Plan Overview

A Data Management Plan created using DMPonline

Title: OqxAB efflux pumps—an emerging threat to the antibiotic nitrofurantoin?

Creator: Danna Gifford

Principal Investigator: Danna Gifford

Data Manager: Danna Gifford

Project Administrator: Danna Gifford

Affiliation: University of Manchester

Funder: Biotechnology and Biological Sciences Research Council (BBSRC)

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ORCID iD: 0000-0002-4990-8816

Project abstract:

Urinary tract infections (UTIs) are one of the most common infections both outside and within hospitals. The antibiotic nitrofurantoin has long been a first-line treatment for UTI because it is effective against the main bacterium that causes UTI, *Escherichia coli*. However, an emerging resistance mechanism known as OqxAB threatens our ability to use nitrofurantoin. OqxAB is a structure bacteria can use to expel antibiotics (an 'efflux pump'). The genes for OqxAB are carried on segments of DNA ('plasmids') that enable it to spread between bacterial strains. Although OqxAB-bearing *E. coli* is thought to be rare in the UK, we have recently detected it in genetically distinct isolates from Manchester hospitals, raising concerns that its prevalence might be increasing.

Our aim is to determine if OqxAB can increase the potential for *E. coli* to evolve resistance to nitrofurantoin. This research is timely because it will enable us to develop a plan of action before OqxAB-bearing *E. coli* becomes widely disseminated in the UK. We will use large-scale genomic analyses, involving hundreds of thousands of publicly available *E. coli* genomes, to determine how widespread OqxAB is today. In parallel, we will perform laboratory experiments to see how OqxAB influences the ability to evolve high-level nitrofurantoin resistance. We will also test whether efflux pump inhibitors can prevent bacteria carrying OqxAB from reaching high-level resistance. This research will clarify whether OqxAB primarily helps bacteria survive early, low-dose antibiotic exposure, or boosts the fitness of strains that are already partially resistant.

Our project will assess the prevalence and potential impact of OqxAB in*E. coli across three work packages (WPs).*

WP1: Determine prevalence and genomic context of *oqxAB* in all available *E. coli* genomes. We will analyse large-scale genomic data—over 374,000 publicly available*E. coli* genomes—along with clinical and environmental data to determine how common OqxAB currently is in the UK and globally. We test whether high-level resistance mutations, particularly in the genes *nfsA* and *nfsB,* are significantly associated with OqxAB, indicative of its ability to drive high-level nitrofurantoin resistance.

WP2: Map OqxAB activity and control across diverse *E. coli* lineages in UTI-like environments We will explore how OqxAB functions and is regulated across diverse*E. coli* strains, including UTI, non-pathogenic and laboratory backgrounds, under conditions physiologically relevant to UTI. We will assess whether OqxAB is inducible in response to nitrofurantoin, how it alters bacterial growth and stress responses, and whether efflux pump inhibitors can restore drug efficacy. We will also determine the breadth of OqxAB-mediated resistance and its potential to persist across treatment and environmental contexts.

WP3: Understand how OqxAB contributes to evolutionary dynamics of nitrofurantoin resistance. Using experimental evolution, we will track how quickly nitrofurantoin resistance emerges in OqxAB-positive strains compared to those lacking the pump. We will test whether OqxAB "buys time" for bacteria to acquire additional mutations required for full-blown resistance, or whether it primarily enhances the fitness of strains that are already resistant. We will also evaluate if efflux inhibition can counter the evolutionary advantages of OqxAB.

Ultimately, our work will generate fundamental insights into how plasmid-encoded efflux pumps like *oqxAB* influence the evolution of antimicrobial resistance. By dissecting the genomic, regulatory, and evolutionary dynamics of *oqxAB*-mediated resistance, we aim to uncover general principles that govern how horizontal and chromosomal resistance mechanisms interact. These findings will advance our understanding of antibiotic durability and resistance evolvability, supporting long-term innovation in antimicrobial research and informing future approaches to preserving drug efficacy.

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OqxAB efflux pumps—an emerging threat to the antibiotic nitrofurantoin?

Manchester Data Management Outline

1. Will this project be reviewed by any of the following bodies (please select all that apply)?

- Funder

2. Is The University of Manchester collaborating with other institutions on this project?

- No - only institution involved

3. What data will you use in this project (please select all that apply)?

- Acquire new data

Antibiotic resistance phenotypes (CSV) and bacterial growth curves (CSV), genomic data of bacteria (FASTQ and derivative analysis files), flow cytometry data (FCS3)

4. Where will the data be stored and backed-up during the project lifetime?

- University of Manchester Research Data Storage Service (Isilon)

5. If you will be using Research Data Storage, how much storage will you require?

- 1 - 8 TB

Genomic data and flow cytometry data are large files, justifying the need for more than 1 TB of space.

6. Are you going to be working with a 3rd party data provider?

- Yes

MicrobesNG (genomics company) stores the data for at least 1 year after acquisition.
Genomic DNA will also be uploaded to the European Nucleotide Archive, as is standard practice in the research field.

7. How long do you intend to keep your data for after the end of your project (in years)?

- 5 - 10 years

Questions about personal information
Personal information, also known as personal data, relates to identifiable living individuals. Special category personal

data is more sensitive information such as medical records, ethnic background, religious beliefs, political opinions, sexual orientation and criminal convictions or offences information. If you are not using personal data then you can skip the rest of this section.
Please note that in line with data protection law (the General Data Protection Regulation and Data Protection Act 2018), personal information should only be stored in an identifiable form for as long as is necessary for the project; it should be pseudonymised (partially de-identified) and/or anonymised (completely de—identified) as soon as practically possible. You must obtain the appropriate ethical approval in order to use identifiable personal data.

8. What type of personal information will you be processing (please select all that apply)?

- No sensitive or personal data

9. Please briefly outline how you plan to store, protect and ensure confidentiality of the participants' information.

No participant data, including any confidential data, will be collected

10. If you are storing personal information (including contact details) will you need to keep it beyond the end of the project?

- Not applicable

11. Will the participants' information (personal and/or sensitive) be shared with or accessed by anyone outside of the University of Manchester?

- Not applicable

12. If you will be sharing personal information outside of the University of Manchester will the individual or organisation you are sharing with be outside the EEA?

- Not applicable

13. Are you planning to use the personal information for future purposes such as research?

- No

14. Who will act as the data custodian for this study, and so be responsible for the information involved?

Danna Gifford

15. Please provide the date on which this plan was last reviewed (dd/mm/yyyy).

2025-04-21

Project details

What is the purpose of your research project?

The project aims to determine the dynamics of antimicrobial resistance evolution in bacteria, facilitated by the OqxAB efflux pump, which will provide insight into evolutionary processes with implications for combating antibiotic resistance and advancing understanding in evolutionary biology.

What policies and guidelines on data management, data sharing, and data security are relevant to your research project?

Data management plan- BBSRC

All applications seeking research grant funding from BBSRC must submit a data management plan. This should include concise plans for data management and sharing as part of the research grant proposal, or provide reasons why data sharing is not possible or appropriate.

The plan will be included in applications as a separate mandatory attachment.

The page limit for the plan is maximum one side of A4.

You must use this document to cover the plans for data management and sharing. Use of this space allocation for any other purpose will result in withdrawal of the application. BBSRC reserves the right to withdraw proposals that do not adhere to these guidelines.

What to include

BBSRC recognises that plans for sharing data will vary according to the type of data collected. Data sharing should be driven by scientific benefit and should also be cost effective. Data should be shared using established standards and existing resources where this is possible.

You may wish to include details of:

- data areas and data types – the volume, type and content of data that will be generated, for example experimental measurements, models, records and images
- standards and metadata – the standards and methodologies that will be adopted for data collection and management and why these have been selected
- relationship to other data available in public repositories
- secondary use – further intended or foreseeable research uses for the completed datasets
- methods for data sharing – planned mechanisms for making these data available, for example through deposition in existing public databases or on request, including access mechanisms
- proprietary data – any restrictions on data sharing due to the need to protect proprietary or patentable data
- timeframes – timescales for public release of data
- format of the final dataset.

See our data sharing policy for full guidance.

Assessment of the data management plan

An application’s data management plan will be assessed by reviewers and BBSRC standard research grant Research Committees or assessment Panels. Standard (sometimes known as ‘responsive’) grants are open to a wide range of research and approaches within BBSRC’s remit.

The plan will be considered separately from the scientific excellence of the proposed research; however, an application’s credibility will suffer if peer review agrees the statement is inappropriate. In the case where a highly-rated proposal has an inappropriate data management plan, research committees and panels may choose to offer conditional awards or provide specific feedback to the applicants. Appropriate plans are expected to be those where the proposed data sharing activities are in-line with current best practice in the field and both the scientific and cost benefits are

Responsibilities and Resources

Who will be responsible for data management?

The project lead, Dr Danna Gifford.

What resources will you require to deliver your plan?

Backup storage provided by The University of Manchester Research IT (Isilon) and publicly accessible databases (European Nucleotide Archive).

Data Collection

What data will you collect or create?

Type of study

The studies encompass laboratory experimental evolution with *Escherichia coli* bacteria. This will involve allowing bacterial populations to evolve and measuring associated changes in antibiotic resistance phenotype and genotype.

Types of data

a) Quantitative data on bacterial growth and population characteristics from laboratory experiments. This will include the frequencies of mutations in bacteria within populations, bacterial phenotyping (e.g. growth rate produced by spectrophotometer and flurometer in the presence and absence of antibiotics).

b) Qualitative data on new resistance mutations arising during laboratory experiments. This will include genomic sequencing data produced by Illumina short read sequencing.

Format and scale of the data

Raw data will be stored in open formats (e.g. text-based CSV, R data objects, current Flow Cytometry Standard format (FCS3.1 or newer), FASTQ). Data initially output into proprietary formats will be immediately exported to open formats. Only open-source analysis tools will be used for downstream analysis of data to ensure reproducibility (e.g. R, breseq). New software generated will be stored in open-source repositories (e.g. GitHub). The use of open formats will facilitate data sharing and long-term data accessibility.

How will the data be collected or created?

Methodologies for data collection / generation

Standards for data collection will be set at the beginning of the project, but will be continually reviewed to ensure that best practices are being followed. This will include e.g. how often data points are collected, the criteria for inclusion in the study, and how negative and positive controls will be included to detect potential mistakes in experimental work. A schema for associating laboratory notebooks with collected data will be made to ensure that the correct metadata is associated with raw data.

Data quality and standards

To ensure data quality, data will be collected by skilled researchers with the appropriate training to use relevant research equipment. The equipment used has checks to ensure data integrity at the point of collection. Data quality will further be maximised through the use of appropriate statistical experimental design to minimise the possibility of spurious results arising due to stochastic noise. At the point of collection, data will be collected by skilled researchers trained FASTQ and FCS3.1 format includes extensive metadata on the machine used for collecting data. Data checksums will be used to ensure that files copied from local RDM provisions to public repositories are done so faithfully.

Documentation and Metadata

What documentation and metadata will accompany the data?

Metadata standards and data documentation

Metadata includes documentation of methods and procedures used to conduct experiments and collect samples. This metadata will be stored with the data, and also available in all resulting publications. This will be stored alongside the databases, which are flexible and allow free-form text documents to be stored alongside data formats e.g. CSV.

Ethics and Legal Compliance

How will you manage any ethical issues?

We do not anticipate any ethical issues arising from the data. Any ethical issues will be managed through referral to departmental or institutional ethics committees.

How will you manage copyright and Intellectual Property Rights (IPR) issues?

Data and publications will be released under Creative Commons Licence 4.0 (CC-BY). External users will be bound by this licence, which is designed to facilitate reuse without restrictions, as long as the original contributor is acknowledged.

Storage and backup

How will the data be stored and backed up?

Data will be stored to meet the standards of GDPR. In the short and medium term (i.e. before publication), data will be stored using The University of Manchester's dedicated Research Data Storage (RDS) facility, which offers 8 TB of backed-up data free at the point of use to research groups. On publication, bacterial phenotyping data will be stored alongside publications in open access databases (e.g. Dryad or Mendeley Data), although there is no community agreed/formal data standard. Bacterial genomic data will be stored in the European Nucleotide Archive (ENA, http://ebi.ac.uk), which allows storage of project metadata. The ENA is one of the community agreed databases for genomic sequence data.

How will you manage access and security?

The project lead (Dr Danna Gifford) on the project will make the decision to supply data. In principle data will be freely accessible without a need for a formal request. Data will be stored in publicly accessible repositories and databases.
The main risk to confidentiality is through unauthorised access to raw data, which can occur if data is stored on a device accessible to the general public. This risk will be mitigated by encrypting the hard drives of laptop computers, preventing access to data without a username and password. Further, the use of VPN via Global Connect will be used to access data on RDM servers. Both of these procedures are part of The University of Manchester's standard IT policy.

Selection and Preservation

Which data should be retained, shared, and/or preserved?

Upon publication, raw data will be made available in a public repository (e.g. Dryad or GitHub) as appropriate. Useful unpublished data will be made available in a public repository on conclusion of the project.

What is the long-term preservation plan for the dataset?

Data will be maintained in an established repository (European Nucleotide Archive for genomic data, Dryad for other types of data, GitHub for software pipelines).

Data Sharing

How will you share the data?

Before publication of an associated manuscript, data will be made available upon request to the project lead. When publication of an associated manuscript/preprint has occurred, data will be made available in a public repository with a doi made available in the publication.

Are any restrictions on data sharing required?

There are no anticipated restrictions on sharing data generated.