Advanced Informatics and Technology for Biomarker Discovery:

Disease-Associated Metabolites and Evidence of Infection in ME/CFS

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Research Project | The ME Association

INTRODUCTION | ME, MY LAB, MY RESEARCH

- Second-year DPhil (PhD) student in the **Nuffield Department of Women's & Reproductive Health (NDWRH)**, University of Oxford
- My research is a joint project with the **Rosalind Franklin Institute (RFI)**
  - Multidimensional Imaging Team (MDI)
  - Mass Spectrometry group
- I also collaborate with **Imperial College** and the **National Phenome Centre (NPC)**

The Rosalind Franklin Institute

National Phenome Centre

SUPERVISORS

Dr. Bela Paizs
Mass spectrometry and computational modelling

Dr. Marcus Gallagher-Jones
Electron microscopy

Prof. Karl Morten
ME/CFS and biomarker discovery

IMPERIAL

UNIVERSITY OF OXFORD

RFI

"Finding new pathways to improve human health, transforming the impossible into reality"

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TECHNOLOGY EXPERTISE

Oxford University | NDWRH

"Advancing women's and reproductive health through research and education"

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DISEASE EXPERTISE

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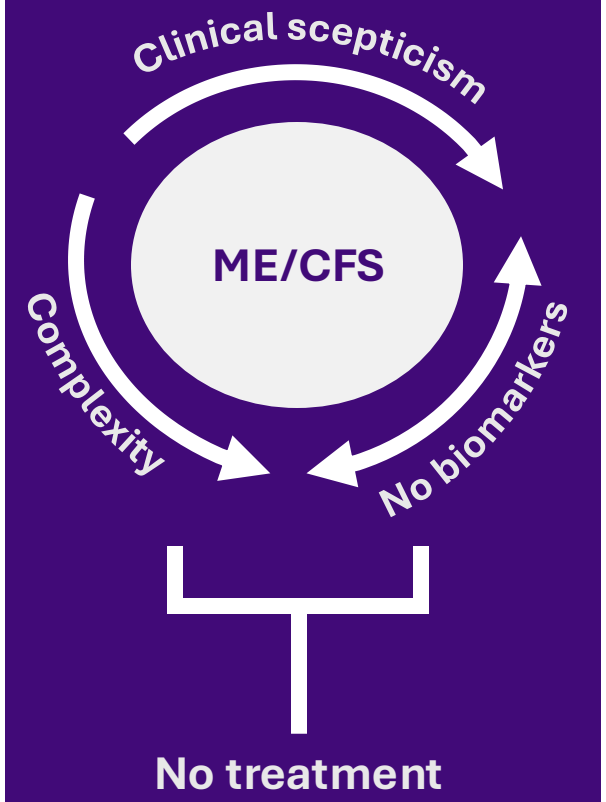
THE CHALLENGE OF ME/CFS | WHY ARE WE STILL STUCK?

How can we track these shifts in the body?

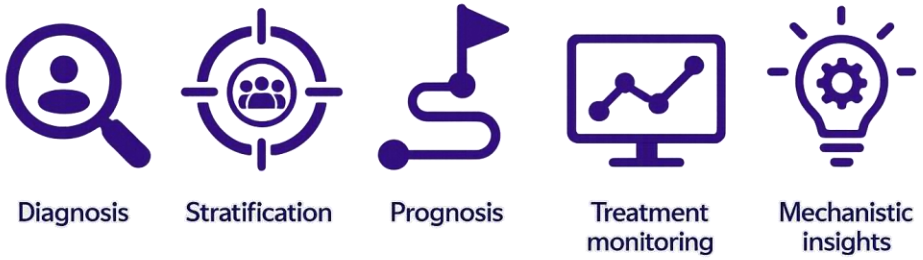


BIOMARKERS | molecular disease signatures

Biomarkers

Biological molecules present in body fluids or tissues that is indicative of normal or abnormal biological processes, or of a disease or medical condition.

Why we need "biomarkers" for diseases?



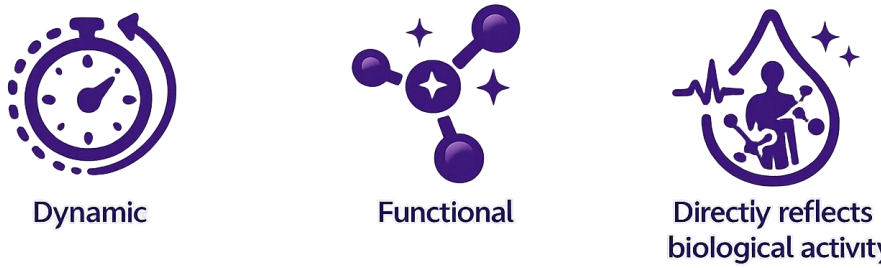
A single biomarker is unlikely for a multisystem disease like ME/CFS; identifying a panel of interacting markers – a "disease fingerprint" – could enable translation.

METABOLOMICS | what small molecules can tell us

Metabolomics

The study of small molecules in our body (called **metabolites**) that reflect how our organs and cells are functioning.

Why study metabolites for diseases?



WHY WE NEED OUR NOVEL TECHNOLOGIES

- Metabolomics allows us to measure thousands of small molecules in the body – but we don't know the identity of many of them
- If we don't know what a molecule is, it is very difficult to understand what role it might play in ME/CFS
- Identifying these molecules could reveal biological differences between patients, help us define ME/CFS subgroups, and ultimately identify potential markers for diagnosis and treatment
- At the **Rosalind Franklin Institute (RFI)**, we have **specialised technology** that can **identify the structure of unknown molecules** – even when only tiny amounts are present

Mass Spectrometry and Liquid Chromatography

Crystallise molecule(s)

+ COMPUTATIONAL PREDICTIONS

Electron Microscope

Confirmed structure of molecule

THE PROJECT | a new way to find biomarkers

Limitations Of Traditional Methods

- Uses only **limited information** from the mass spectrometer
- Relies on **AI** to **predict structures**, which can be **inaccurate**
- **No microscope validation** (requires large sample amounts)
  - **Often not possible** with patient samples

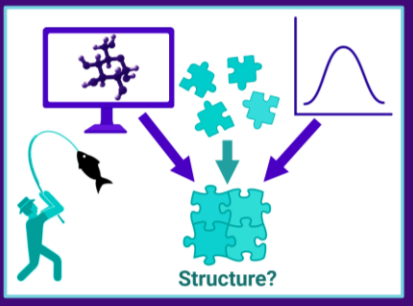
→ **KEY DISEASE MARKERS MAY BE MISSED**

We can find tiny amounts of important molecules and reveal their 3D shapes

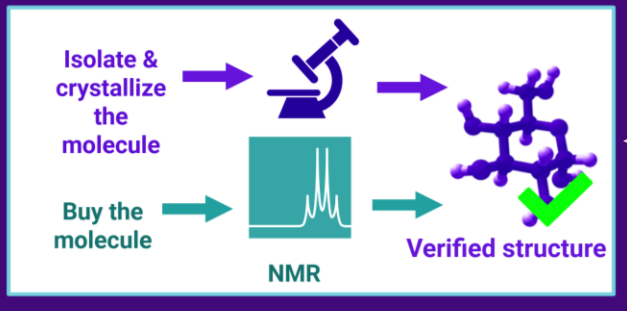
Our Workflow Is More Flexible

1. FIND IMPORTANT MOLECULES

2. ADVANCED STRUCTURAL ANALYSIS



3. MULTI-METHOD VALIDATION



FIND ROLE IN DISEASE

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The ME/CFS Cohorts We Are Studying:

1. Exercise intervention cohort [9]

NICOLAUS COPERNICUS UNIVERSITY IN TORUŃ

2. Cryotherapy cohort [10,11]

NICOLAUS COPERNICUS UNIVERSITY IN TORUŃ

3. Post-exertional malaise cohort [12]

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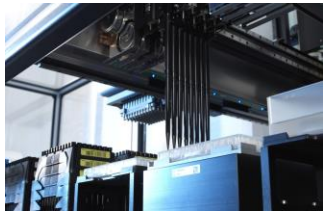
OUR PROGRESS SO FAR | Applying method to disease molecules

1 Our method worked successfully on molecules made in our laboratory

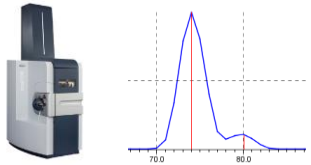
10. Lumsden et *al.*, ChemRxiv (2026)

A. Made the molecules

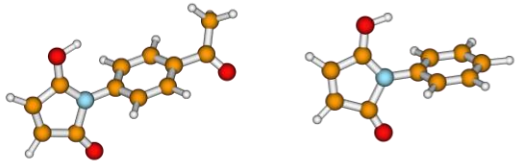


PRODUCED 32 MOLECULES AT ONCE

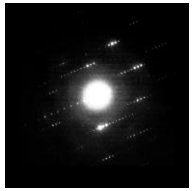
B. Collected their mass spectrometry data

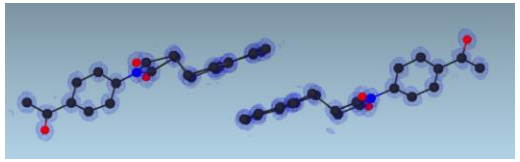


C. Computed their possible structures



D. Confirmed the structures with the microscope

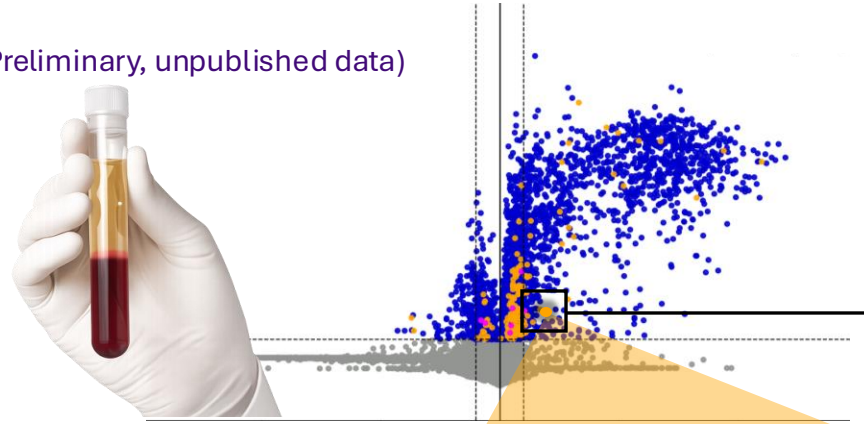




2 We successfully applied our method to an ME/CFS-related molecule

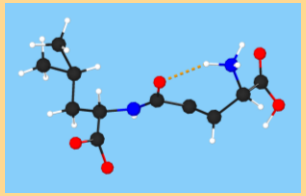
ME/CFS vs Healthy molecules

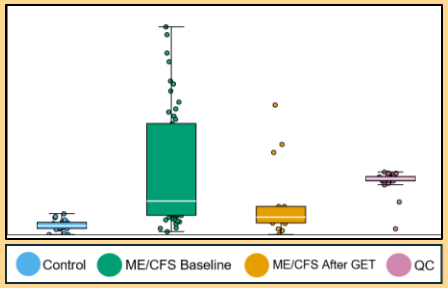
(Preliminary, unpublished data)



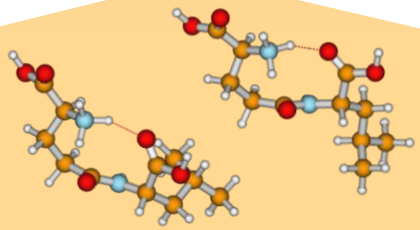
A molecule that increases in ME/CFS

Confirmed as **γ-Glu-Leu** by microscope and fragmentation modelling





*It was unclear from computer analysis whether the molecule was **γ-Glu-Leu** or **γ-Glu-Ile**, which are extremely similar*



Possible structures

Mass spectrometry data

FUTURE PLANS

Compare different patient groups to find shared disease-related molecules

Find molecules that are different in people with ME/CFS (absent in healthy people)

Test different ways of preparing and analysing the samples to find more molecules

Find out if important molecules are linked to known ME/CFS disease pathways


Thanks for listening!

CITATIONS

(1) **Nature Portfolio (2025)** *Metabolomics*. Nature Portfolio.

(2) **The Rosalind Franklin Institute**. *The Rosalind Franklin Institute: New pathways to improve health*. Available at https://www.rfi.ac.uk/

(3) **Hitachi High-Tech (2026)** *Transmission Electron Microscope HT7800 Series. Hitachi High-Tech*.

(4) **World Pharma Today (2022)** *Bruker launches timsTOF SCP for unbiased single cell 4D-proteomics and next-gen timsTOF Pro 2 with unprecedented proteomic depth*

(5) **Oxford University Hospitals NHS Foundation Trust (2026)** *History of the John Radcliffe Hospital*. Oxford University Hospitals NHS Foundation Trust.

(6) **Prenetics (2026)** *Early Detection | Insighta*. Prenetics.

(7) **Created with BioRender.** *Biorender*. Available at https://www.biorender.com

(8) **Kromtekindo Utama (2021)** *AQUITY H-Class PLUS System*. Available at https://kromtekindo.com/2021/12/30/acquity-uplc-h-class-plus-system/

(9) **Zhao, L. *et al*. (2026)** 'The efficacy of exercise in patients with myalgic encephalomyelitis/chronic fatigue syndrome: A systematic review and meta-analysis', *Journal of Psychosomatic Research*, 207, 112677.

(10) **Kujawski, S. *et al*. (2023)** 'Effects of whole-body cryotherapy and static stretching are maintained 4 weeks after treatment in most patients with chronic fatigue syndrome', *Cryobiology*. doi: 10.1016/j.cryobiol.2023.05.003.

(11) **Kujawski, S. *et al*. (2022)** 'Combination of whole body cryotherapy with static stretching exercises reduces fatigue and improves functioning of the autonomic nervous system in Chronic Fatigue Syndrome', *Journal of Translational Medicine*, 20, 279.

(12) **Pears, K. (2023)** *ME Association Research Review: Post-Exertional Malaise (PEM) in ME/CFS and Long Covid*. The ME Association. Available at: https://meassociation.org.uk/2023/12/me-association-research-review-post-exertional-malaise-pem/

(13) **OpenAI (2026)** *ChatGPT* (GPT-5) [Large language model]. OpenAI.

(14) **Lumsden et *al*., 2026.** *Integrating Ion Mobility-Resolved Tandem Mass Spectrometry and Microcrystal Electron Diffraction for Structural Elucidation*. ChemRxiv.