

**Negative correlations point to amino acid biosynthesis as a target of phenolic inhibitors. Amino acid biosynthesis is important for growth in the presence of iron chelators and at least one ionic liquid.**

### **Phenolic Acid – Iron Chelator Negative Correlation**

The profile of 22Dipyridyl, an iron chelator, negatively correlates with 3 phenolic acids profiles, Ferulic Acid, Coumaric Acid, and Sinapic Acid. This seems to be driven by deletions that are resistant in phenolic acid by sensitive in 22Dipyridyl. There are 9 genes shared across these three comparisons with that pattern. There is no GO enrichment or obvious functional profile. There are 3 amino acid biosynthesis genes.

SLM6  
ARG4  
LYS12  
RAD57  
TRP1  
YGR022C  
YPT7  
HMI1  
CBC2

### **Phenolic Amide – Iron Chelator Negative Correlation**

The profile of 22Dipyridyl, an iron chelator, negatively correlates with 2 phenolic amide profiles, Feruloyl Amide and Coumaroyl Amide. This, again, is driven largely by deletions that are resistant in phenolic amide but sensitive to iron chelation. There are 40 genes driving the pattern here. There is complete overlap with the 9 genes driving the Phenolic Acid – Iron Chelator relationship.

There is also significant GO enrichment here for a number of amino acid biosynthesis categories.

*alpha-amino acid biosynthetic process* 0.0003346329601981131  
*cellular amino acid biosynthetic process* 0.0005769963417414045  
*alpha-amino acid metabolic process* 0.0008249115763239895  
*cellular amino acid metabolic process* 0.015379793867665652  
*organic acid biosynthetic process* 0.01732071665615443  
*carboxylic acid biosynthetic process* 0.01732071665615443

### **Phenolic Acid – Cationic toxin/IL**

The profiles of EMIMCl (a cationic toxin) and Vanillic Acid (a phenolic acid) are negatively correlated. This is driven by 13 genes that are resistant in phenolic acid by sensitive in EMIMCl. There is almost complete overlap of those genes driving the Phenolic amide- Iron chelator and Phenolic acid – Iron chelator relationships, with only one gene being unique here (AIM22). There is no significant GO enrichment, however, there are again a number of amino acid biosynthesis genes present.

SLM6  
ARG4  
LYS12  
RAD57  
TRP1  
YGR022C  
YPT7  
HMI1

CBC2  
HIS7  
HIS6  
SHE9  
MPO1  
PCP1  
AIM22

### Looking at individual gene tradeoffs

Genes with large logFC dynamic ranges between inhibitors are enriched for deletions with low logFC in 22Dipyridyl and high logFC values in CV (a cationic toxin/IL). The logFC profiles of these inhibitors are not significantly correlated per my prior method, however, there are 31 deletions with a logFC difference greater than 10 between the two inhibitors. Those 31 deletions are enriched for amino acid biosynthesis.

*alpha-amino acid biosynthetic process* 0.001139743362405481  
*alpha-amino acid metabolic process* 0.0017964370541555508  
*cellular amino acid biosynthetic process* 0.0018506936929194053  
*organic acid biosynthetic process* 0.00336433620260306  
*carboxylic acid biosynthetic process* 0.00336433620260306  
*cellular amino acid metabolic process* 0.025521542976634823  
*carboxylic acid metabolic process* 0.03142400037843871  
*oxoacid metabolic process* 0.04856467035499416