected classification based on current average grades.

1st		0
2:1		0
2:2		0
3rd		0
Pass		0
Merit		0
Distinction		0

13.b Provide the name of the institution that awarded this degree, eg, University of Sheffield

No responses

13.c Provide the subject of this degree (eg, Animal Behaviour, Psychology, Mathematics)

No responses

13.d In what year was this degree awarded (YYYY)? If yet to be awarded please state 'pending'.

No responses

14 The Doctoral Training Partnership aims to bring together different academic disciplines. Please select the most appropriate discipline(s) for yourself based on your recent study/experience.

Medicine and dentistry (clinical)	0
Subjects allied to medicine	0
Biological sciences	0
Veterinary science	0
Agriculture and related subjects	0
Physical sciences	0
Mathematical sciences	0
Computer science	0
Engineering and technology	0
Architecture and related subjects	0
Social sciences	0
Law	0
Business and administration studies	0
Mass communications and documentation	0

Multi answer: Percentage of respondents who selected each answer option (e.g. 100% would represent that all this question's respondents chose that option)

-
- 15** Please outline 2 examples of your achievements in research related activities (e.g. undergraduate, masters or postgraduate work experience). (Maximum of 1250 characters including spaces).

No responses

-
- 16** Please outline 2 examples of your achievements in non-research related activities (e.g. outside of academic study). (Maximum of 1250 characters including spaces).

No responses

-
- 17** Please describe why you have chosen this project (e.g. your interest/understanding of the research question, your skills/experience that fit with this project). (Maximum of 1250 characters including spaces).

No responses

-
- 18** What do you hope to gain from doing a PhD with the GW4 BioMed2 MRC DTP? (Maximum of 1000 characters including spaces).

No responses

19 Please provide any additional relevant information to support your application (maximum of 1000 characters including spaces). Please note that completion of this section is not compulsory.

No responses

20 What is your age?

No responses

21 Do you have any disabilities?

None	0
A specific learning difficulty, such as dyslexia, dyspraxia or AD(H)D	0
A social/communication impairment such as Asperger's syndrome/other autistic spectrum disorder	0
A longstanding illness or health condition, such as cancer, HIV, diabetes, chronic heart disease, or epilepsy	0
A mental health condition, such as depression, schizophrenia or anxiety disorder	0
A physical impairment or mobility issues, such as difficulty using arms or using a wheelchair or crutches	0
Deaf or a serious hearing impairment	0
Blind or a serious visual impairment uncorrected by glasses	0
A disability, impairment or medical condition that is not listed above	0
Prefer not to say	0

22 What is your ethnic group?

White	0
Gypsy or Traveller	0
Other White background	0
Black or Black British - Caribbean	0
Black or Black British - African	0
Other Black background	0
Asian or Asian British - Indian	0
Asian or Asian British - Pakistani	0
Asian or Asian British - Bangladeshi	0
Chinese	0
Other Asian background	0
Mixed - White and Black Caribbean	0
Mixed - White and Black African	0
Mixed - White and Asian	0
Other mixed background	0
Arab	0
Other ethnic background	0
Unknown	0
Prefer not to say	0

23 How would you describe your national identity?

No responses

24 What is your gender?

Male	0
Female	0
Other	0
Prefer not to say	0

25 What was the occupation of your main household earner when you were about age 14?

Modern professional and traditional profession occupations such as: teacher, nurse, musician, social worker, police officer (sergeant or above), software designer, accountant, solicitor, medical practitioner, scientist, engineer	0
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Senior, middle or junior managers or administrators such as: finance manager, chief, executive, large business owner, office manager, retail manager, bank manager, restaurant manager, warehouse manager	0
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Clerical and intermediate occupations such as: secretary, personal assistant, call centre agent, clerical worker, nursery nurse	0
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Technical and craft occupations such as: motor mechanic, plumber, printer, electrician, gardener, train driver	0
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Routine, semi-routine, manual and service occupations such as: postal worker, machine operative, security guard, caretaker, farm worker, catering assistant, sales assistant, cleaner, porter, labourer, waiter/waitress, bar staff	0
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Long term unemployed: (claimed unemployment benefit for more than 1 year) | 0

Small business owner who employs less than 25 people such as: corner shop owner, small plumbing company, single cafe owner, taxi owner, garage owner | 0

Other: such as retired, this question does not apply to me, I don't know | 0

I prefer not to say | 0

26 If you finished school after 1980, were you eligible for free school meals at any point during your school years?

Yes | 0

No | 0

Not applicable (finished school before 1980 or went to school overseas) | 0

I don't know | 0

I prefer not to say | 0

27 Did either of your parents attend university or gain a degree (e.g. BA/BSc or equivalent) by the time you were 18?

No, neither of my parents attended university | 0

Yes, one or both of my parents attended university | 0

Do not know/ not sure | 0

I prefer not to say | 0

28 How did you find out about this PhD opportunity?

Email from GW4 BioMed forwarded by my university	0
Email from the project supervisor	0
GW4 BioMed DTP Website	0
Via link from another website	0
Personal recommendation ie from friend or colleague	0
FindaPhD.com	0
General Postgrad event	0
Social Media - Twitter/Facebook	0
University Careers Service	0
Other	0

Multi answer: Percentage of respondents who selected each answer option (e.g. 100% would represent that all this question's respondents chose that option)

29 Please confirm that you have read the data protection statement and understand how your information will be collected and shared as specified in the application form. If you do not agree with the terms, please exit the survey without submitting.

Yes, I have read and accept these terms	0
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