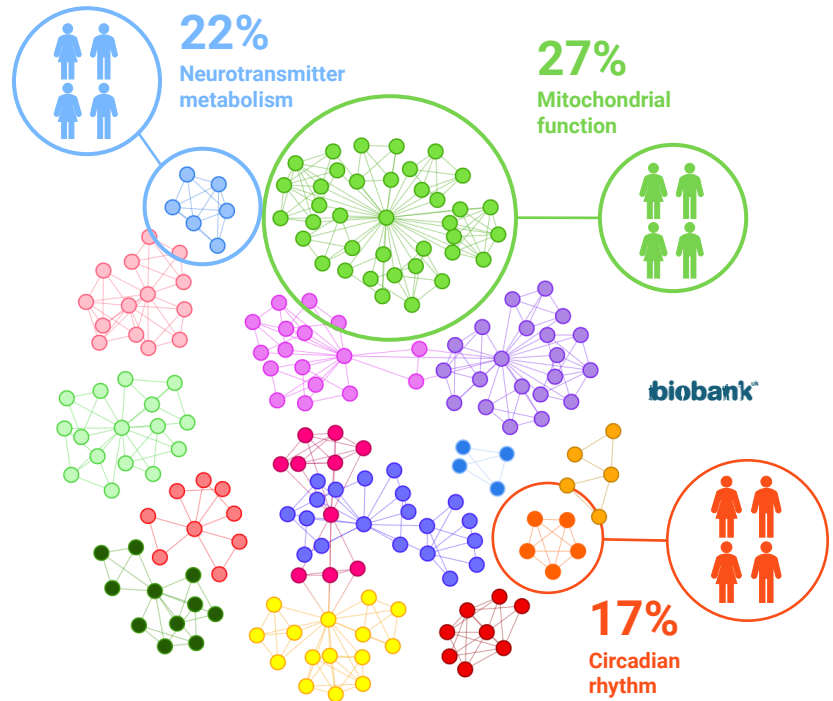# Beginning to Unravel the Biological Drivers of ME

ME is a very complex disease that has many different causes and risk factors.

We have for the first time potentially identified some of the different genetic mechanisms causing ME/CFS (shown as colours) and used this to stratify patients.

We've validated that patients with specific underlying genes/mechanisms have symptoms that match this mechanism (e.g. fatigue vs autoimmune).

Only patients with the green mechanism will respond to a drug targeting this gene.

Patients with other disease mechanisms will not respond – making it essential to validate the biological basis of the disease.

22%
Neurotransmitter metabolism

27%
Mitochondrial function

biobank*

17%
Circadian rhythm

We're currently replicating these results in DecodeME's much larger, better characterized patient populations as part of the LOCOME grant supported by Innovate UK. We're now aiming to:

- validate simple saliva/blood genotyping tests for ME, CFS and long COVID
- identify actively protective biology that may prevent people getting ME / help them recover
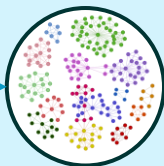- identify and validate drug repurposing candidates that may help some ME patients

action for m·e

THE UNIVERSITY OF EDINBURGH

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precisionlife · **action for m.e** · **Decode ME** The ME/CFS DNA Study · **LOCOME**

ME/CFS
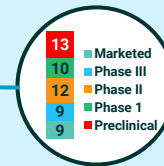disease risk/protective signatures

ME/CFS
mechanistic stratification

Candidate Selection
best fit of drug to mechanism/trial
(safe, well-tolerated / high prevalence)

Drug Repurposing Candidates
Pipeline of existing drugs for each
patient subgroup / mechanism

13 — Marketed
10 — Phase III
12 — Phase II
9 — Phase 1
9 — Preclinical

Clinical Validation · **precisionlife** ✕ **metrodora**

Patient sampling, surveys & genotyping

Identification of patient's disease risk/protective signatures and disease mechanism/s

Patient Recruitment
• Identifying high-risk patients with specific mechanism
• Recommendation of therapy targeting patient's specific ME/CFS mechanism
• Recruitment criterion for repurposing efficacy trial

Efficacy Trial
Testing of repurposed
therapy targeting patient's
specific ME/CFS mechanism
(*n* of 30-50)

Approval
Regulatory approval
for therapy proved
efficacious in
ME/CFS

For more
information,
please follow
the link

We're recruiting 4,000 patients at Metrodora to validate the new diagnostic tests. We currently have 7 ME, CFS and long COVID drug repurposing candidates in active consideration for trials

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