

Assessing Endothelial Dysfunction in ME/CFS



Graz, Austria

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Nitric oxide (NO) as a signaling molecule in the cardiovascular system



Photo from the Nobel Foundation archive.

Robert F. Furchgott

Prize share: 1/3

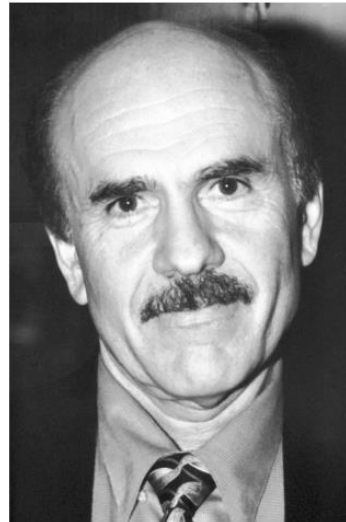


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Louis J. Ignarro

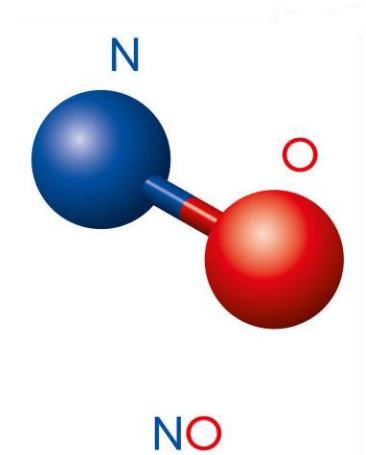
Prize share: 1/3



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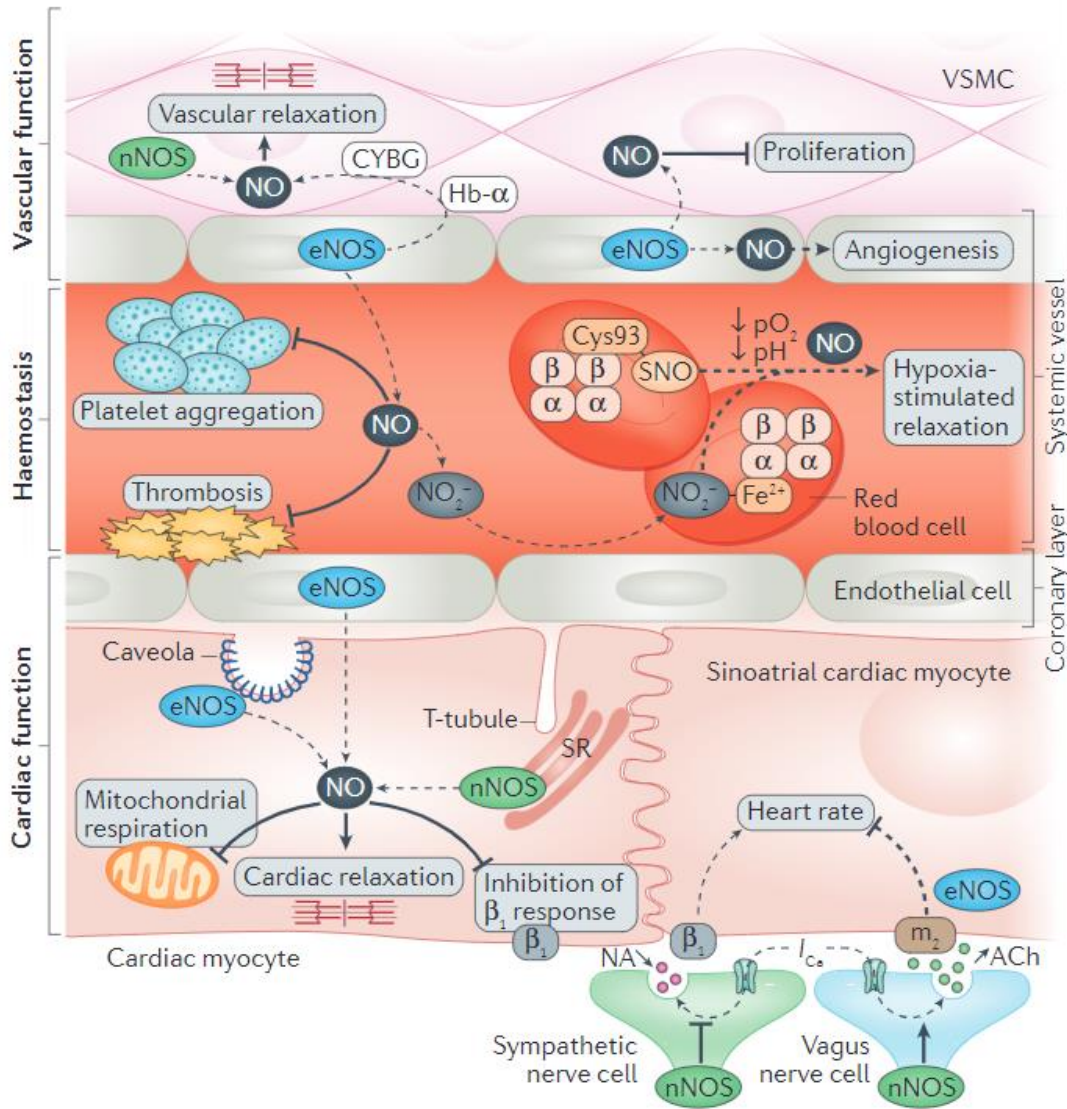
Ferid Murad

Prize share: 1/3



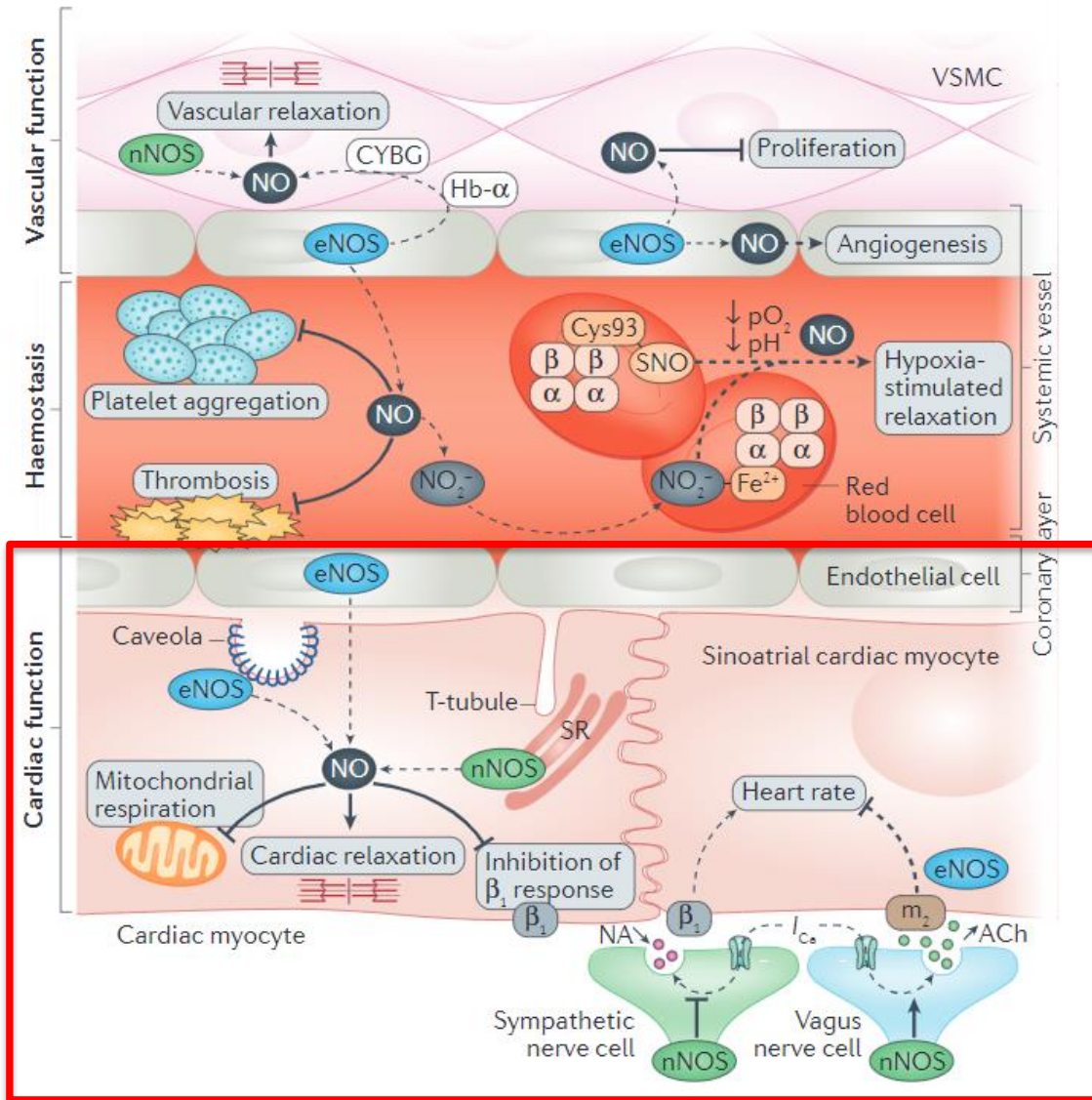
The Nobel Prize in Physiology or Medicine 1998





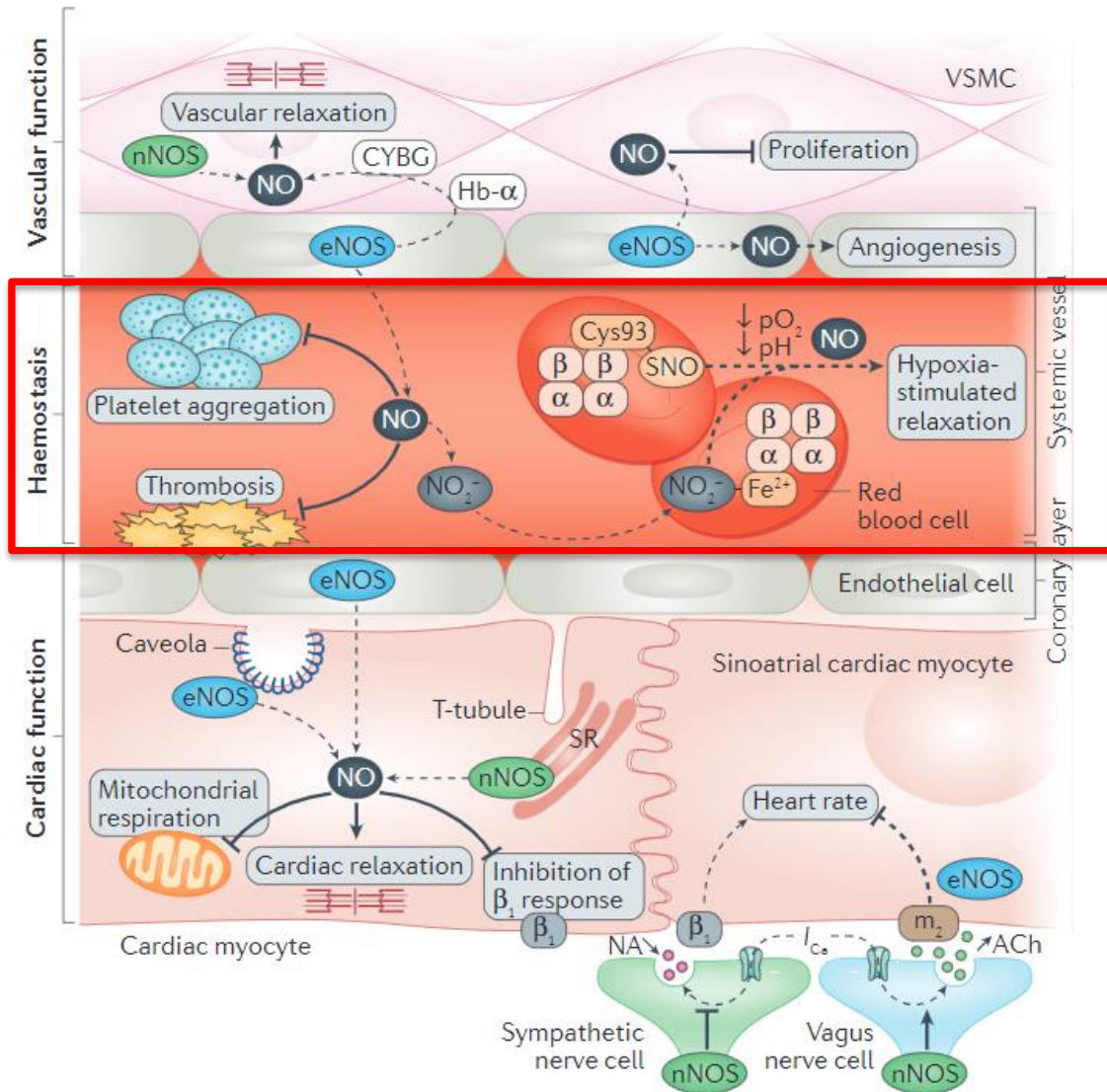
NO signaling in cardiovascular tissues





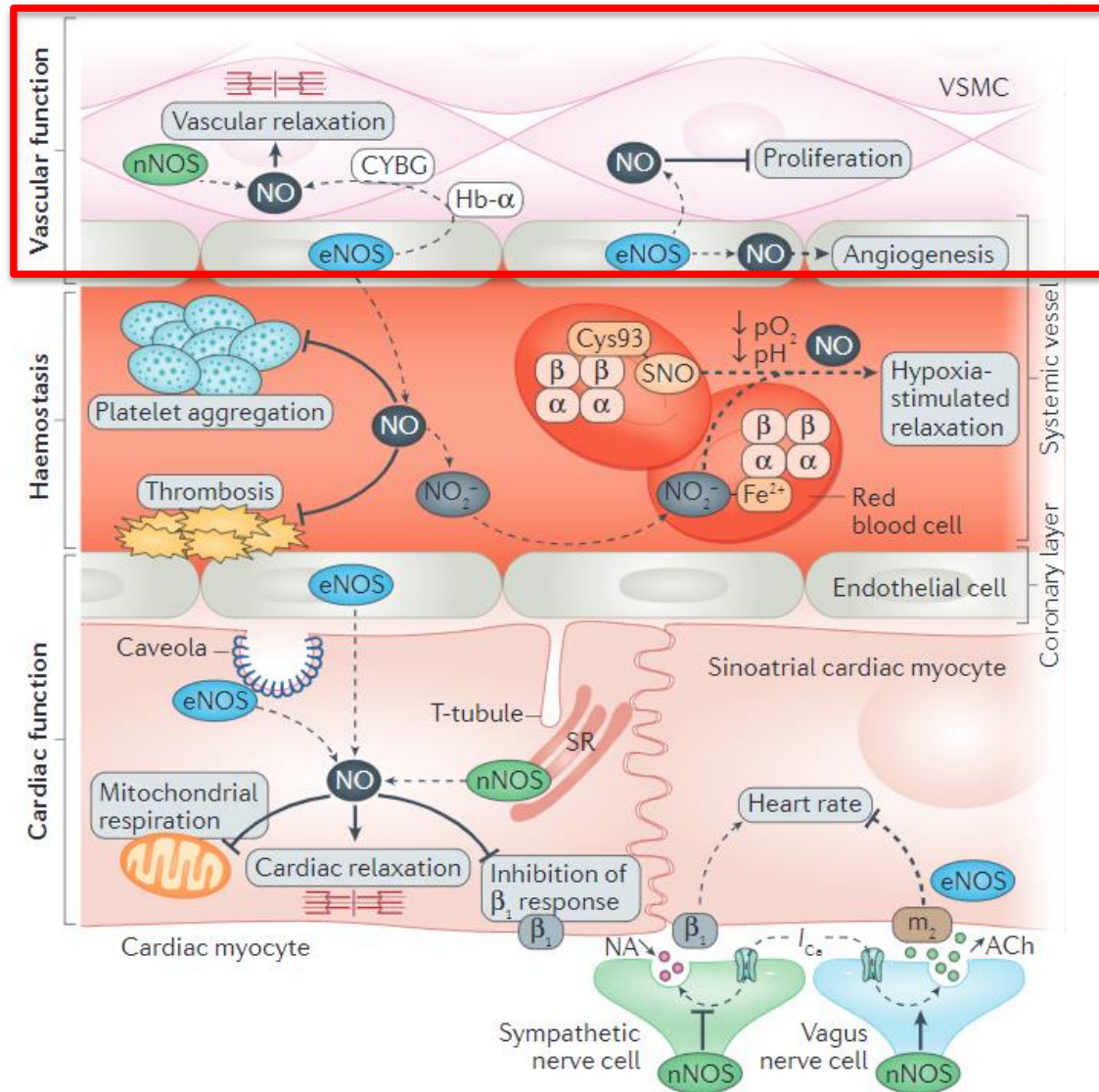
NO signaling in cardiovascular tissues





NO signaling in cardiovascular tissues

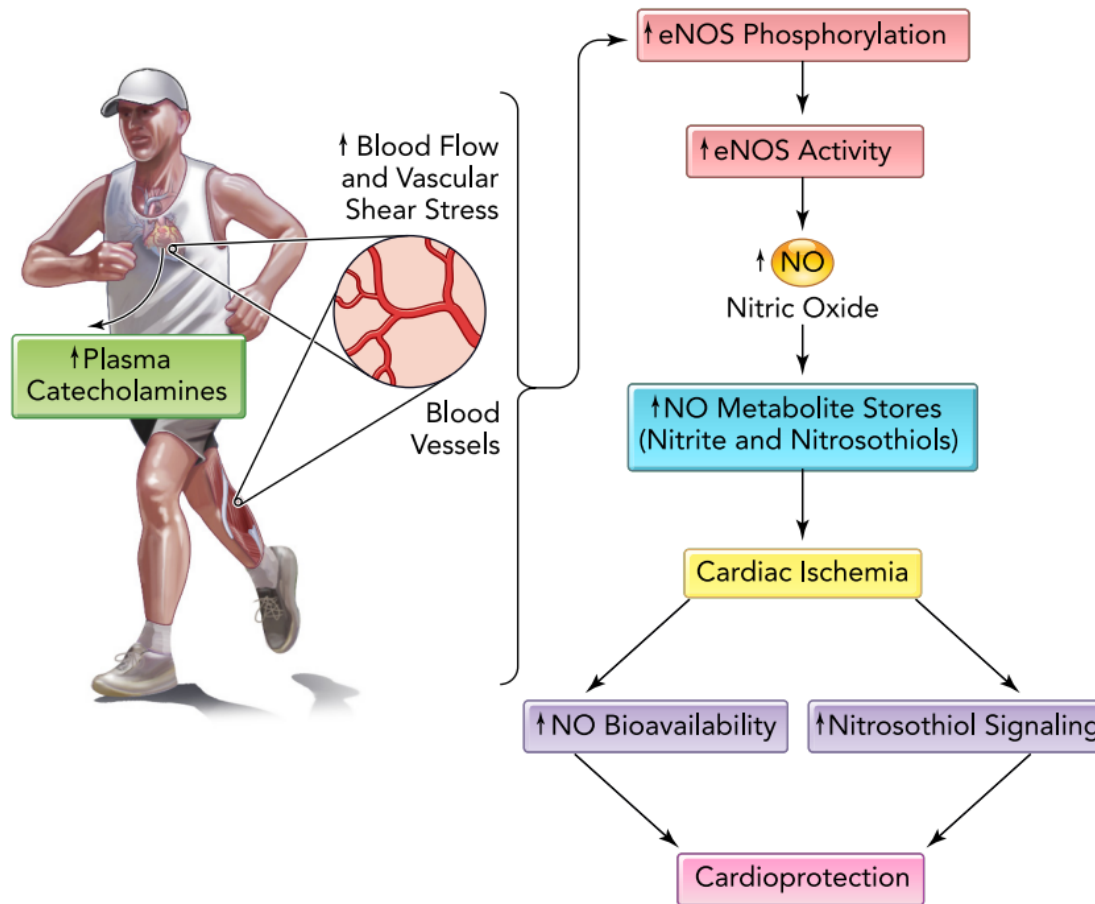




NO signaling in cardiovascular tissues



Exercise and nitric oxide homeostasis



ME/CFS is a complex illness and symptoms of ME/CFS may seem similar to many other illnesses. ME/CFS requires **three** symptoms:

1 Not being able to participate in routine activities that were possible before becoming ill, such as work, school, social life, and/or personal life, that:

- **Lasts** for more than **6 months**
- Is accompanied by **fatigue** that is:
 - Often serious
 - Just started (not lifelong)
 - Not the result of ongoing activities
 - Not from more than usual effort
 - Not made better by rest

2 Post-exertional malaise (PEM). Worsening of symptoms after physical, mental, or emotional effort that would not have caused a problem before the illness. This is sometimes referred to as “crashing” by people with ME/CFS.

3 Unrefreshing sleep. People with ME/CFS may not feel better even after a full night of sleep (e.g., feeling just as tired upon waking up as before going to bed).

In addition, **at least one** of the following symptoms is also required:

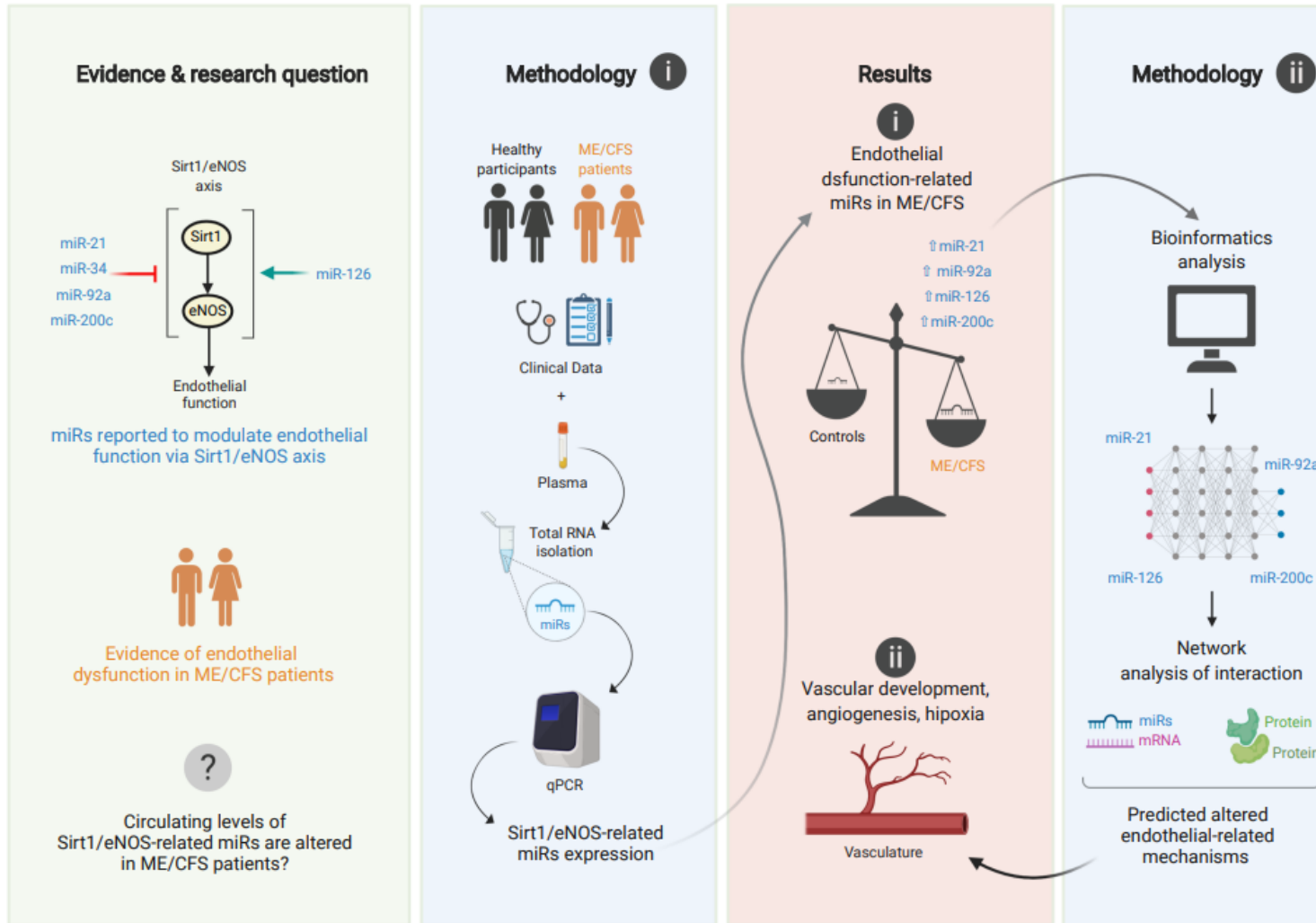


Impaired memory or ability to concentrate. People with ME/CFS may have trouble remembering, learning new things, concentrating, or making decisions.

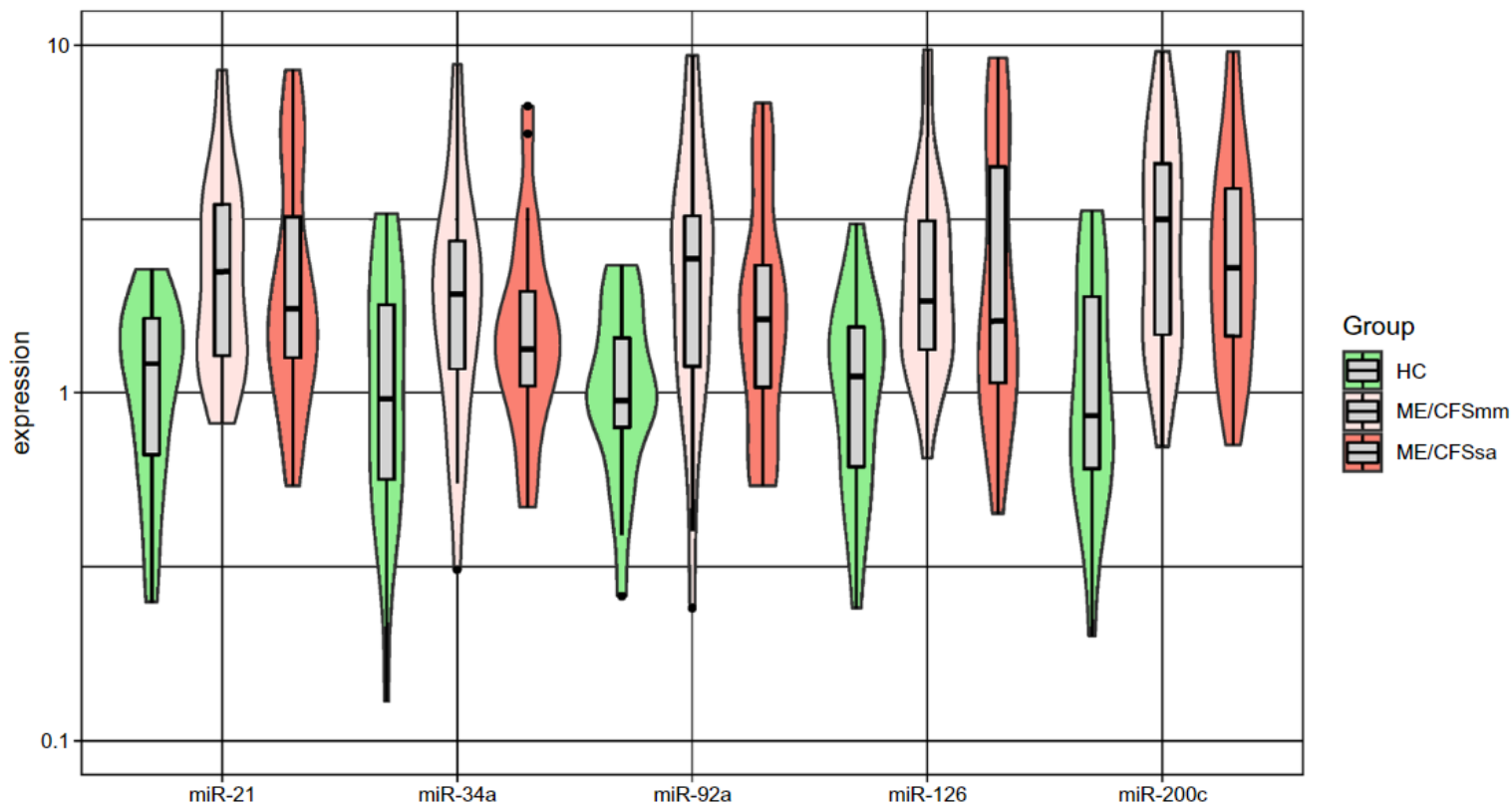


Orthostatic Intolerance (symptoms that occur when standing upright). People with ME/CFS may feel lightheaded or dizzy when standing upright and may even faint.

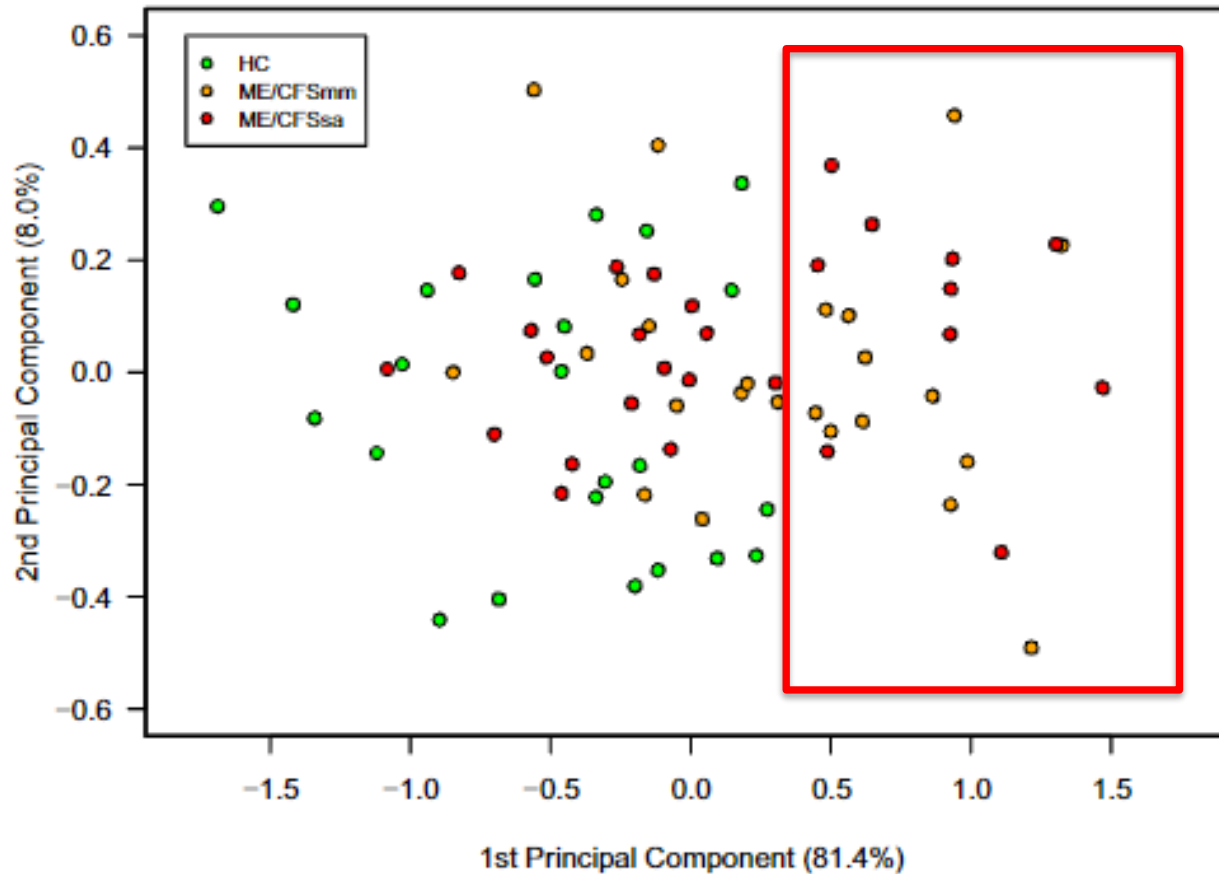




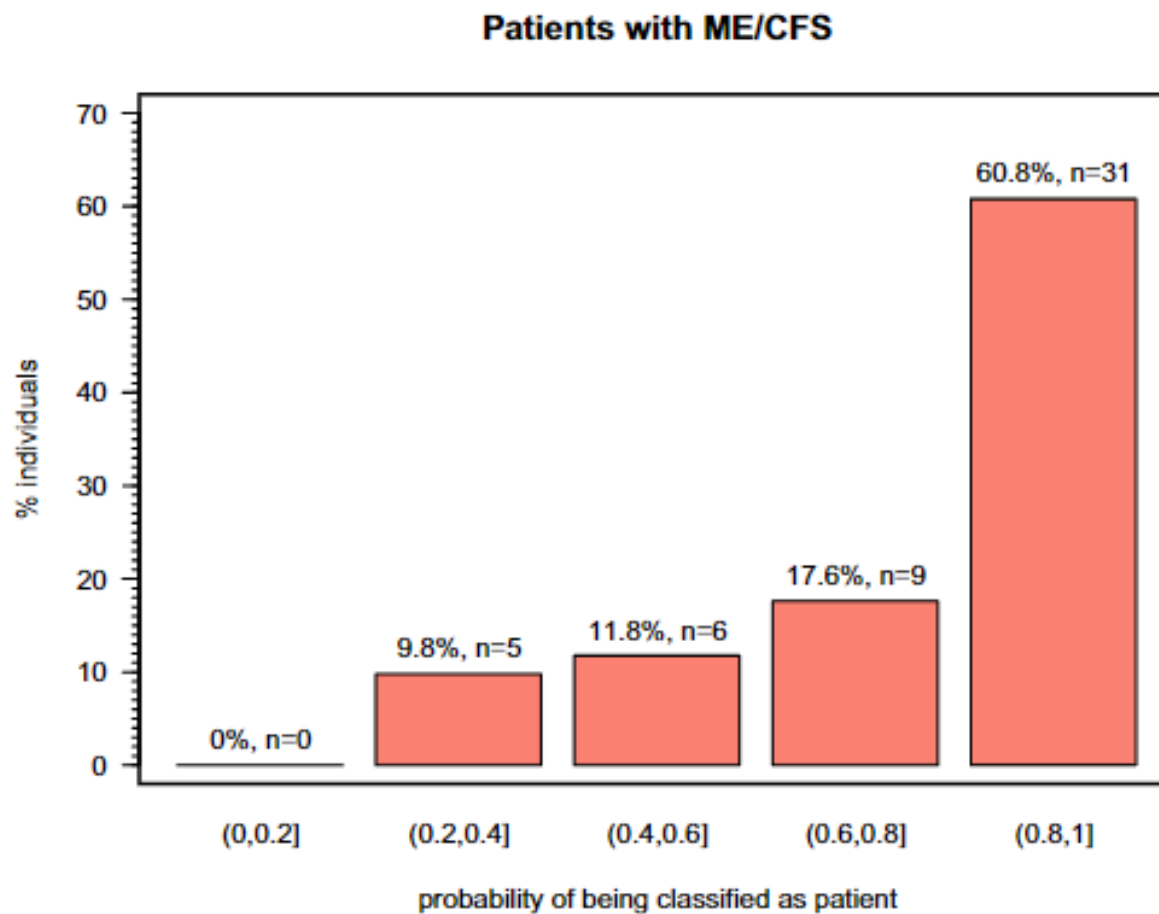
miRs associated with ED are increased in plasma from ME/CFS patients



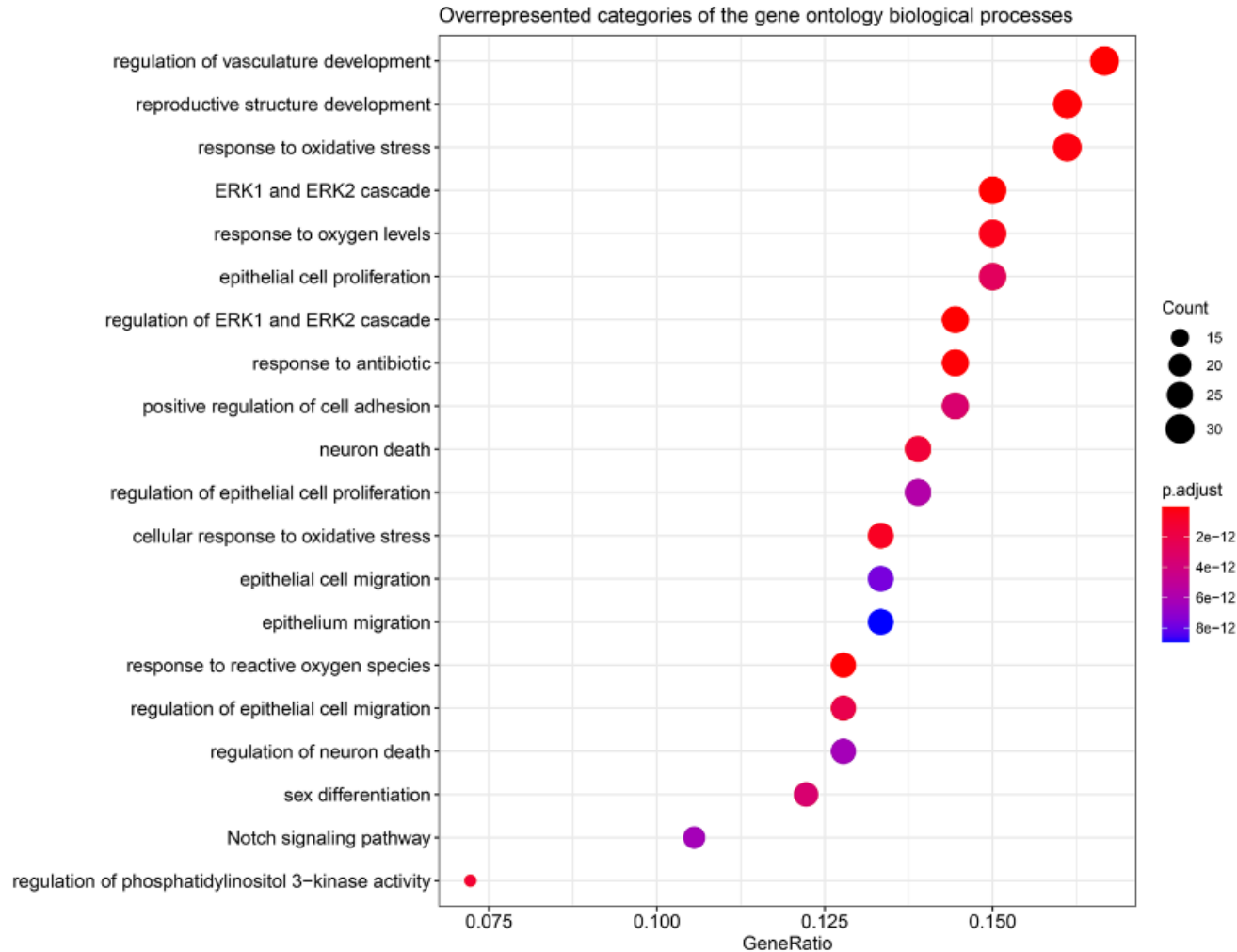
A subset of ME/CFS patients were different from HC in the abundance of these miRs



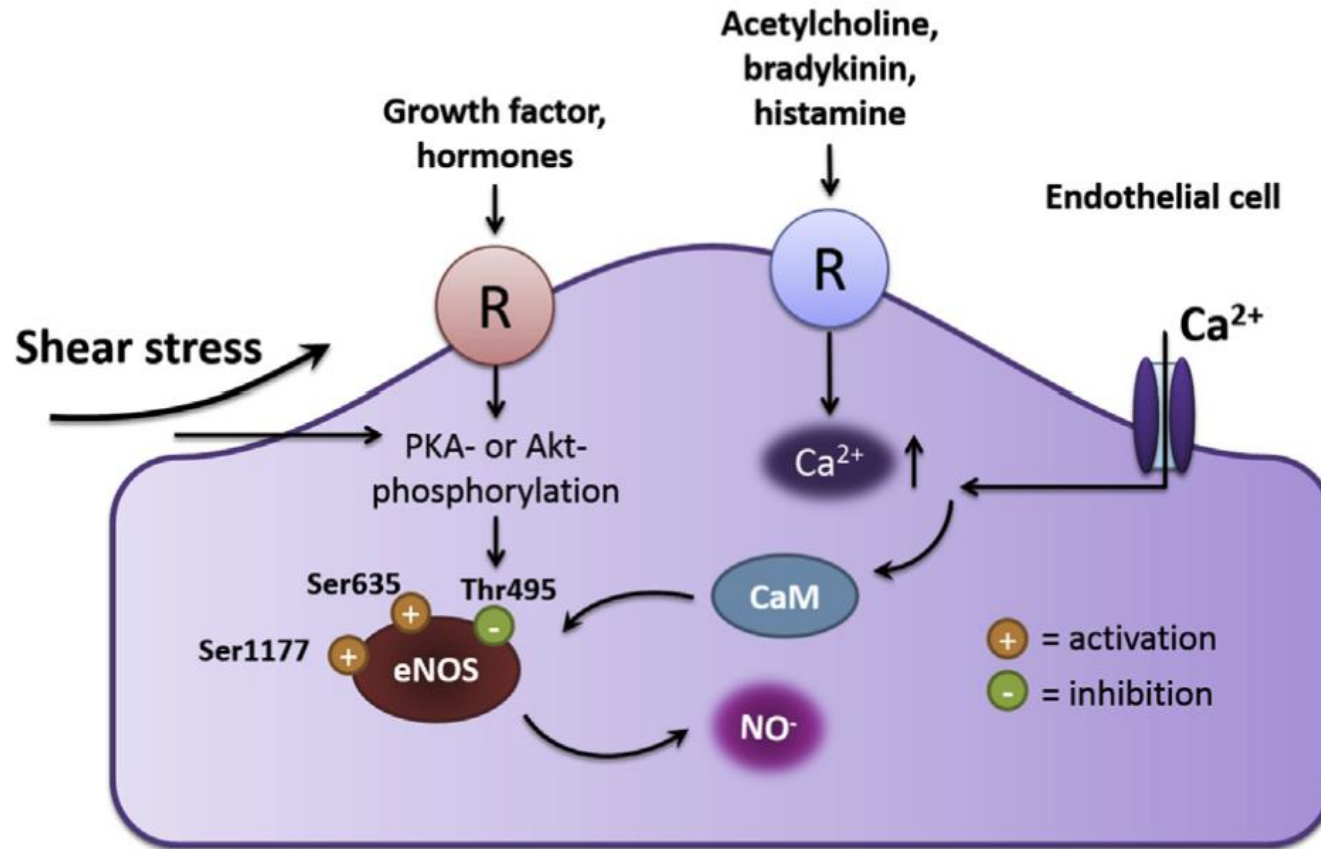
We were able to correctly classify ~60% of the patients with a probability of 80%

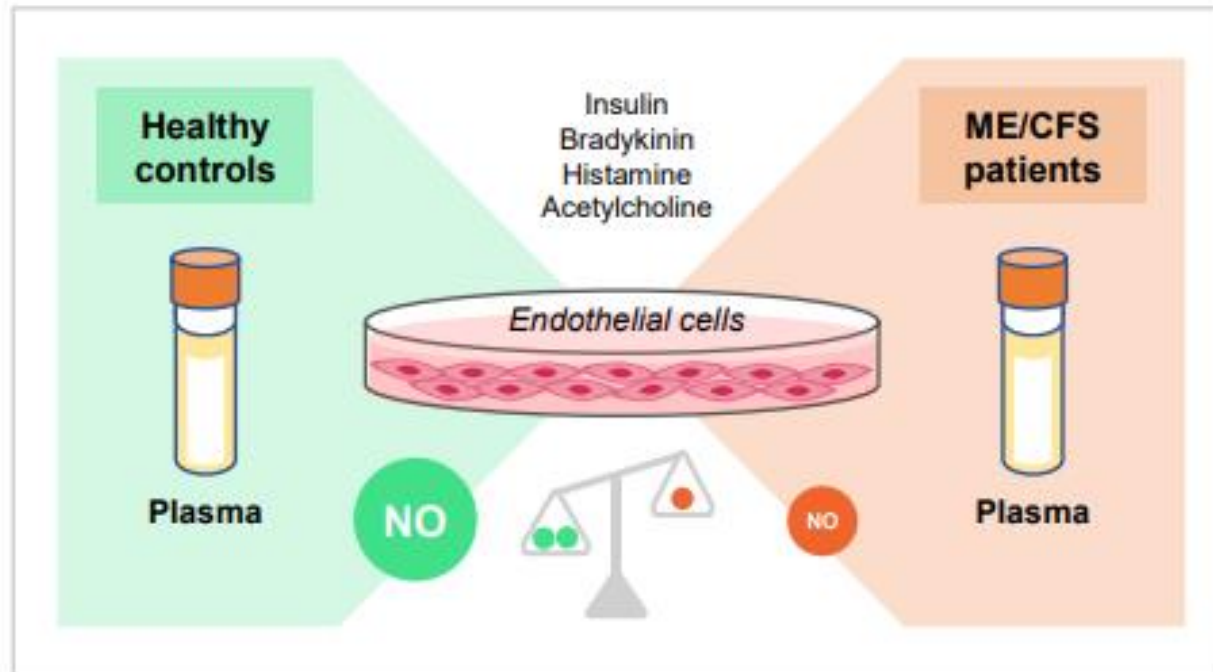


Association between our set of miRs and endothelial-related processes

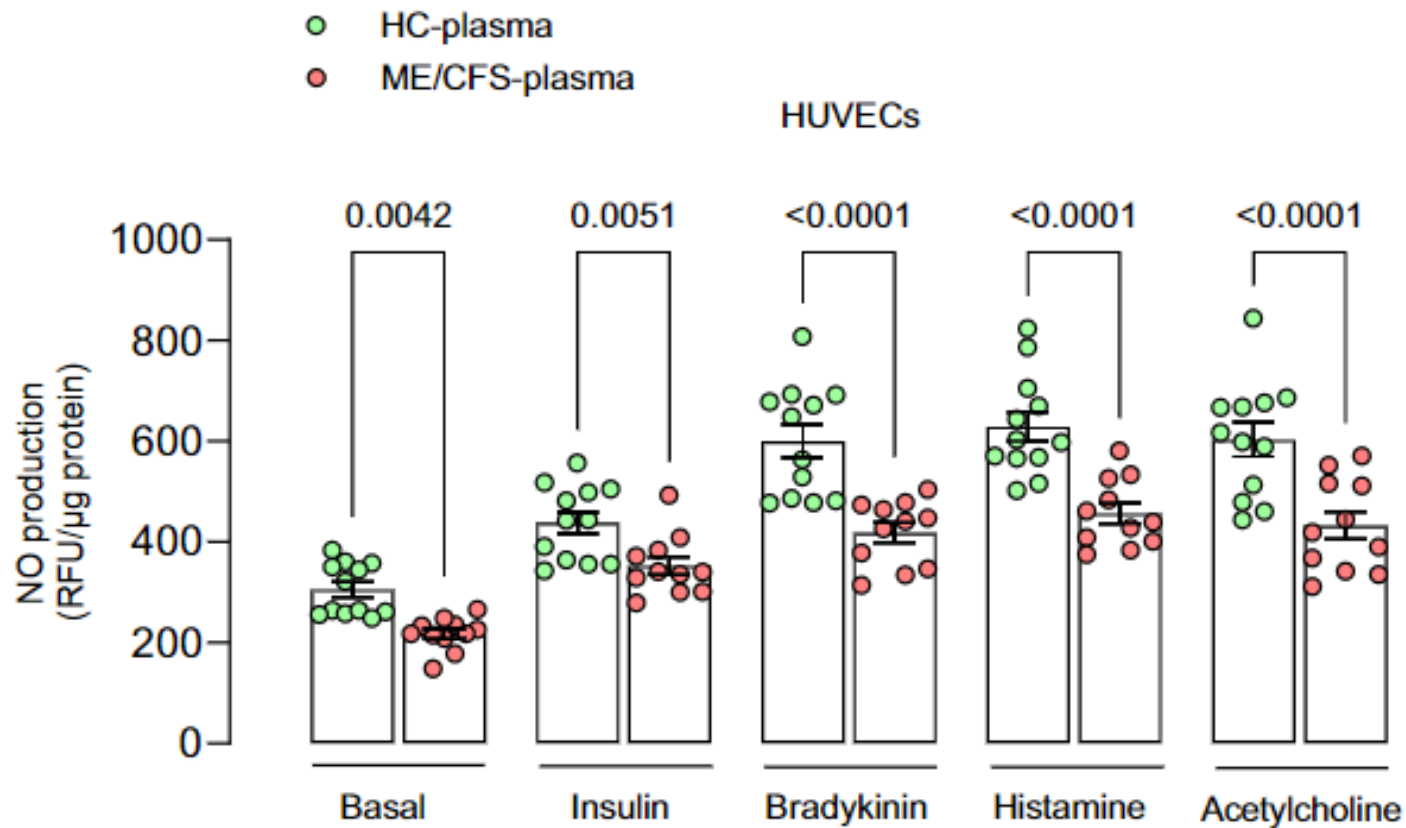


eNOS regulation in endothelial cells

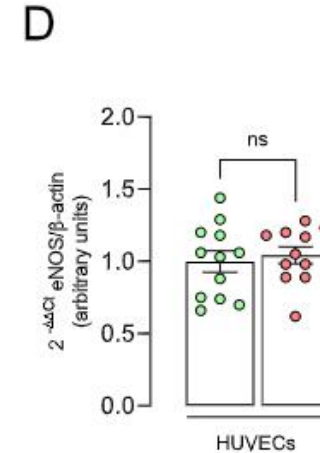
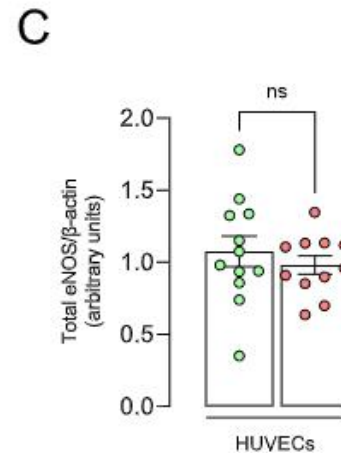
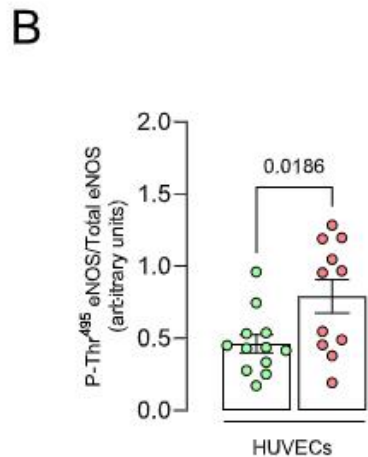
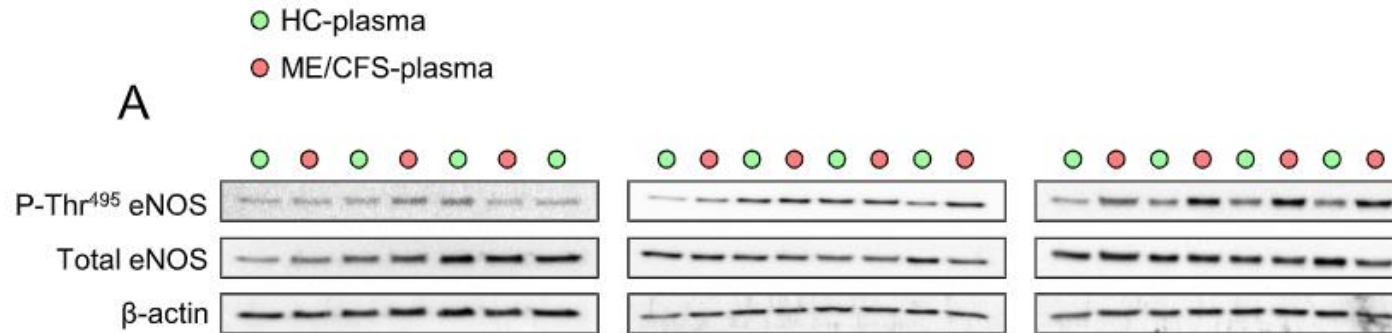




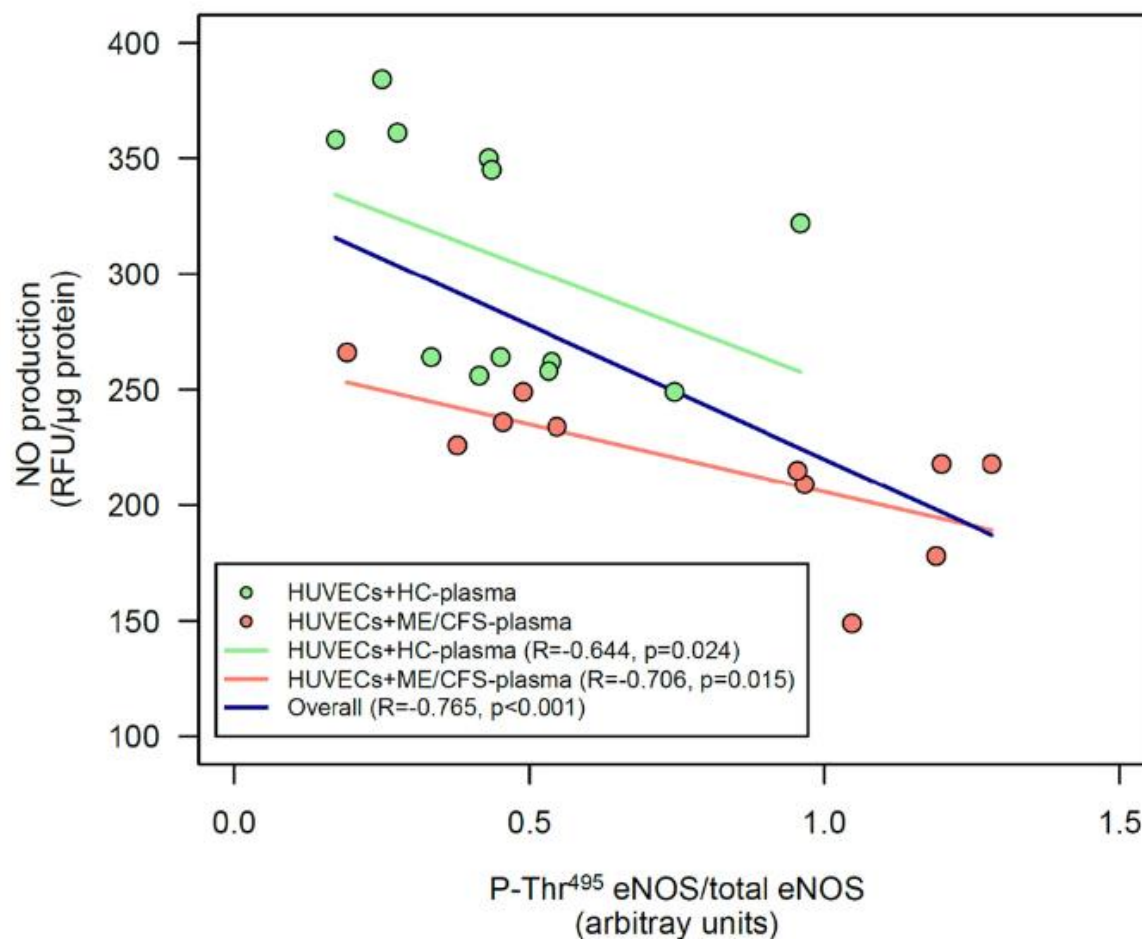
NO production is reduced in endothelial cells exposed to plasma from ME/CFS patients



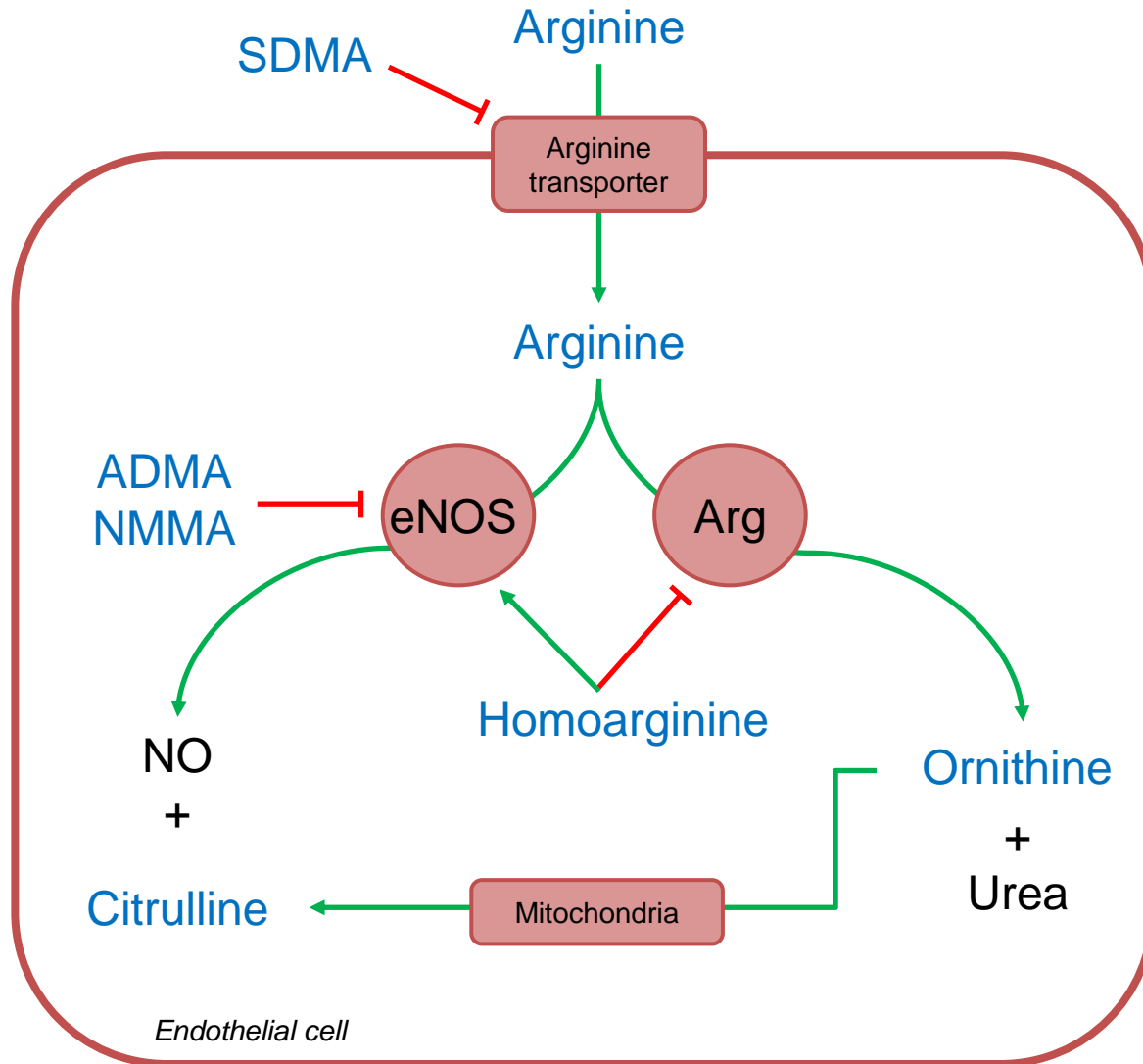
Endothelial cells exposed to plasma from ME/CFS patients show higher phosphorylation of eNOS at Thr⁴⁹⁵



Reduced NO production might be linked to phosphorylation of eNOS at Thr⁴⁹⁵

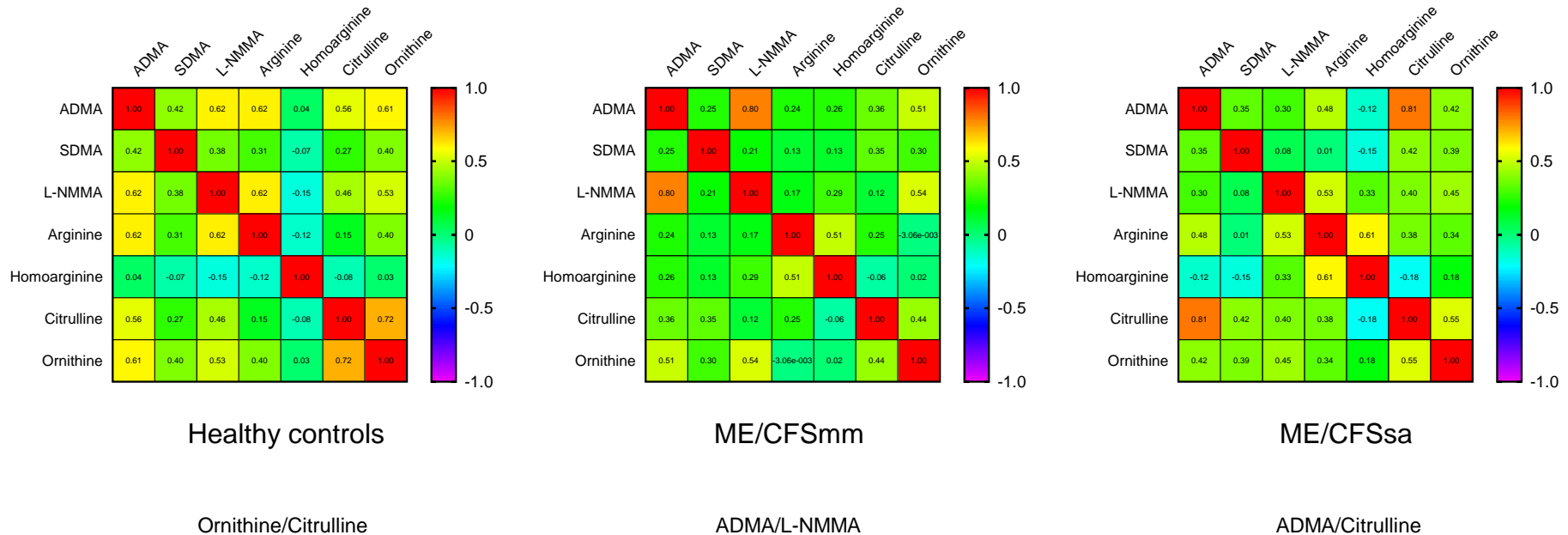


Arginine metabolism in ME/CFS



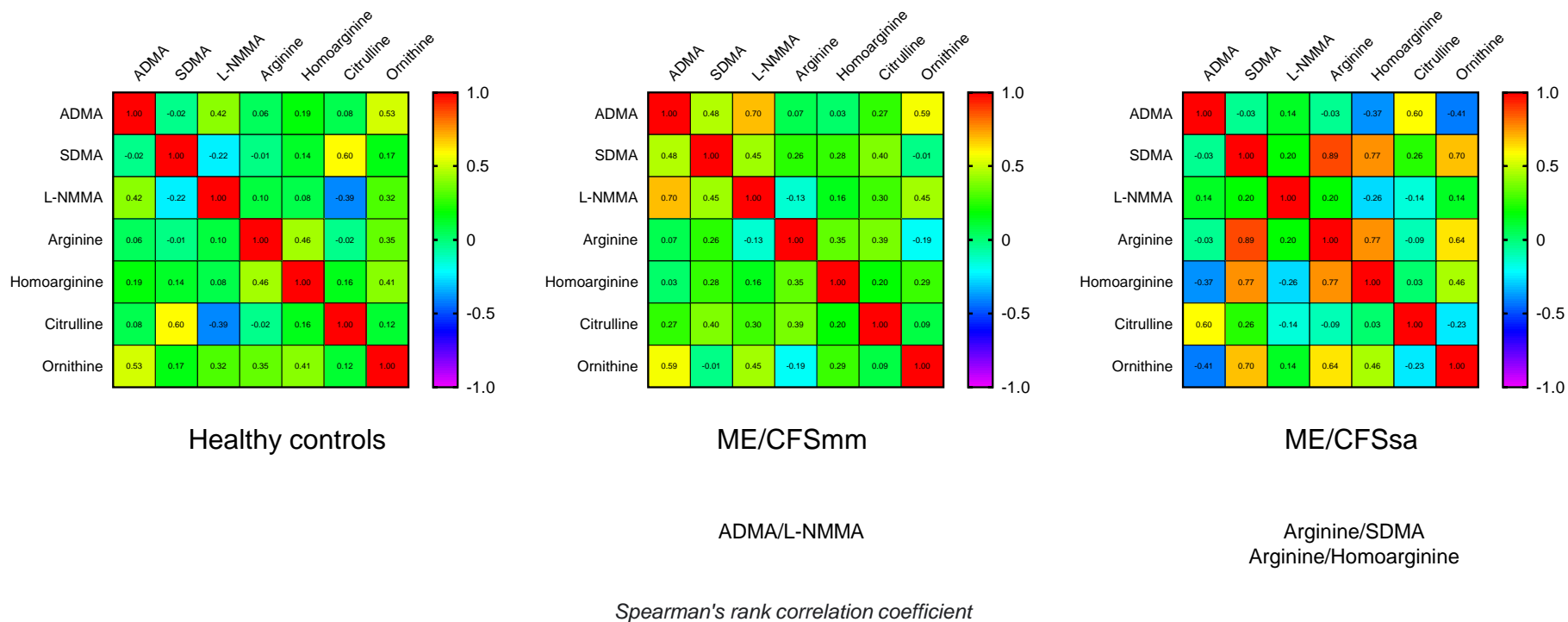
CUREME
Leading research into ME/CFS

Arginine metabolism in our female cohort of ME/CFS patients



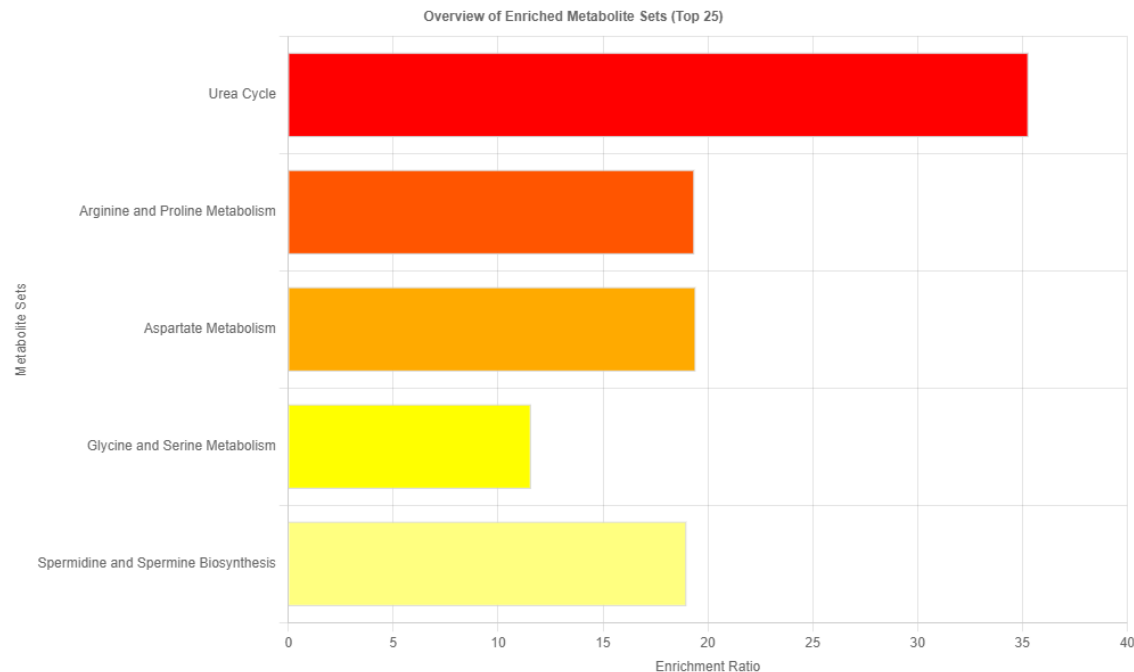
Spearman's rank correlation coefficient

Arginine metabolism in our male cohort of ME/CFS patients



Preliminary conclusions

- Our preliminary analysis suggests that L-arginine metabolites are dysregulated in ME/CFS compared to healthy controls, especially in our male cohort.
- In this line, L-arginine and L-homoarginine show an opposite pattern by comparing male and female ME/CFS patients with their respective healthy counterparts.
- Interestingly, the urea cycle seems to be the most relevant pathway based on our metabolite set enrichment analysis (Figure below).



Acknowledgements

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