

ROOTS AND RESILIENCE: A PASIFIKA ACADEMIC JOURNEY



GENOMICS AOTEAROA WORKSHOP, WELLINGTON
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genomics
aotearoa

Psychotria insularum (matalafi) – a traditional medicine used in Samoa



- Locals call the plant ‘matalafi’
- Highly treasured anti-inflammatory medicine typically reserved for serious illnesses.

“Understand matalafi’s molecular mechanism using yeast chemical genomics”

Using yeast as a model organism to determine *P. insularum* molecular mechanism of action

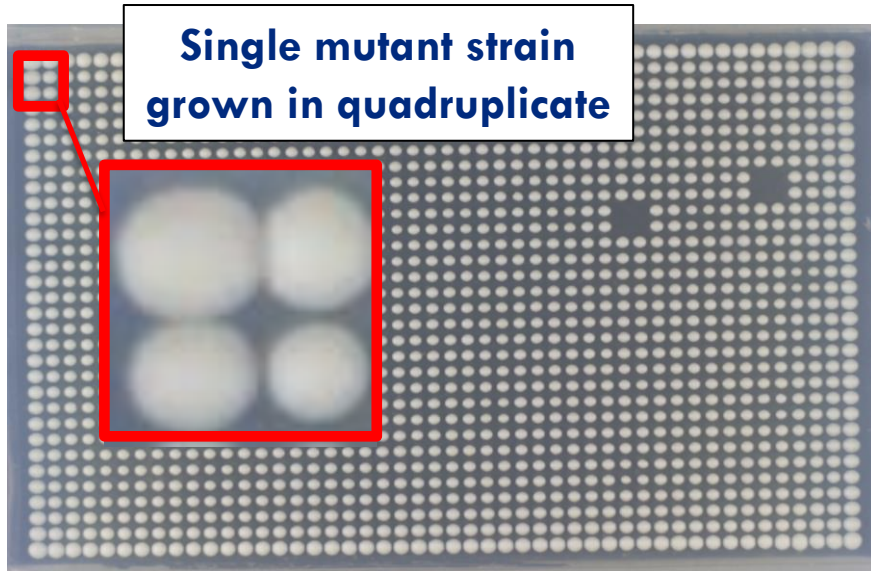


- *Saccharomyces cerevisiae* (baker's yeast).
- Cheap and quick to grow.
- Many biological processes that happen in yeast also happen in humans.
- Easily genetically modified to study **how natural products affect biological processes**.
 - Yeast gene deletion mutant library.
 - GFP-tagged protein yeast library.

The yeast gene deletion mutant library



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- Library contains ~6200 mutant strains.
- Each quadruplicate mutant has a single gene deleted from its genome.
- Compare non-treated with treated yeast

Analogy

Home game (control)



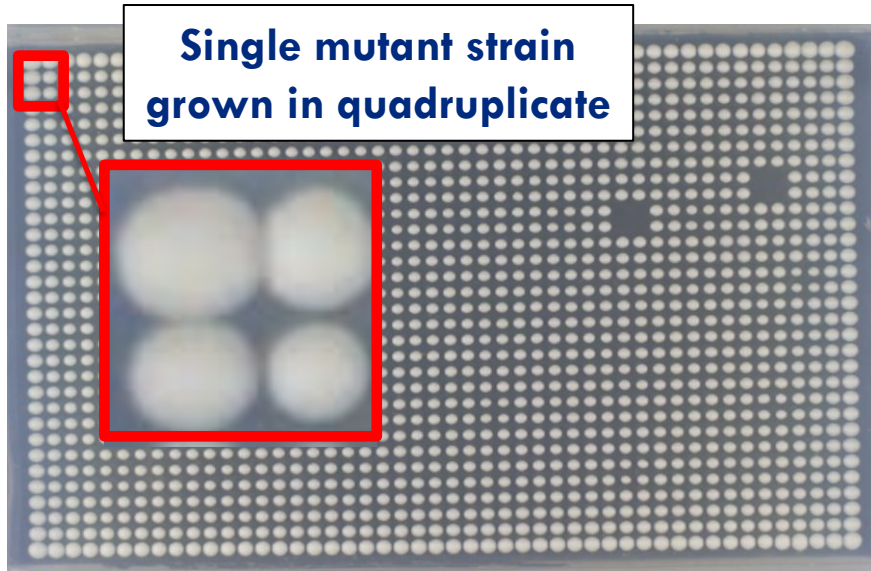
Away game (variable)



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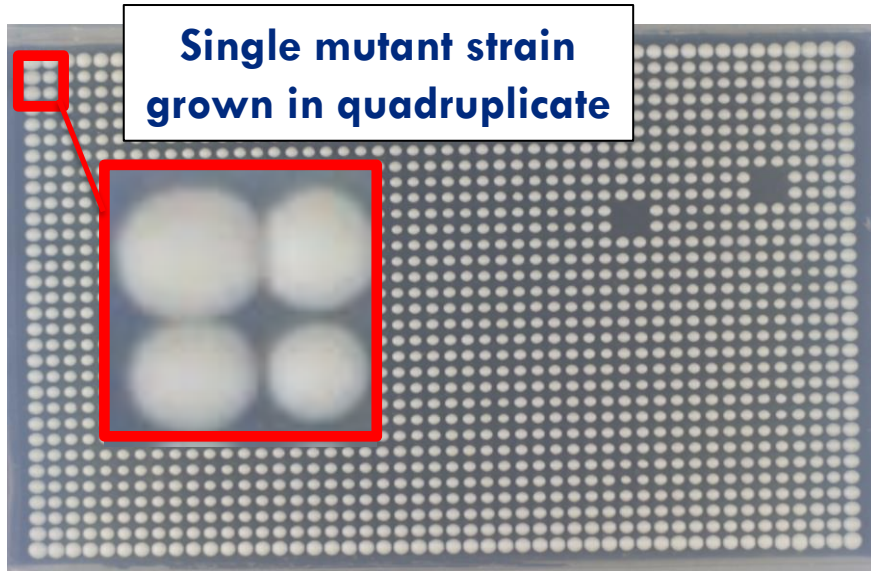
Away game (variable)



The yeast gene deletion mutant library



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Single mutant strain
grown in quadruplicate

- Library contains ~6200 mutant strains.
- Each quadruplicate mutant has a single gene deleted from its genome.
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Analogy

Home game (control)

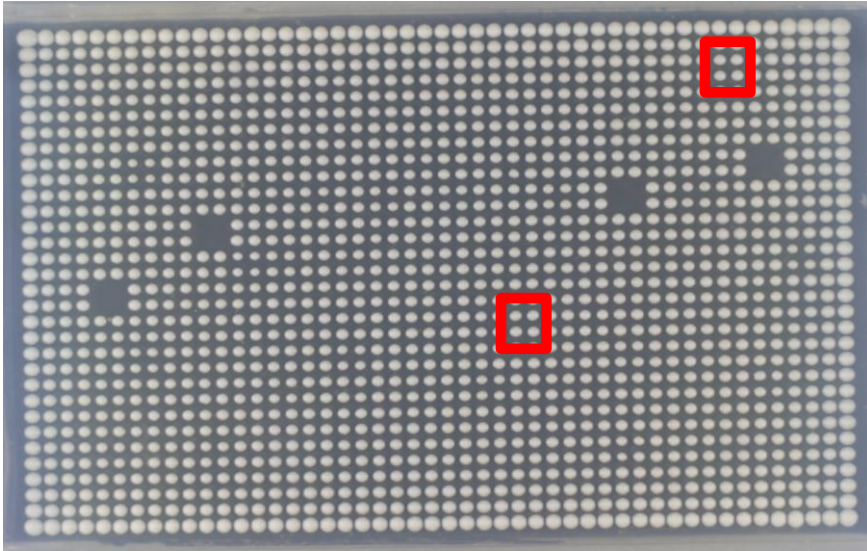


Away game (variable)

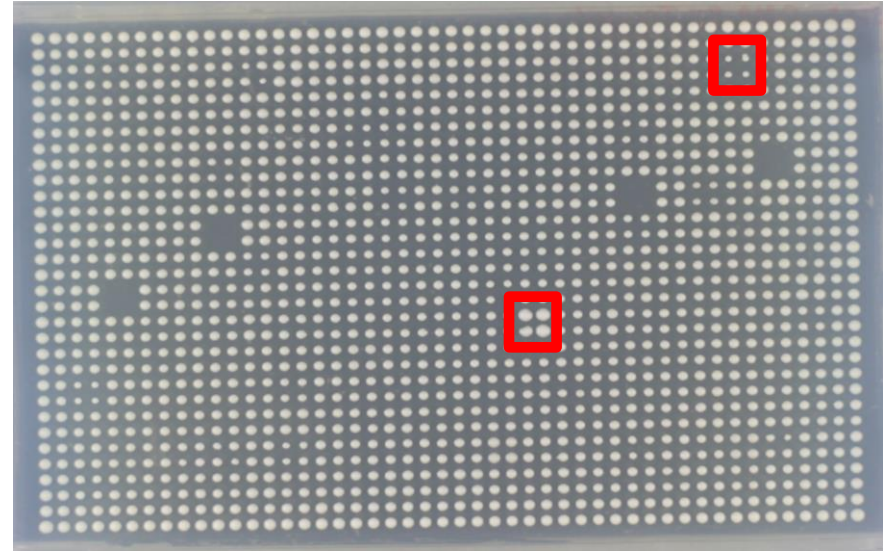


P. insularum and the yeast gene deletion mutant library

Absence of matalafi

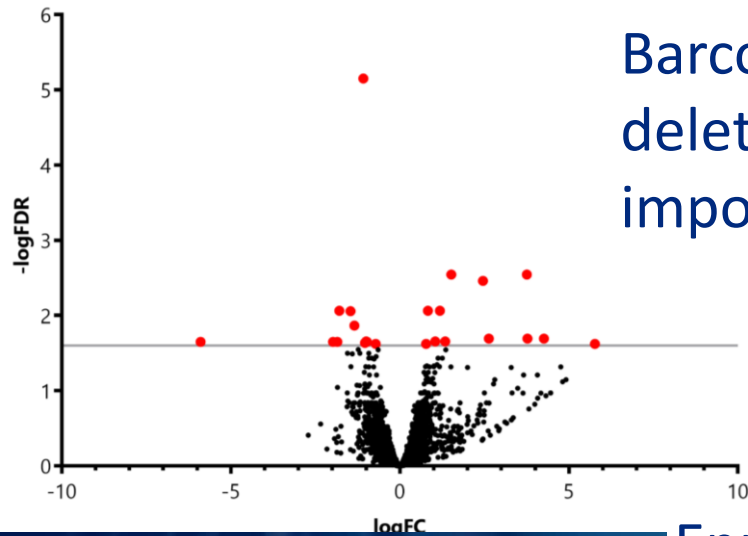


Presence of matalafi



- We examined the yeast gene deletion library in the absence/presence of matalafi homogenate to identify affected mutant strains and implicated genes.
- Growth of each gene deletion strain quantified as a ratio of treated vs untreated.

P. insularum and the yeast gene deletion mutant library



Barcode sequencing of gene deletions identified 23 genes of importance.

THE GENE ONTOLOGY RESOURCE

The mission of the GO Consortium is to develop a comprehensive, **computational model of biological systems**, ranging from the molecular to the organism level, across the multiplicity of species in the tree of life.

The Gene Ontology (GO) knowledgebase is the world's largest source of information on the functions of genes. This knowledge is both human-readable and machine-readable, and is a foundation for computational analysis of large-scale molecular biology and genetics experiments in biomedical research.

Search GO term or Gene Product in AmiGO ...

Any ● Ontology ● Gene Product

GO Enrichment Analysis ?

Powered by PANTHER

Your gene IDs here...

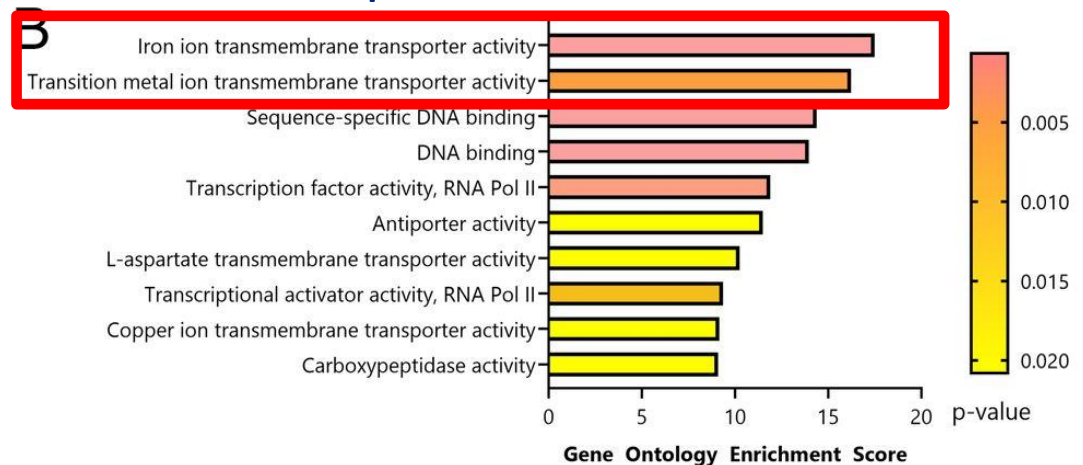
biological process

Homo sapiens

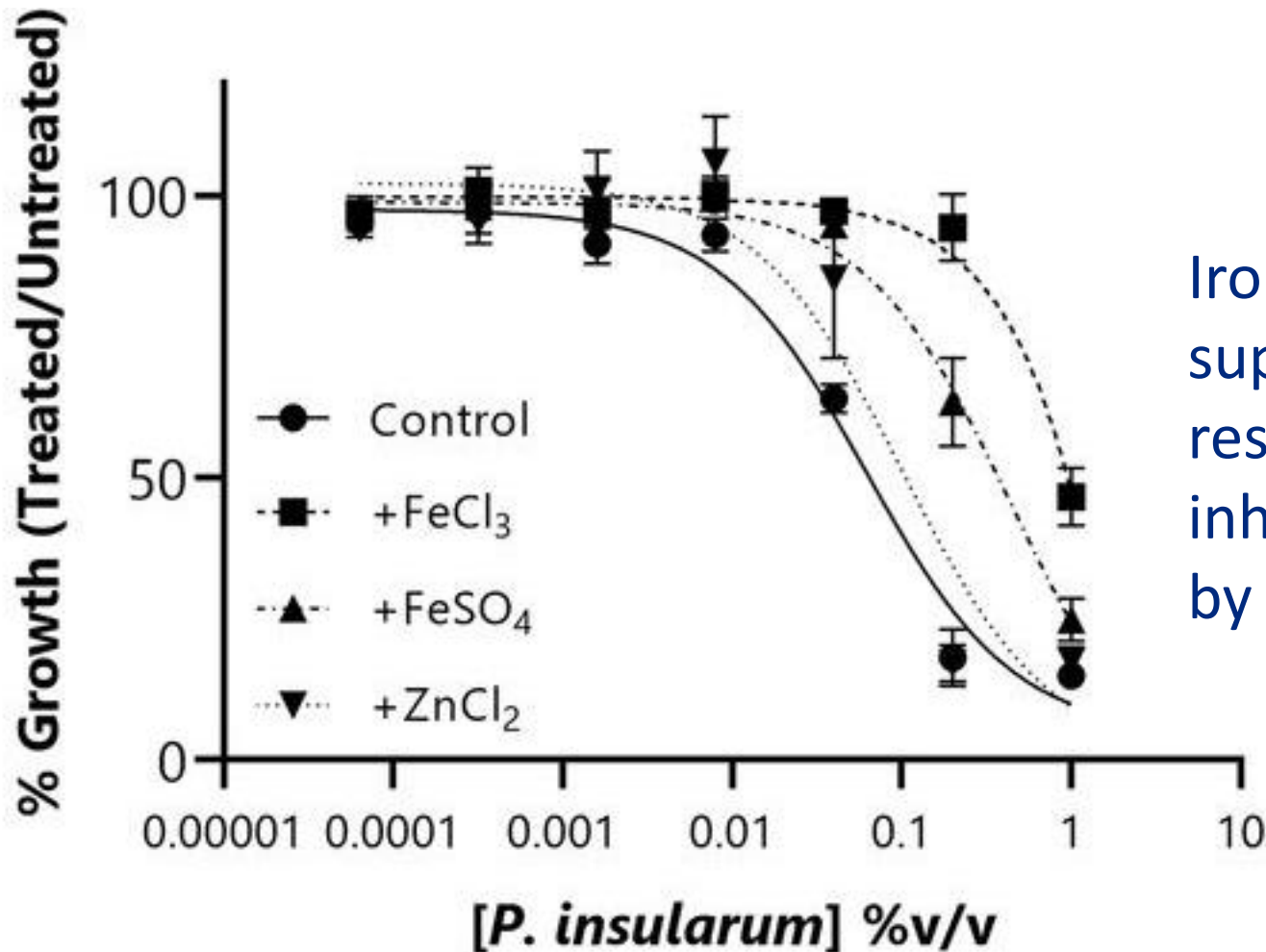
Examples Launch >

Hint: can use UniProt ID/AC, Gene Name, Gene Symbols, MOD IDs

Enrichment analysis revealed importance of metal ion transporters



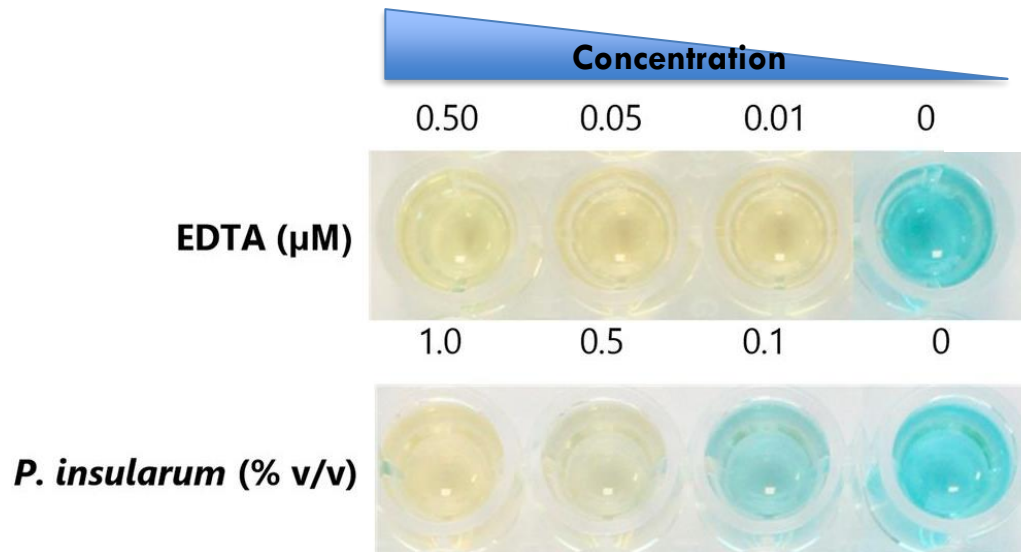
P. insularum and the iron rescue assay



Iron supplementation rescued growth inhibition induced by *P. insularum*.

P. insularum and the iron chelation assay

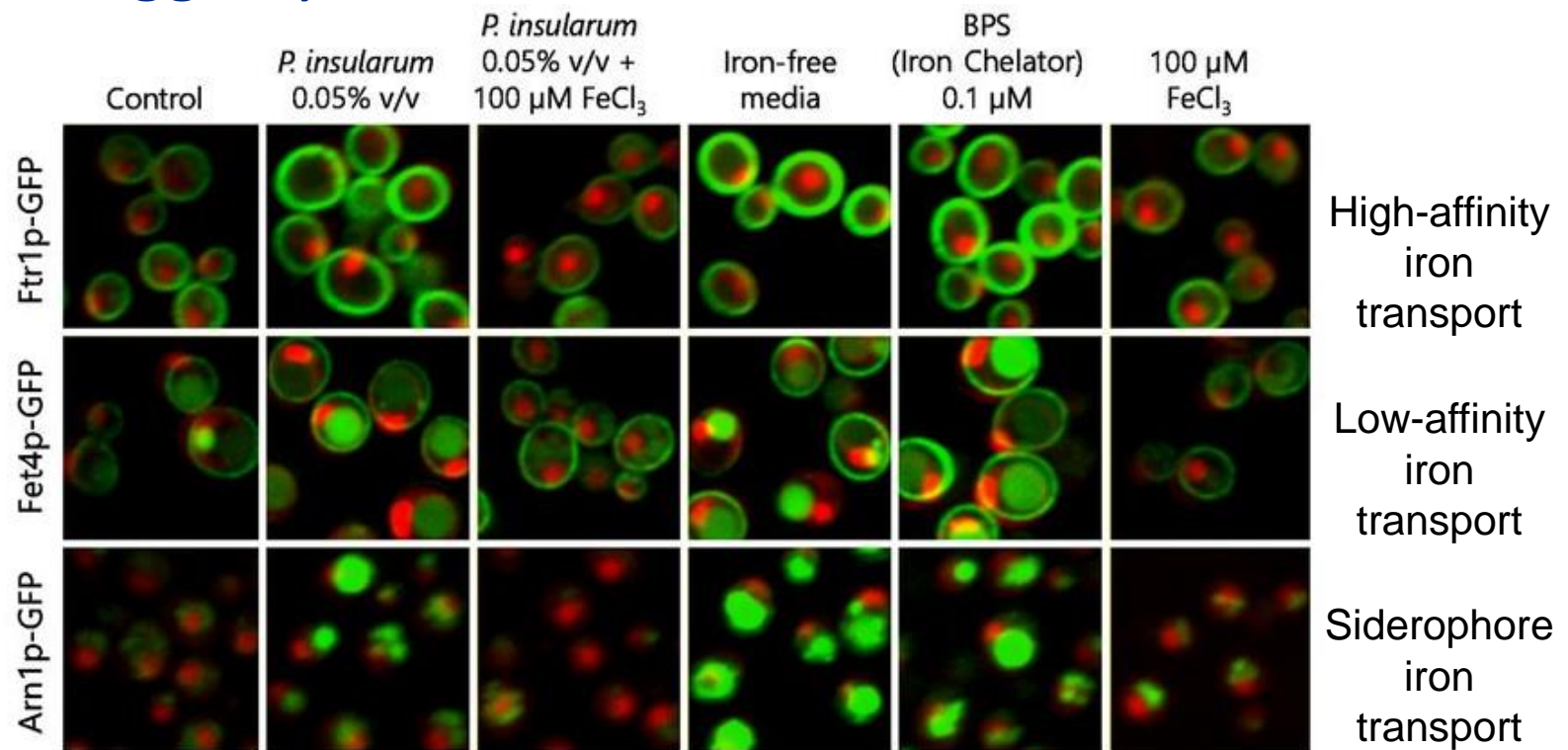
Chrome Azurol S iron chelation assay



P. insularum chelates iron
in a cell-free assay.

P. insularum and the GFP-tagged protein library

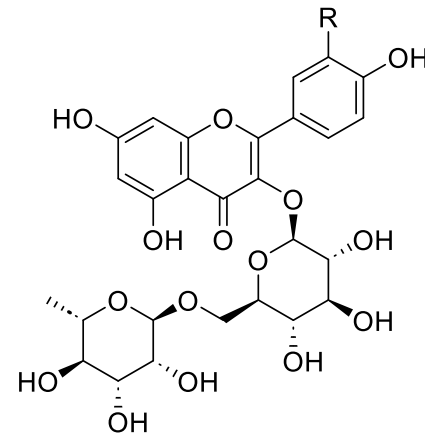
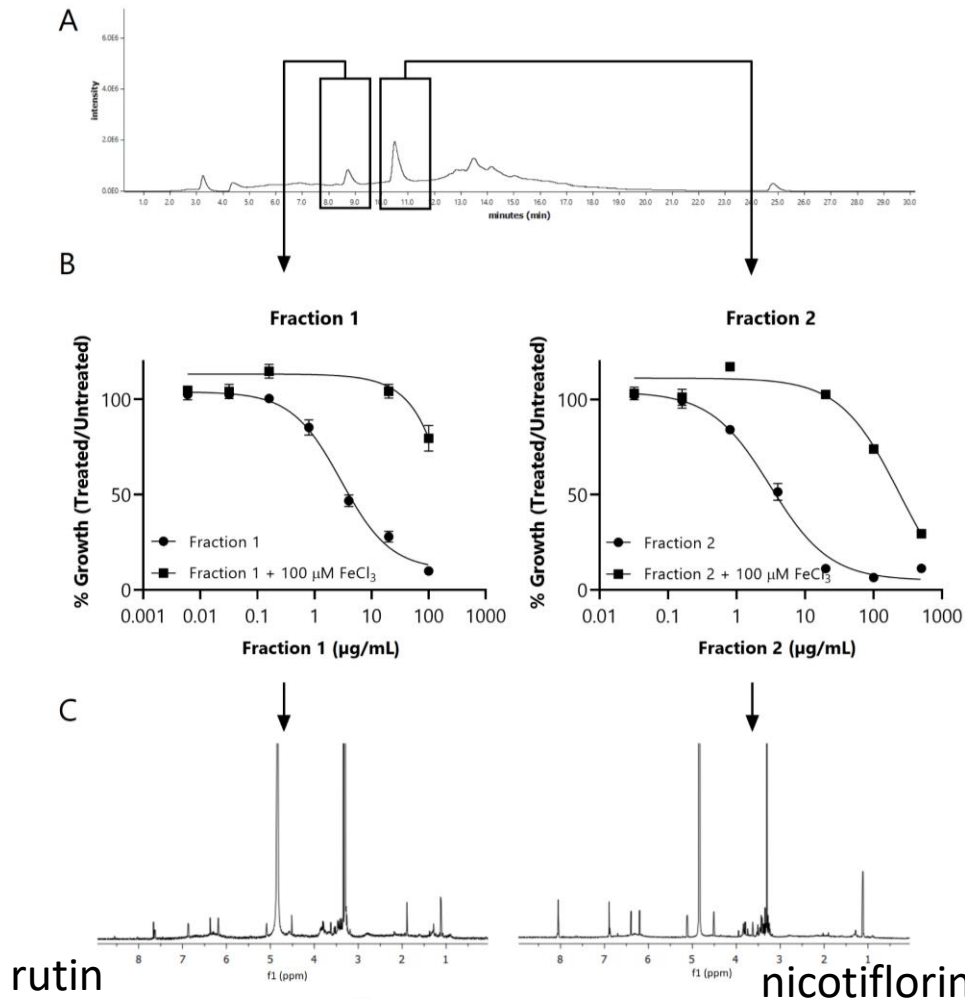
- We measured protein abundance in 84 GFP-tagged yeast strains



- P. insularum* homogenate increases the expression of GFP-tagged iron transport proteins.

Bioassay-guided fractionation of *P. insularum*

- Bioactivity-guided isolation led to identification of rutin and nicotiflorin as iron chelators in matalafi.

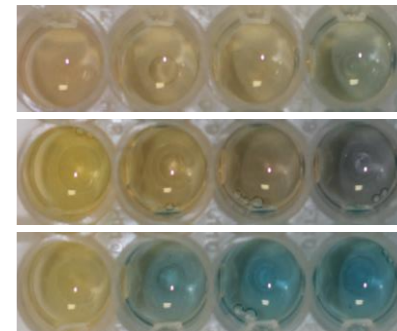


Concentration

EDTA

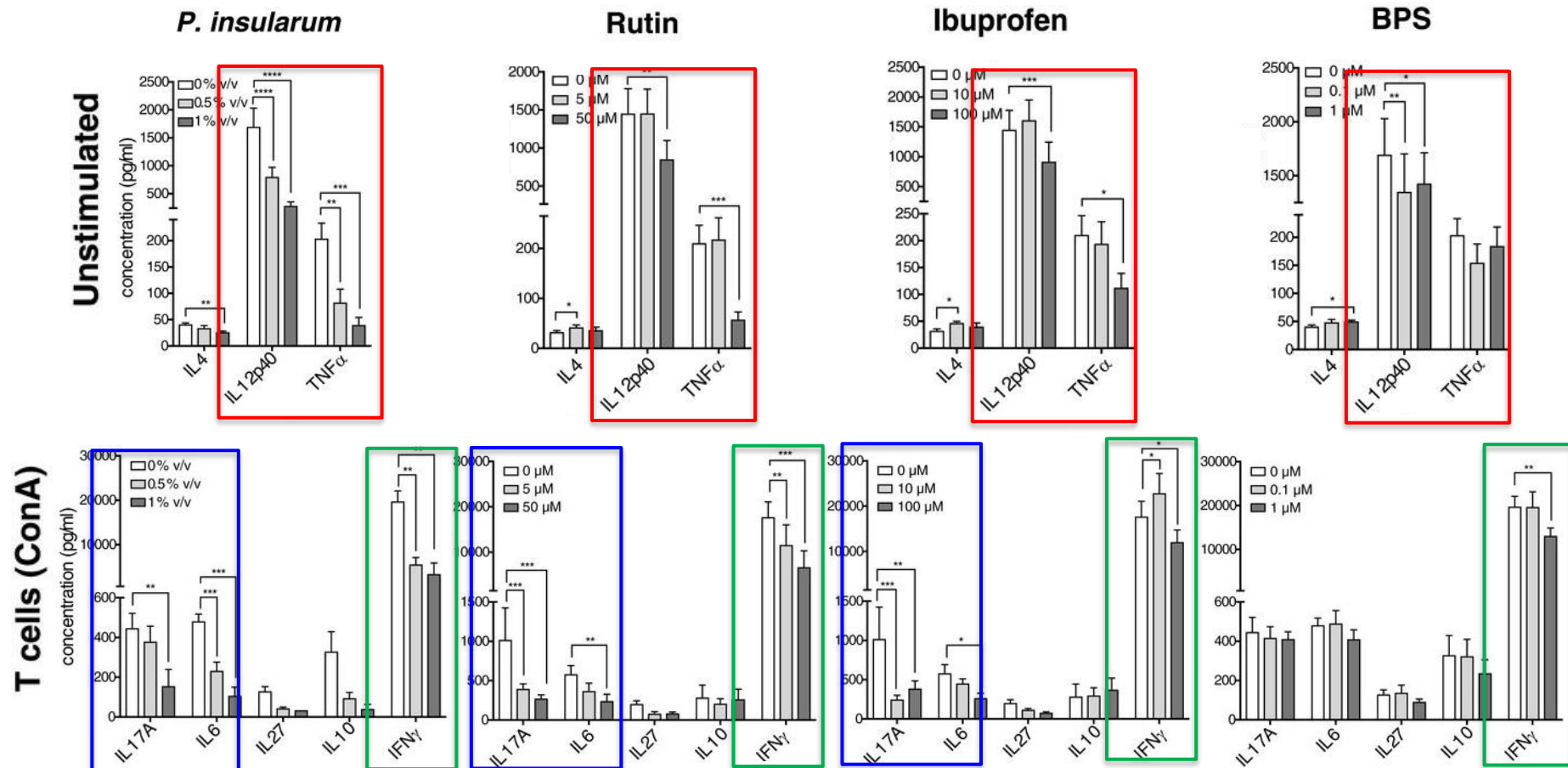
Rutin

Nicotiflorin



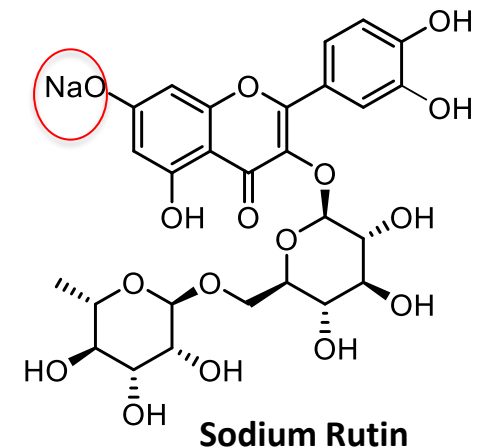
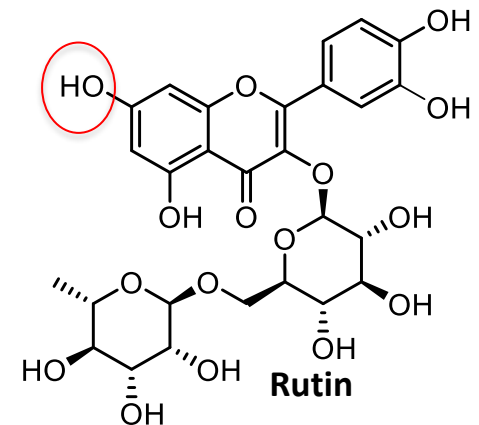
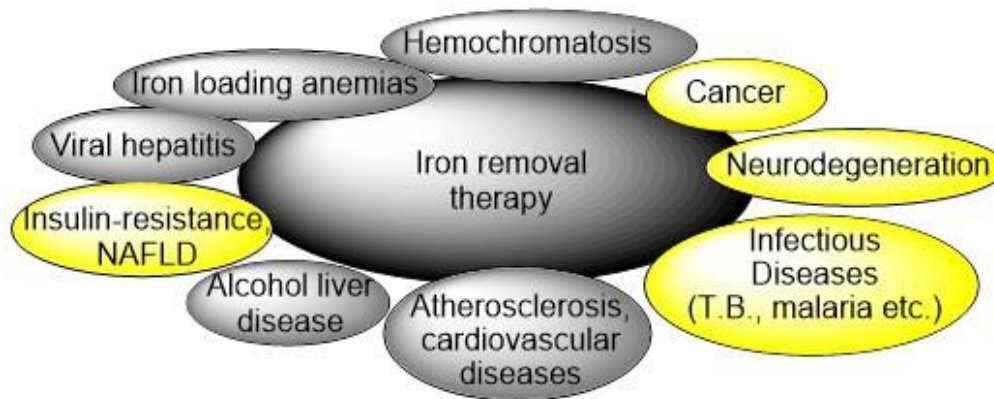
Immunomodulatory properties of *P. insularum* in murine splenocytes

- Anti-inflammatory activity of *P. insularum* homogenate and rutin is comparable to ibuprofen and BPS in murine splenocytes.



Iron-overload disease

- Iron overload is clinically treated by iron chelation therapy



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FOR MOLECULAR BIODISCOVERY



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