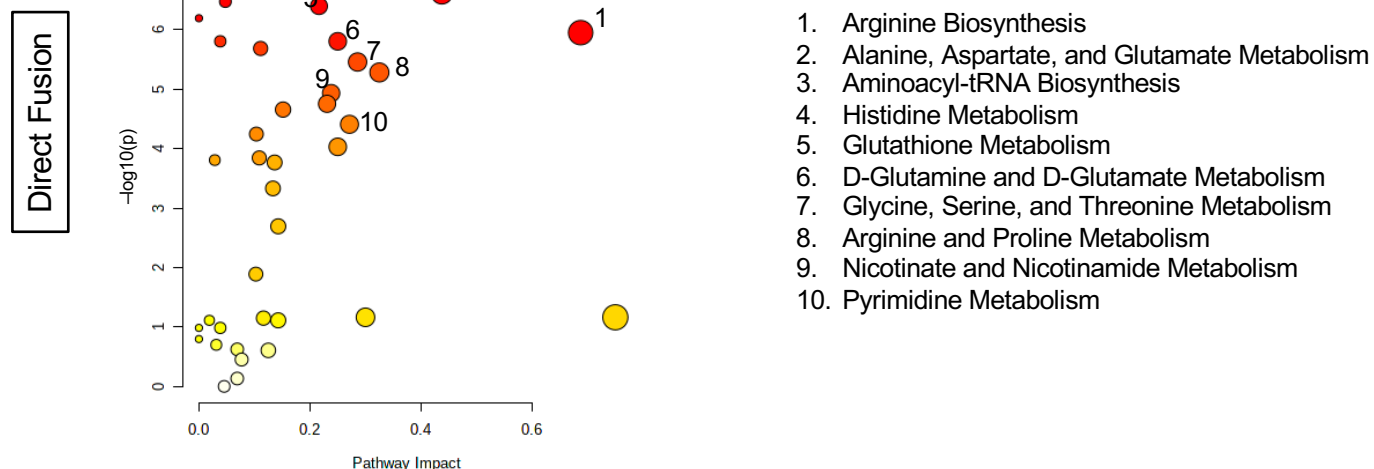
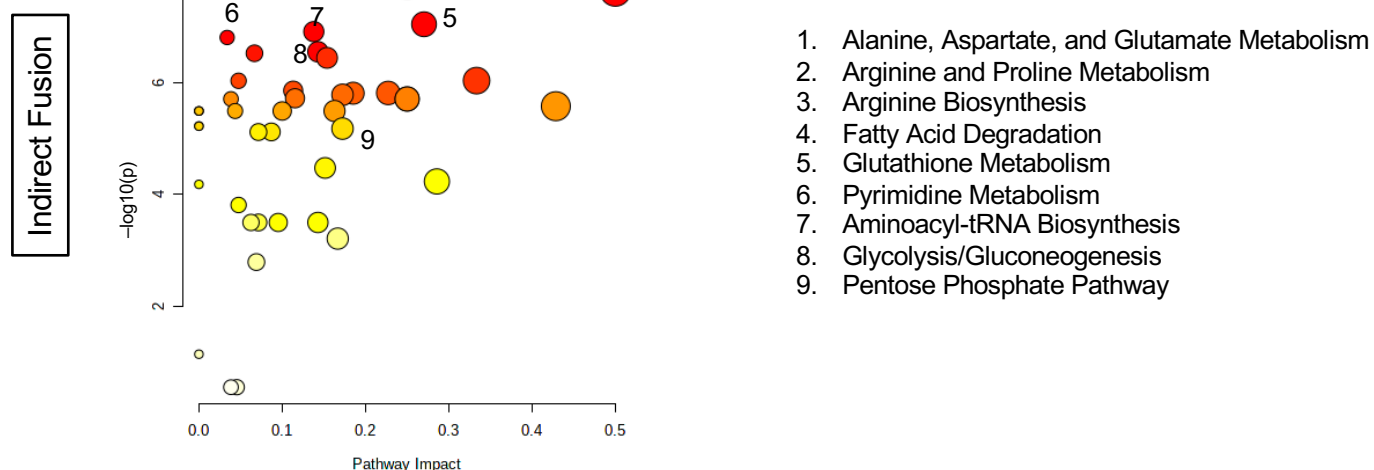


**Figure S1.** Western blot analysis confirms direct induction of mitochondrial fusion occurs independent of Drp1 expression. **(A)** tetracycline-inducible Mfn2, **(B)** Drp1 knockout, and **(C)** leflunomide treated KPC cells were probed for Mfn2, Drp1, and Vinculin as a loading control.

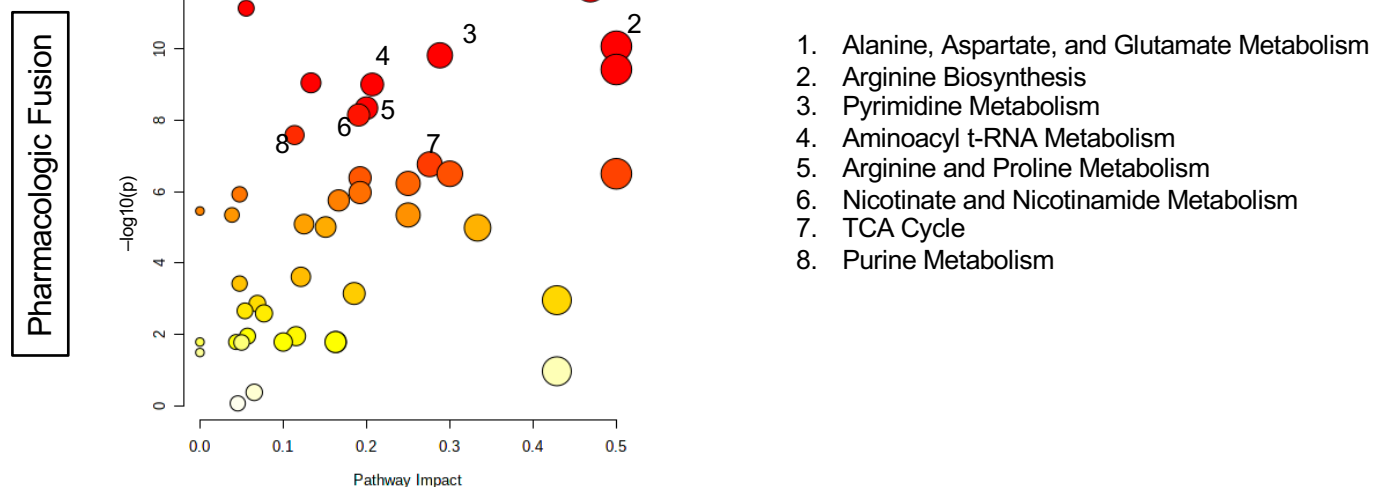
### Tet-On Mfn2 Pathway Analysis



### sgDrp1 Pathway Analysis



### Lef Pathway Analysis

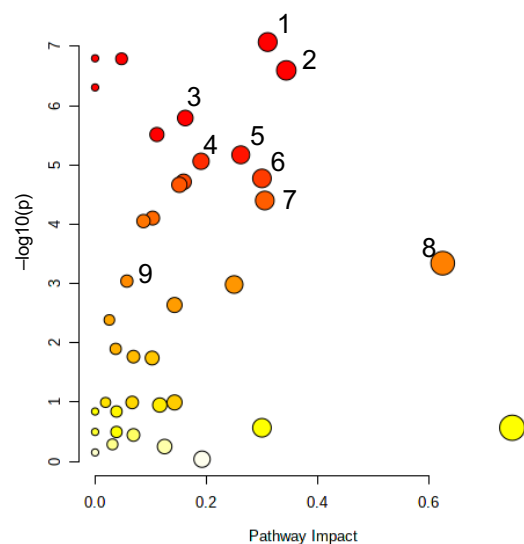


**Figure S2.** Pathway analysis generated from discriminant metabolites identified by univariate Student's *t*-test.



### Tet-On Mfn2 Pathway Analysis

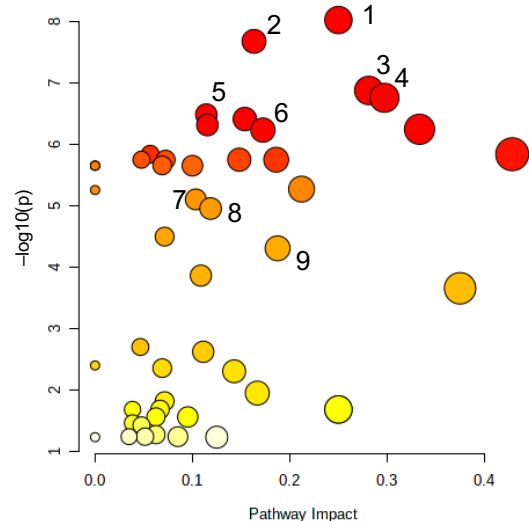
Direct Fusion



1. Alanine, Aspartate, and Glutamate Metabolism
2. Arginine Biosynthesis
3. Pyrimidine Metabolism
4. Aminoacyl t-RNA Metabolism
5. Arginine and Proline Metabolism
6. Nicotinate and Nicotinamide Metabolism
7. TCA Cycle
8. Purine Metabolism

### sgDrp1 Pathway Analysis

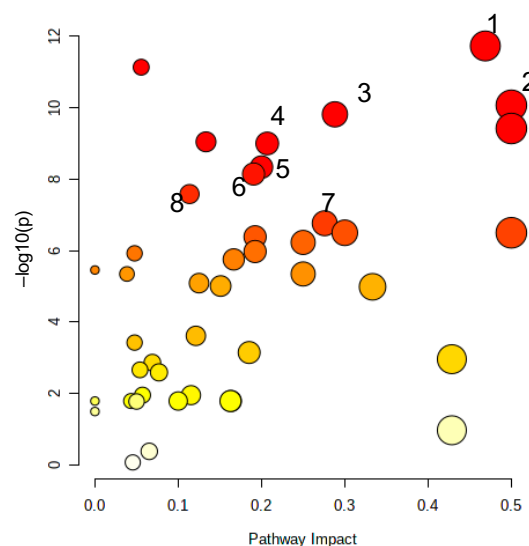
Indirect Fusion



1. Arginine and Proline Metabolism
2. Fatty Acid Degradation
3. Alanine, Aspartate, and Glutamate Metabolism
4. Glutathione Metabolism
5. Glycolysis/Gluconeogenesis
6. TCA Cycle
7. Pentose Phosphate Pathway
8. Pyrimidine Metabolism
9. Arginine Biosynthesis

### Lef Pathway Analysis

Pharmacologic Fusion

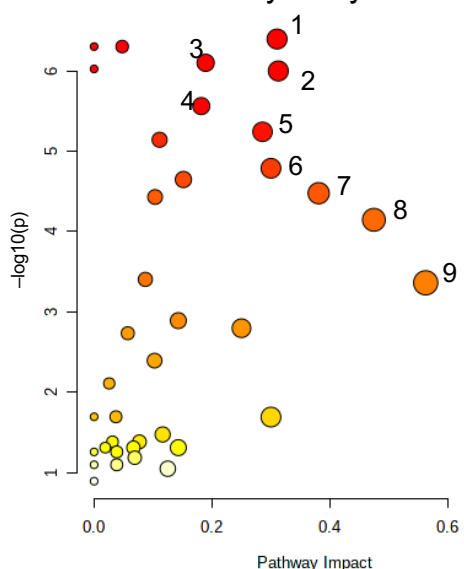


1. Alanine, Aspartate, and Glutamate Metabolism
2. Arginine Biosynthesis
3. Pyrimidine Metabolism
4. Aminoacyl t-RNA Metabolism
5. Arginine and Proline Metabolism
6. Nicotinate and Nicotinamide Metabolism
7. TCA Cycle
8. Purine Metabolism

**Figure S3.** Pathway analysis generated from discriminant metabolites identified by SAM.

### Tet-On Mfn2 Pathway Analysis

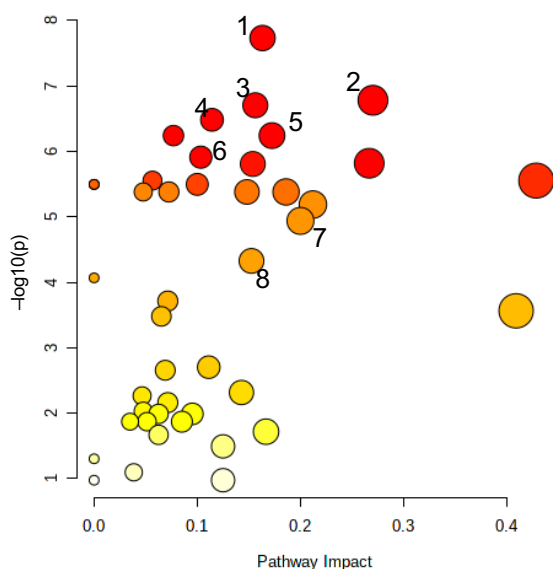
Direct Fusion



1. Aminoacyl-tRNA Biosynthesis
2. Alanine, Aspartate, and Glutamate Metabolism
3. Glutathione Metabolism
4. Purine Metabolism
5. Glycine, Serine, and Threonine Metabolism
6. Arginine and Proline Metabolism
7. Nicotinate and Nicotinamide Metabolism
8. Pyrimidine Metabolism
9. Arginine Biosynthesis

### sgDrp1 Pathway Analysis

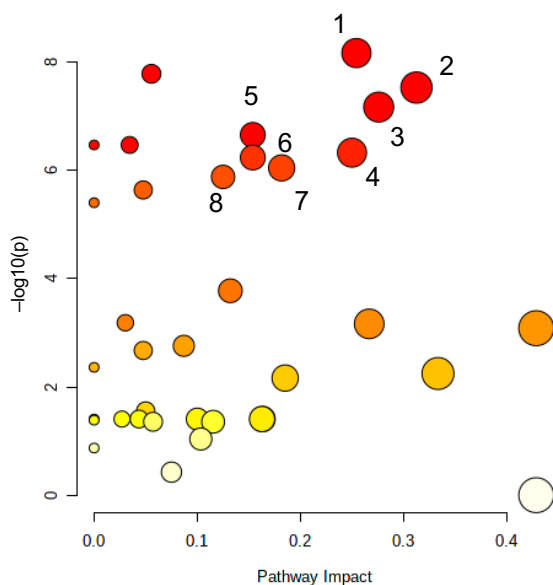
Indirect Fusion



1. Fatty Acid Degradation
2. Glutathione Metabolism
3. Alanine, Aspartate, and Glutamate Metabolism
4. Glycolysis/Gluconeogenesis
5. TCA Cycle
6. Pentose Phosphate Pathway
7. Arginine and Proline Metabolism
8. Pyrimidine Metabolism

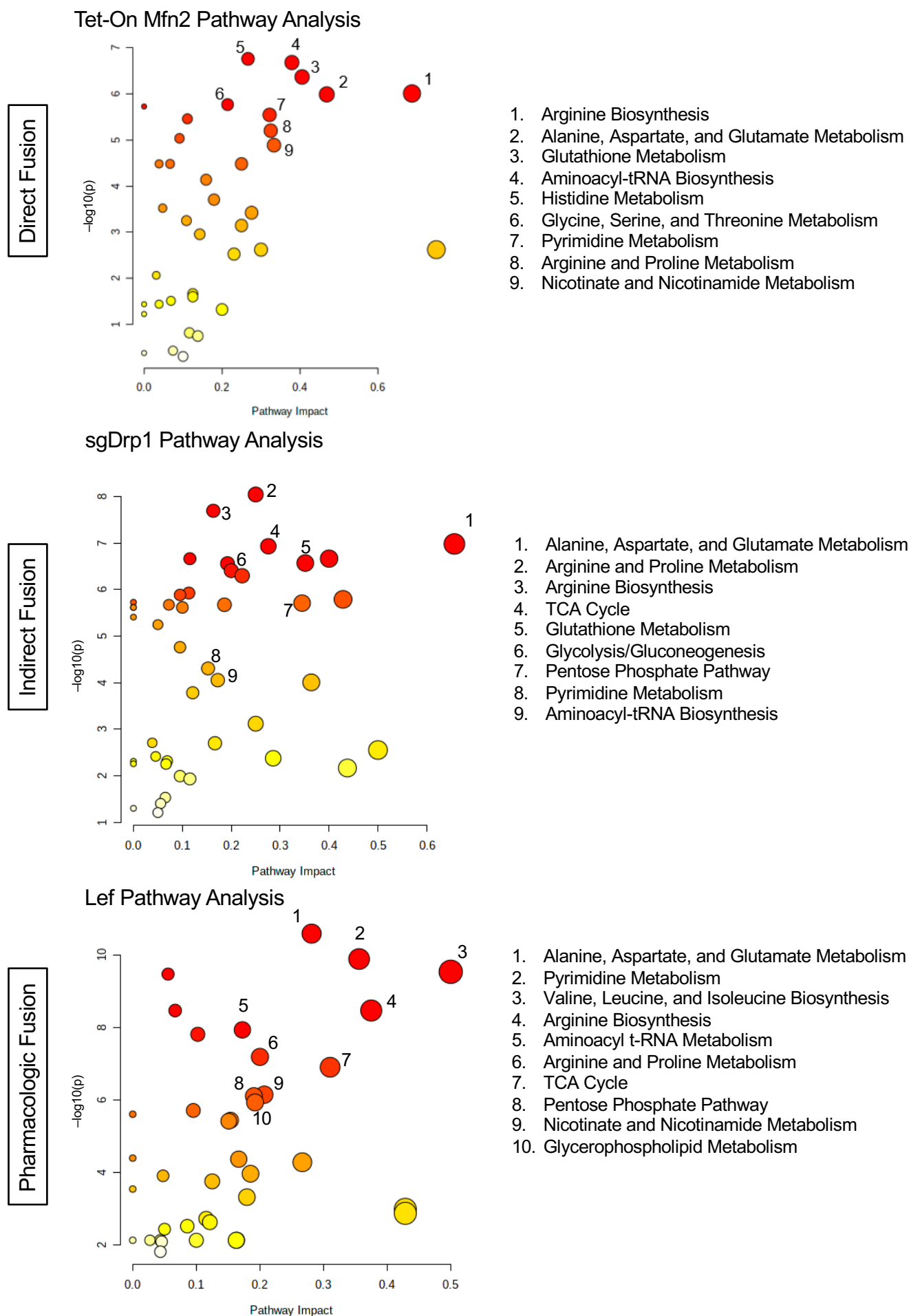
### Lef Pathway Analysis

Pharmacologic Fusion

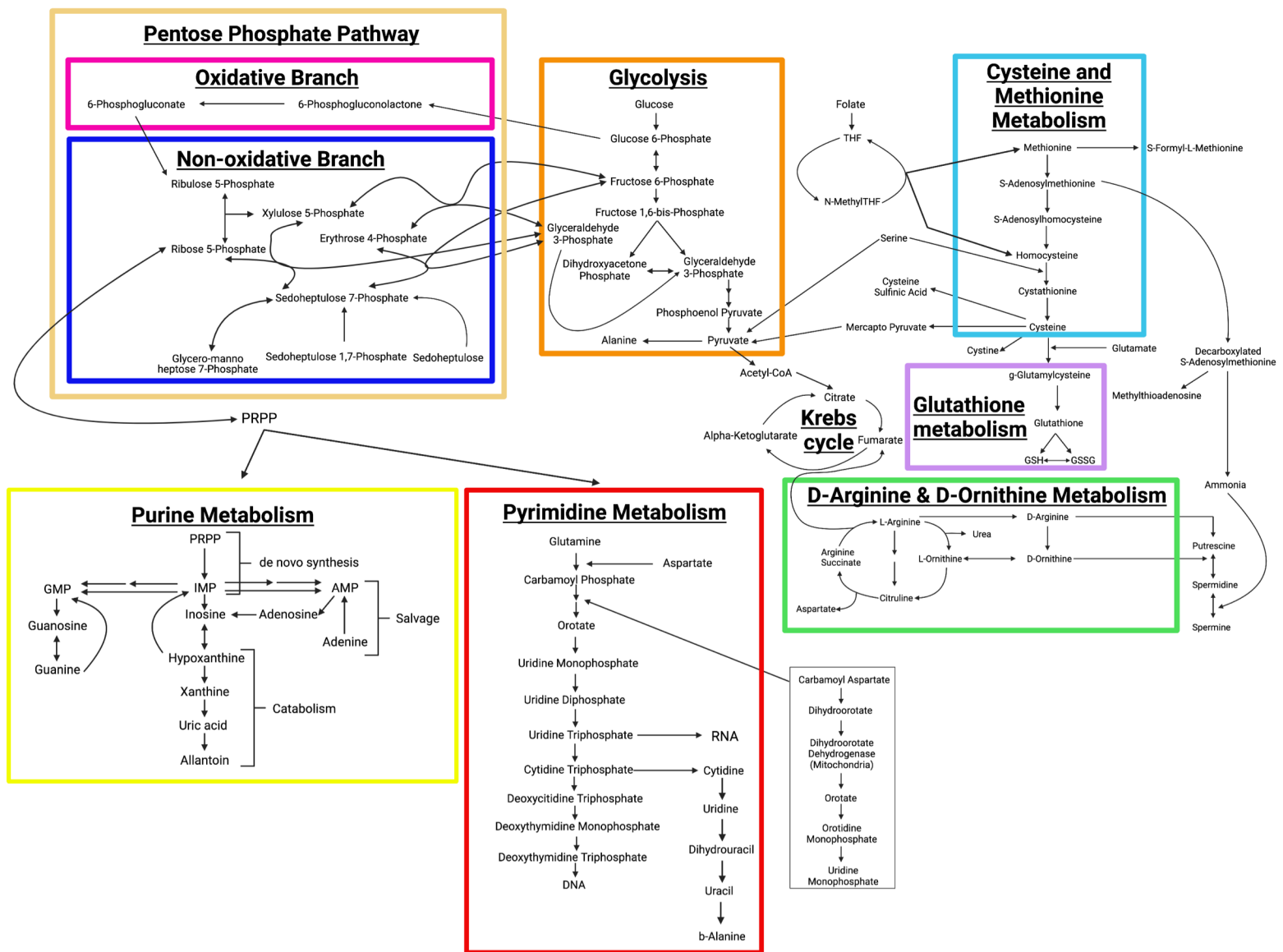


1. Pyrimidine Metabolism
2. Alanine, Aspartate, and Glutamate Metabolism
3. TCA Cycle
4. Valine, Leucine, and Isoleucine Biosynthesis
5. Glyoxylate and Dicarboxylate Metabolism
6. Glycerophospholipid Metabolism
7. Purine Metabolism
8. Arginine Biosynthesis

**Figure S4.** Pathway analysis generated from discriminant metabolites identified by PLS-DA VIP.



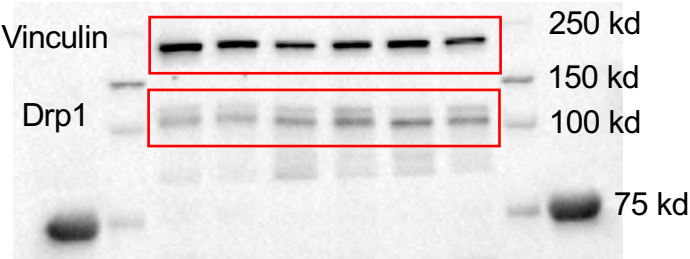
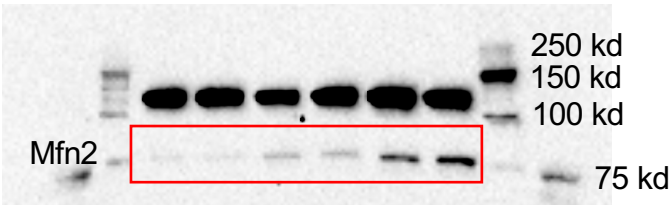
**Figure S5.** Pathway analysis generated from discriminant metabolites identified by RF classification.



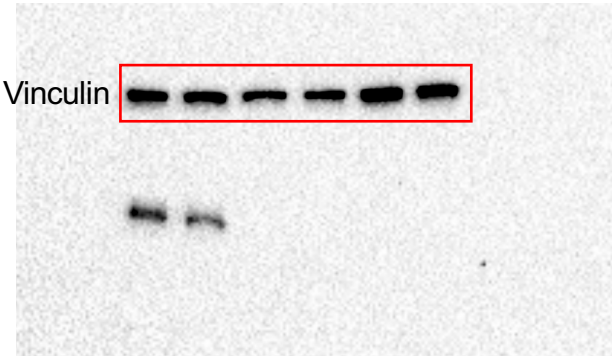
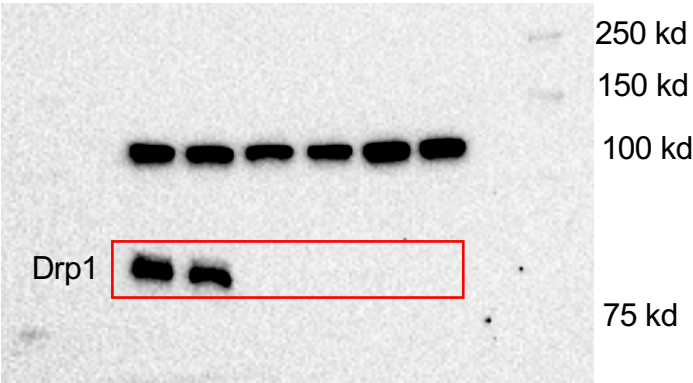
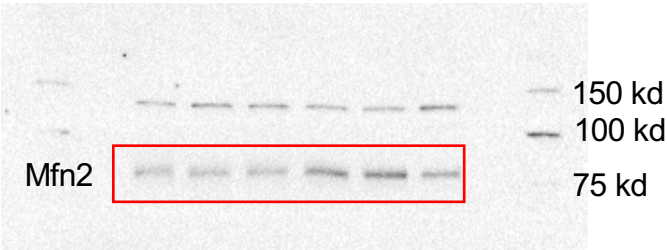
**Figure S6.** Significantly altered metabolic pathways in fusion induced KPC cells interconnected. Top 8 altered metabolic pathways identified from our overlapped discriminant metabolite set in fused KPC cells are mapped to show their interdependent relationships among each other.

**Figure S7.** Full Uncut Western Blots

From Figure S6A



From Figure S6B



From Figure S6C

