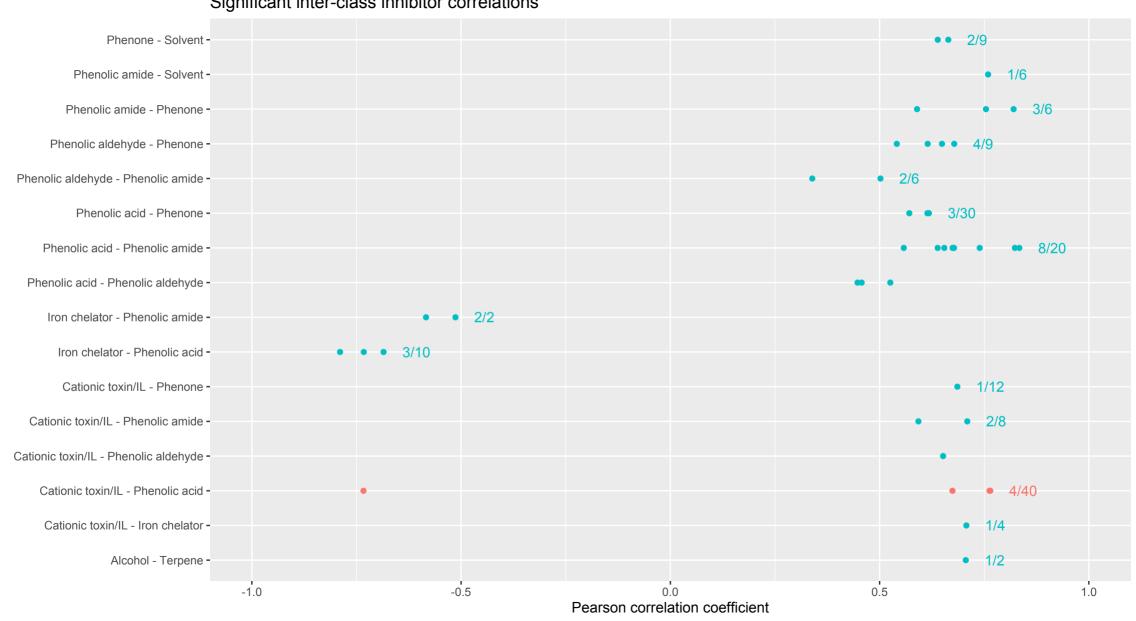
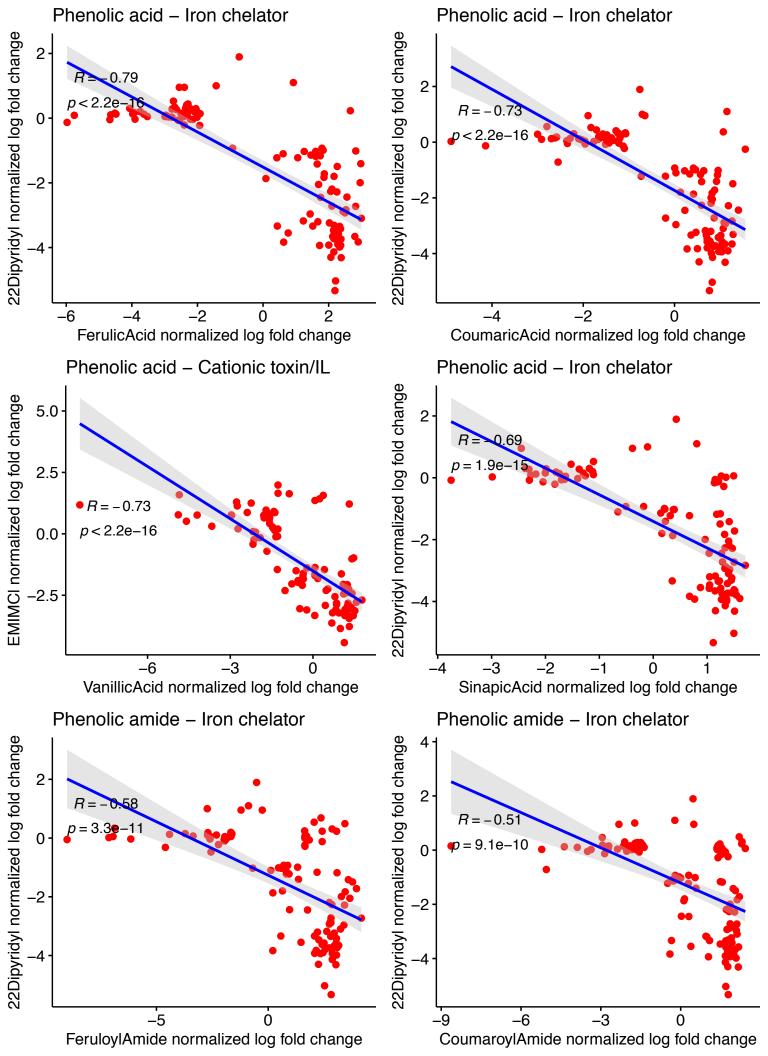
bol	Phenone – Phenone $ 5 - \\ R = 0.88 \\ p < 2.2e-16 $	Phenolic acid – Phenolic acid $ \begin{array}{c} 2.5 \\ R = 0.88 \\ p < 2.2e - 16 \end{array} $
2 Commaricy Comm	-7.5 -5.0 -2.5 0.0 2.5	-2.5- -5.0- -7.5- -4 -3 -2 -1 0 1
Phenolic acid – Phenolic amide R = 0.83 p < 2.2e-16	Phenolic amide – Phenolic acid R = 0.82 p < 2.2e-16	SinapicAcid normalized log fold change Phenone – Phenone 2.5 – R = 0.85 p < 2.2e-16 0.0 – Phenone – Phenone
FerulicAcid normalized log fold change	Dioyola —4 ——————————————————————————————————	-2.5 -5.0 -6 -4 AcetoSyringone normalized log fold change
Phenolic amide – Phenone $R = 0.82$ $p < 2.2e-16$	Phenolic acid – Cationic toxin/IL R=0.76 p<2.2e-16	Phenolic acid – Phenolic acid $R = 0.82$ $p < 2.2e - 16$
Phenolic acid – Cationic toxin/IL	Phenolic acid – Iron chelator	Phenolic amide – Phenolic amide
10 - R = 0.76 p < 2.2e – 16	R = -0.79 $p < 2.2e - 16$ R = -0.79 $p < 2.2e - 16$	3 - R = 0.76 p < 2.2e - 16
Phenolic amide – Solvent R = 0.76	Phenolic acid – Phenolic amide R = 0.74	Phenolic amide – Phenone 2.5 - R = 0.75
2 - p < 2.2e-16 egual 2 - p < 2.2e-16 p < 2.2e-16	p < 2.2e-16 p < 2.2e-16 p < 2.2e-16	DOUBLE -2.55.05
-5 FeruloylAmide normalized log fold change Phenolic amide – Cationic toxin/IL $10 - R = 0.71$ $p < 2.2e - 16$		-7.5 -5 FeruloylAmide normalized log fold change Phenolic acid – Phenolic acid $R = 0.76$ $p < 2.2e - 16$
CV normalized log fold change	B = -0.73 p < 2.2e-16 P = -0.73 p < 2.2e-16	Do 0 2
FeruloylAmide normalized log fold change Cationic toxin/IL – Cationic toxin/IL 2 R = 0.85 p < 2.2e-16	CoumaricAcid normalized log fold change Phenolic acid – Cationic toxin/IL 10- R = 0.67 p < 2.2e-16	VanillicAcid normalized log fold change Phenolic aldehyde – Phenolic aldehyde R = 0.76 p < 2.2e-16
BMIMCI normalized log for	op log fold of the state of the	0.0- -2.5- -5.0-
EMIMCI normalized log fold change Phenolic acid – Cationic toxin/IL 5.0- But a control of the	VanillicAcid normalized log fold change Cationic toxin/IL – Phenone R = 0.69 p < 2.2e-16	Vanillin normalized log fold change Phenolic acid – Phenolic amide R = 0.67 p < 2.2e-16
DATE DOWN DATE DOWN DATE DATE DATE DATE DATE DATE DATE DATE	OCV normalized log fold change	VanillicAcid normalized log fold change
Terpene – Alcohol 3 - R = 0.71 p < 2.2e-16	Phenolic acid – Phenolic acid $R = 0.71$ $p < 2.2e - 16$	Phenolic aldehyde – Cationic toxin/IL 15 10 R = 0.65 p < 2.2e-16
Outpings -6 -10 -5 0 5 MBO normalized log fold change Phenolic acid – Phenolic amide	VanillicAcid normalized log fold change Phenolic aldehyde – Phenolic aldehyde	Vanillin normalized log fold change Phenone – Phenone
R = 0.68 p < 2.2e-16	ormalized Ic	$\begin{array}{cccccccccccccccccccccccccccccccccccc$
Phenolic amide – Phenolic acid 2.5 - R=0.65	Solvent – Phenone A B = 0.66	-5.0 -7.5 -5.0 Acetovanillone normalized log fold change Cationic toxin/IL – Cationic toxin/IL
p = 5.1e-16 p = 5.1e-16 p = 5.1e-16	p = 5.9e-16 p = 5.9e-16 p = 5.9e-16	10- R = 0.64 p = 6.1e-16
$ \begin{array}{c} -7.5 \\ -5 \\ \text{FeruloylAmide normalized log fold change} \end{array} $ Phenolic amide – Phenolic acid $ \begin{array}{c} R = 0.64 \\ p = 1.9e-15 \end{array} $	DMSO normalized log fold change Phenolic aldehyde – Phenone B = 0.65	-5.0 -2.5 0.0 2.5 5.0 NAO normalized log fold change Phenolic acid – Iron chelator $2 R = -0.69$ $p = 1.9e - 15$
CommaricAcid normalized log fold of the command of	AcetoSyringon normalized log foldon per 1.9e-15	2 - 2
FeruloylAmide normalized log fold change Cationic toxin/IL – Iron chelator Page 1.71 Page 2.3e–15	Vanillin normalized log fold change Phenolic acid – Phenone $R = 0.62$ $p = 3.8e-15$	$-4 \qquad -3 \qquad -2 \qquad -1 \qquad 0 \qquad 1$ SinapicAcid normalized log fold change Phenolic amide – Cationic toxin/IL $R = 0.59$ $p = 9.7e-15$
Sol paziladi –4 – – – – – – – – – – – – – – – – – –	Poetro Po	
EMIMCI normalized log fold change Phenolic amide – Phenone R = 0.59 p = 5.4e-14	Phenolic acid – Phenone R = 0.61 p = 8.6e-14	CoumaroylAmide normalized log fold change Phenolic acid – Phenone R = 0.57 p = 1.3e-12
AcetoSylingone more lived leg feld change	Phonelie aldebude. Phonene	-4 -6 CoumaricAcid normalized log fold change
CoumaroylAmide normalized log fold change Phenolic acid – Phenolic acid	Phenolic aldehyde – Phenone R=0.61	Phenolic acid – Phenolic amide
CoumaroylAmide normalized log fold change Phenolic acid – Phenolic acid R = 0.64 p = 2e-11	2- R= 0.61 p= 2.6e-11	R = 0.56 $p = 3e - 11$
Phenolic acid – Phenolic acid $R = 0.64$ $p = 2e-11$	p=2.6e-11 p=2.6e-11 p=2.6e-11 Vanillin normalized log fold change Solvent – Phenone	R = 0.56 $p = 3e-11$
Phenolic acid – Phenolic acid $R = 0.64$ $p = 2e - 11$ Phenolic acid – Phenolic acid $R = 0.64$ $p = 2e - 11$ Vanillic Acid normalized log fold change Phenolic amide – Iron chelator $R = 0.58$ $P = 3.3e - 11$	p=2.6e-11 p=2.6e-11 p=2.6e-11 p=2.6e-11 p=2.6e-11 vanillin normalized log told change Solvent – Phenone Solvent – Phenone 2.5	$R = 0.56$ $\rho = 3e-11$ -6 VanillicAcid normalized log fold change
Phenolic acid — Phenolic acid R = 0.64 p = 2e-11 Vanillic Acid normalized log fold change Phenolic amide — Iron chelator Phenolic amide — Iron chelator Phenolic addehyde — Phenolic acid Phenolic aldehyde — Phenolic acid	The top of the property of th	Phenolic aldehyde – Phenolic amide Phenolic aldehyde – Phenolic amide Phenolic aldehyde – Phenolic amide
Phenolic acid — Phenolic acid R = 0.64 p = 2e-11 Phenolic amide — Iron chelator Phenolic addehyde — Phenolic acid	Degraph of the property of the	Phenolic aldehyde – Phenolic amide Phenolic aldehyde – Phenolic amide
Phenolic acid – Phenolic acid #=0.84 p=20-11 Phenolic amide – Iron chelator Phenolic amide – Iron chelator Phenolic addehyde – Phenolic acid Phenolic aldehyde – Phenolic acid #=0.53 p=3.49-10 Aldehyde – Aldehyde Aldehyde – Aldehyde #=0.5 p=2.38-90	$\rho = 2.66 - 11$ $\rho = 2.66 - 11$ -2 $\sqrt{2}$ $\sqrt{2}$ $\sqrt{2}$ $\sqrt{2}$ $\sqrt{2}$ $\sqrt{2}$ $\sqrt{2}$ $\sqrt{3}$ $\sqrt{4}$ $\sqrt{2}$ $\sqrt{4}$ $\sqrt{2}$ $\sqrt{4}$	Phenolic aldehyde – Phenolic amide
Phenolic acid – Phenolic acid \$ -0.64 \$ -2.2-11 T = -0.55 \$ -2.3-11 Phenolic article – Iron chelator Feruloy/Amide normalized log fold change Phenolic aldehyde – Phenolic acid # -0.53 \$ -3.3-10 Addehyde – Aldehyde Aldehyde – Aldehyde Aldehyde – Aldehyde # -0.53 # -0.5	Solvent - Phenone Solvent - Phenone Solvent - Phenone B = 0.64 p = 1e-10 DMSO normalized log told change Phenolic amide - Iron chelator The post of the pos	Phenolic aldehyde – Phenolic amide Phenolic aldehyde – Phenolic acid M=0.45 p=2e-07
Phenolic addehyde – Phenolic add Phenolic addehyde –	Solvent - Phenonic and e- Iron chelator Phenolic aldehyde - Phenone The solvent - Phenonic and the solvent - Phenolic and the solvent - Phenonic and the s	Phenolic aldehyde – Phenolic amide Phenolic aldehyde – Phenolic acid
Phenoic add Phenoic and Phenoi	Solvent – Phenone 23	Phenolic aldehyde – Phenolic amide
Phenolic and Phenolic acid Phenolic arids - Iron chelator	Solvent - Phenone Solvent - Phenone Phenolic amice - Iron chelator Annual Solvent - Phenone The Camerophysic rumalized by but change Phenolic amice - Iron chelator Annual Solvent - Phenone The Camerophysic rumalized by but change Phenolic addenyde - Phenone Annual Solvent - Phenone The Camerophysic rumalized by but change Phenolic addenyde - Phenone The Camerophysic rumalized by but change Phenolic addenyde - Phenone The Camerophysic rumalized by but change Phenolic addenyde - Phenone The Camerophysic rumalized by but change Phenolic addenyde - Phenone The Camerophysic rumalized by but change Phenolic addenyde - Phenone The Camerophysic rumalized by but change Phenolic addenyde - Phenone The Camerophysic rumalized by but change	Phenolic aldehyde – Phenolic amide

Significant inter-class inhibitor correlations





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, Feruloy 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 0.008249115763239895 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 process0.0017964370541555508 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

