

Irradiation causes alterations of polyamine, purine and sulfur metabolism in red blood cells and multiple organs

**Micaela Kalani Roy,^{1,#} Francesca La Carpia,^{2,#} Francesca Cendali,¹ Sebastian Fernando², Chiara Moriconi²,
Boguslaw S. Wojczyk², Lin Wang², Travis Nemkov,¹ Eldad A Hod,² Angelo D'Alessandro^{1*}**

¹ Department of Biochemistry and Molecular Genetics, University of Colorado Denver – Anschutz Medical Campus,
Aurora, CO, USA 80045

² Columbia University Irving Medical Center, New York, NY, USA 10032

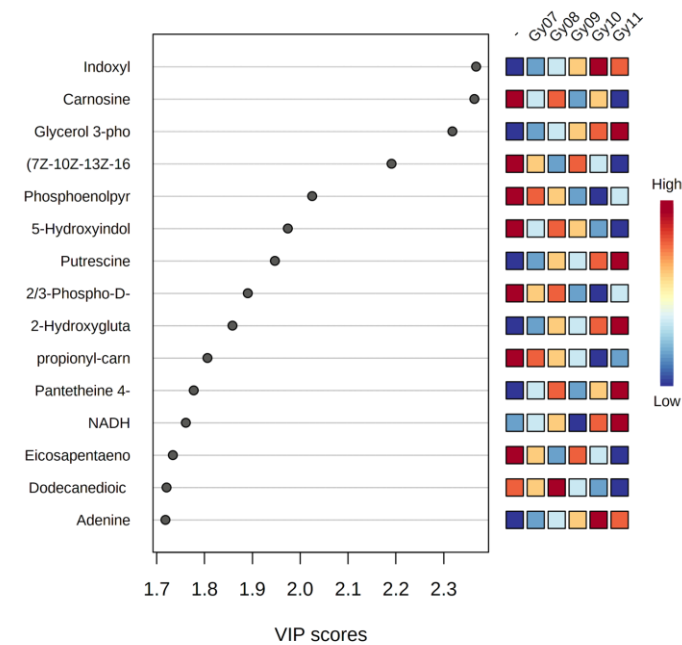
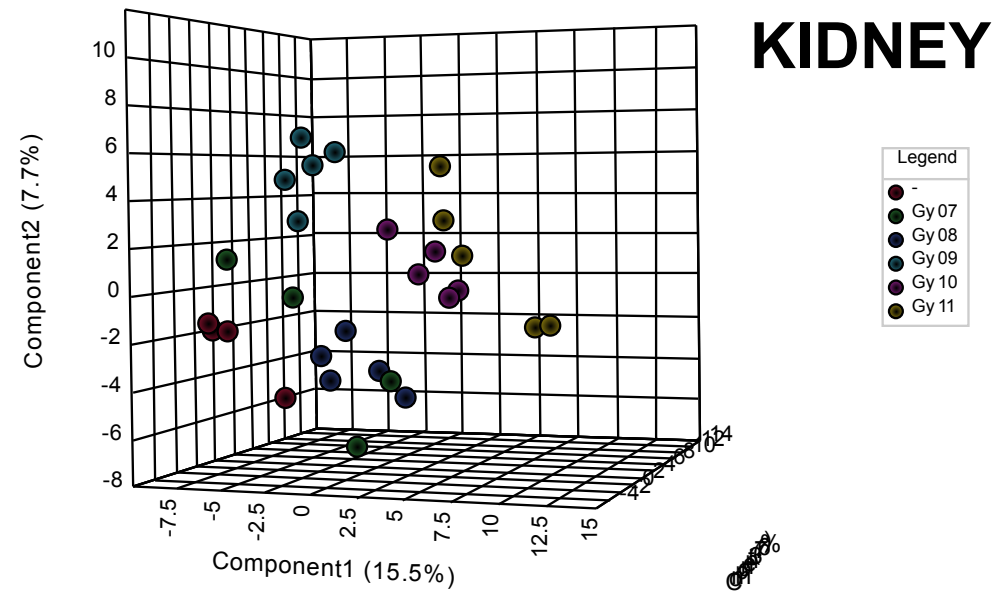
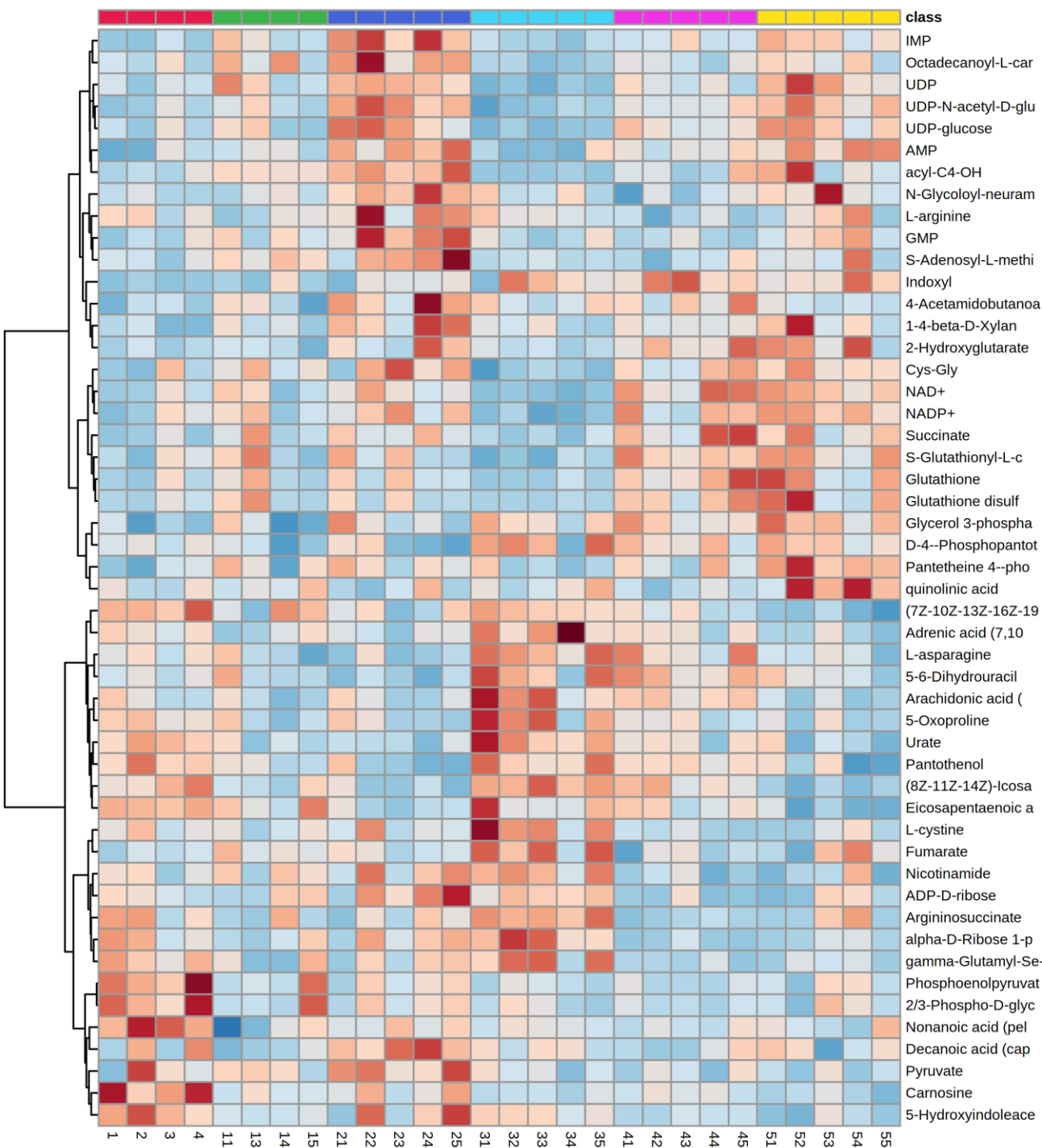
These authors contributed equally and share the first authorship

***Corresponding authors:**

Angelo D'Alessandro, PhD
Department of Biochemistry and Molecular Genetics
University of Colorado Anschutz Medical Campus
12801 East 17th Ave., Aurora, CO 80045
Phone # 303-724-0096
E-mail: angelo.dalessandro@ucdenver.edu

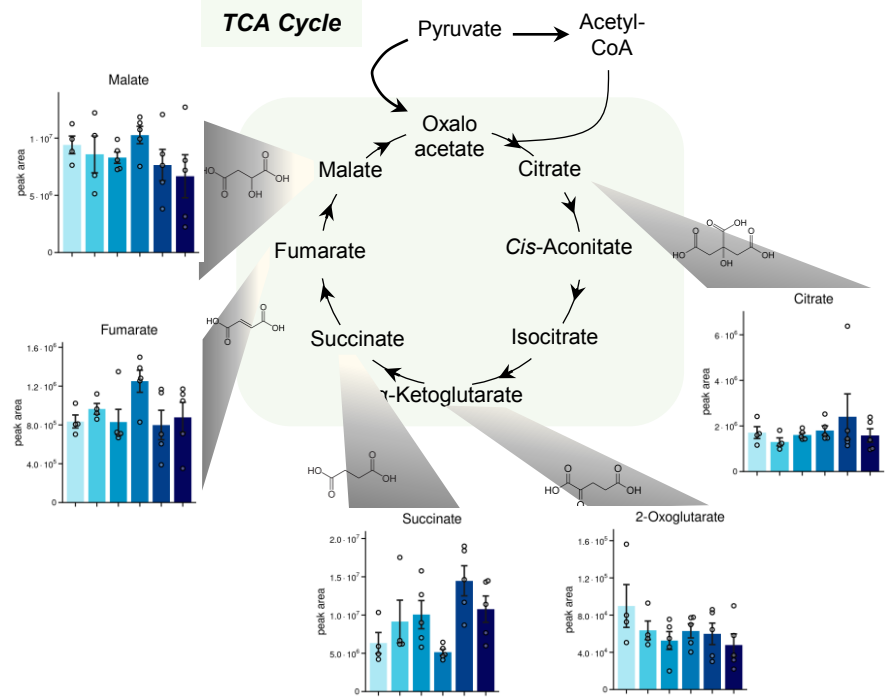
Table of Content:

- **Supplementary Figure 1 – Impact of irradiation on different organs and biofluids in mice;**
- **Supplementary Figure 2 – Impact of intravenous iron supplementation and irradiation on different organs and biofluids in mice.**
- **Supplementary Table 1.xlsx – Raw data and elaborations. Uploaded as a separate file.**
Raw mass spectrometry data for this study are available for free download at the Metabolomics Workbench website, with the following IDs: ST002031-ST002041.
DOI: <http://dx.doi.org/10.21228/M8771V>

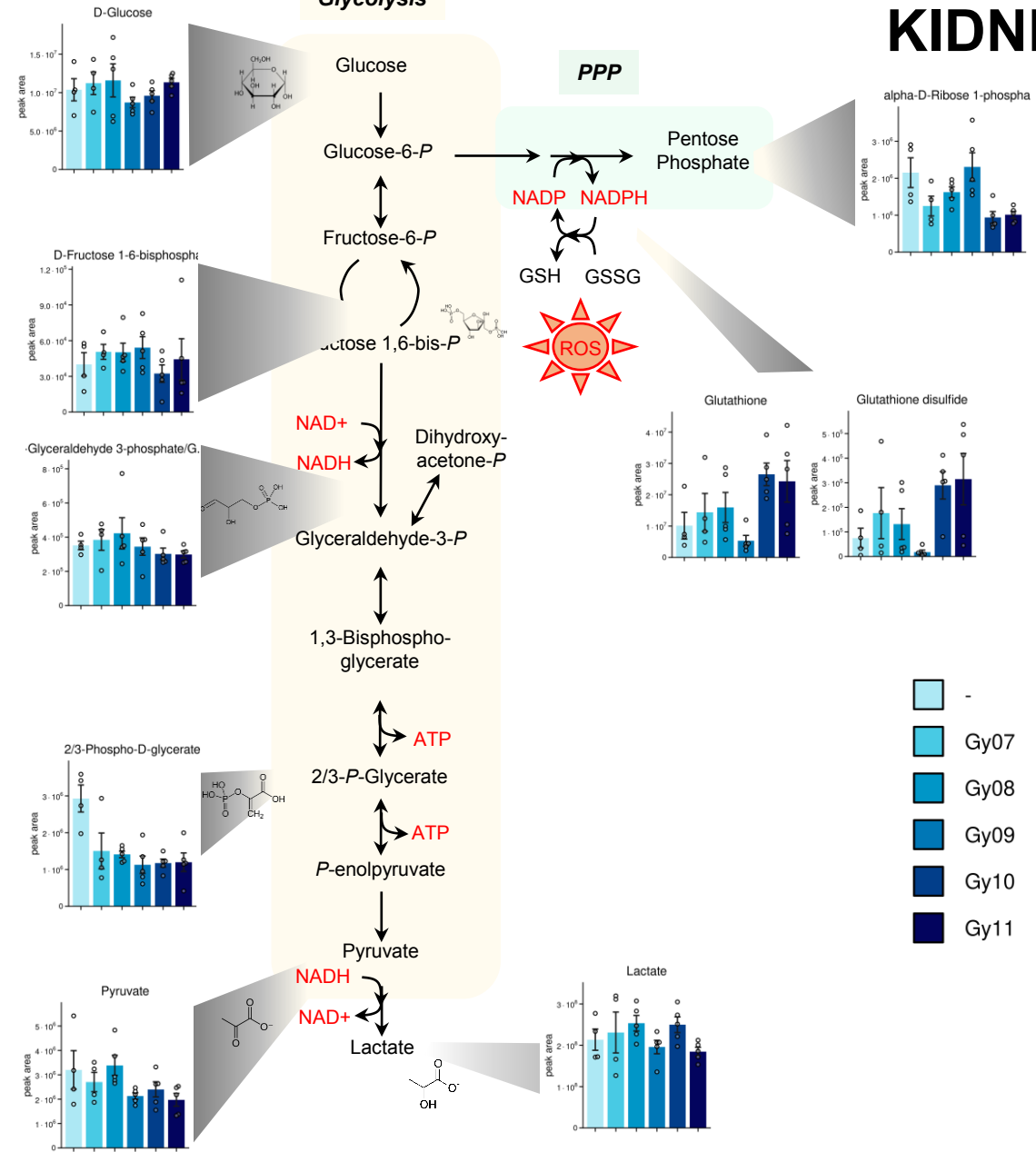


Supp Fig 1.A – Heat map (top 50 ANOVA), Principal Component Analysis and VIP Score plots for kidney metabolites in response to radiation.

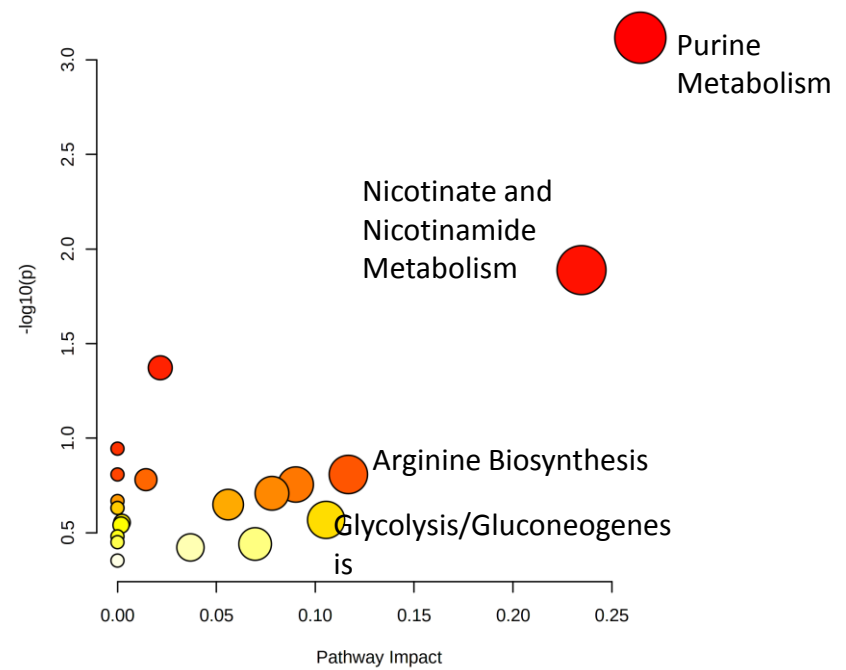
TCA



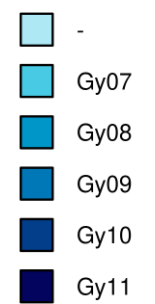
Glycolysis



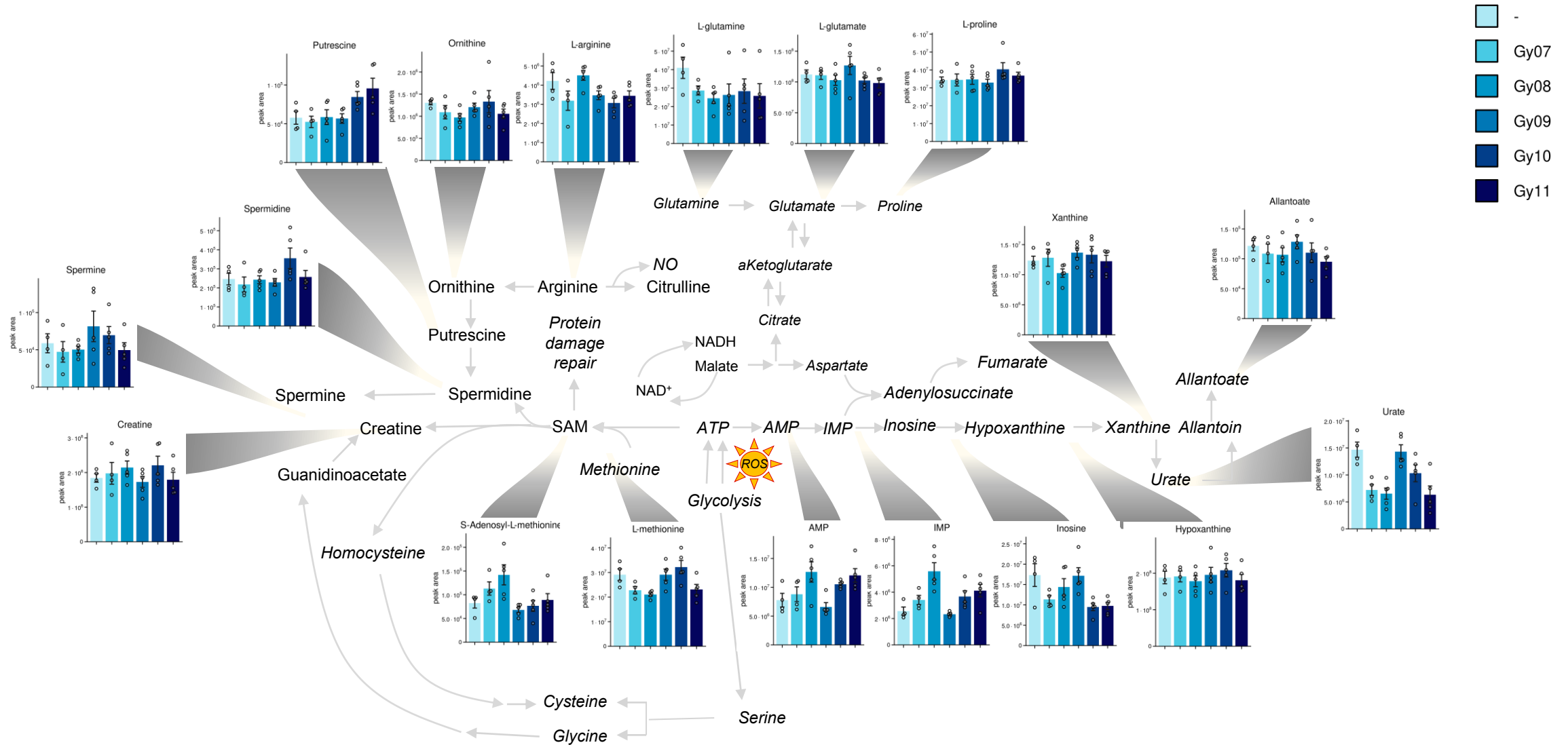
KIDNEY



Supp Fig 1.B – Bar plots on the impact of radiation on the TCA cycle, glycolysis and pathway analysis of top metabolic effects in kidneys.

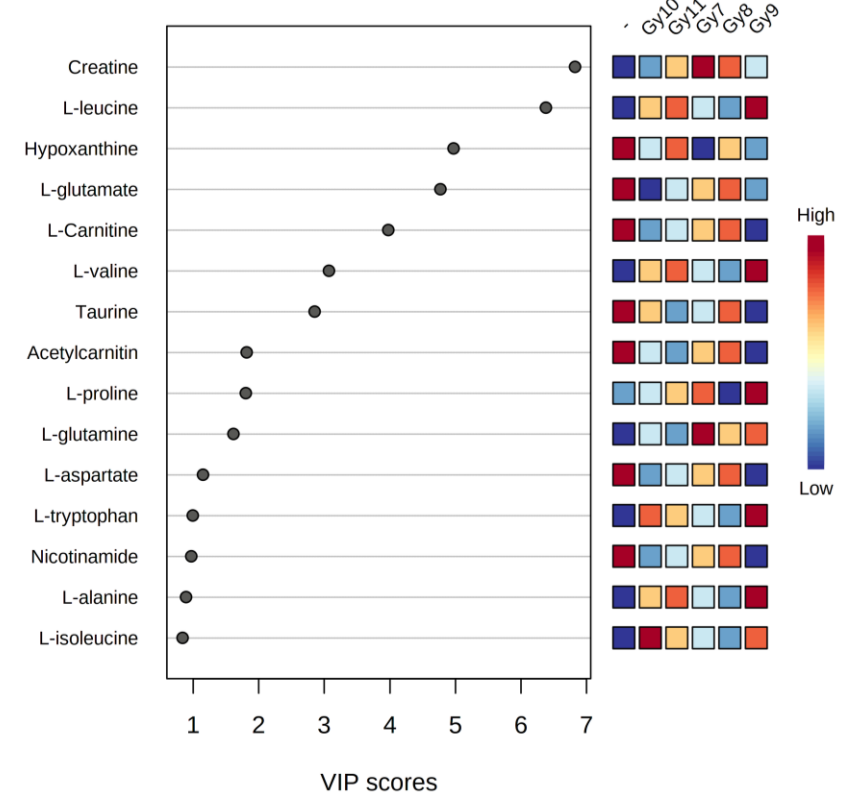
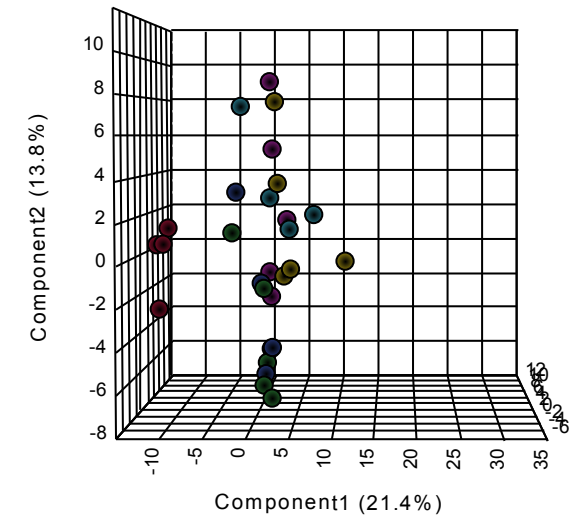
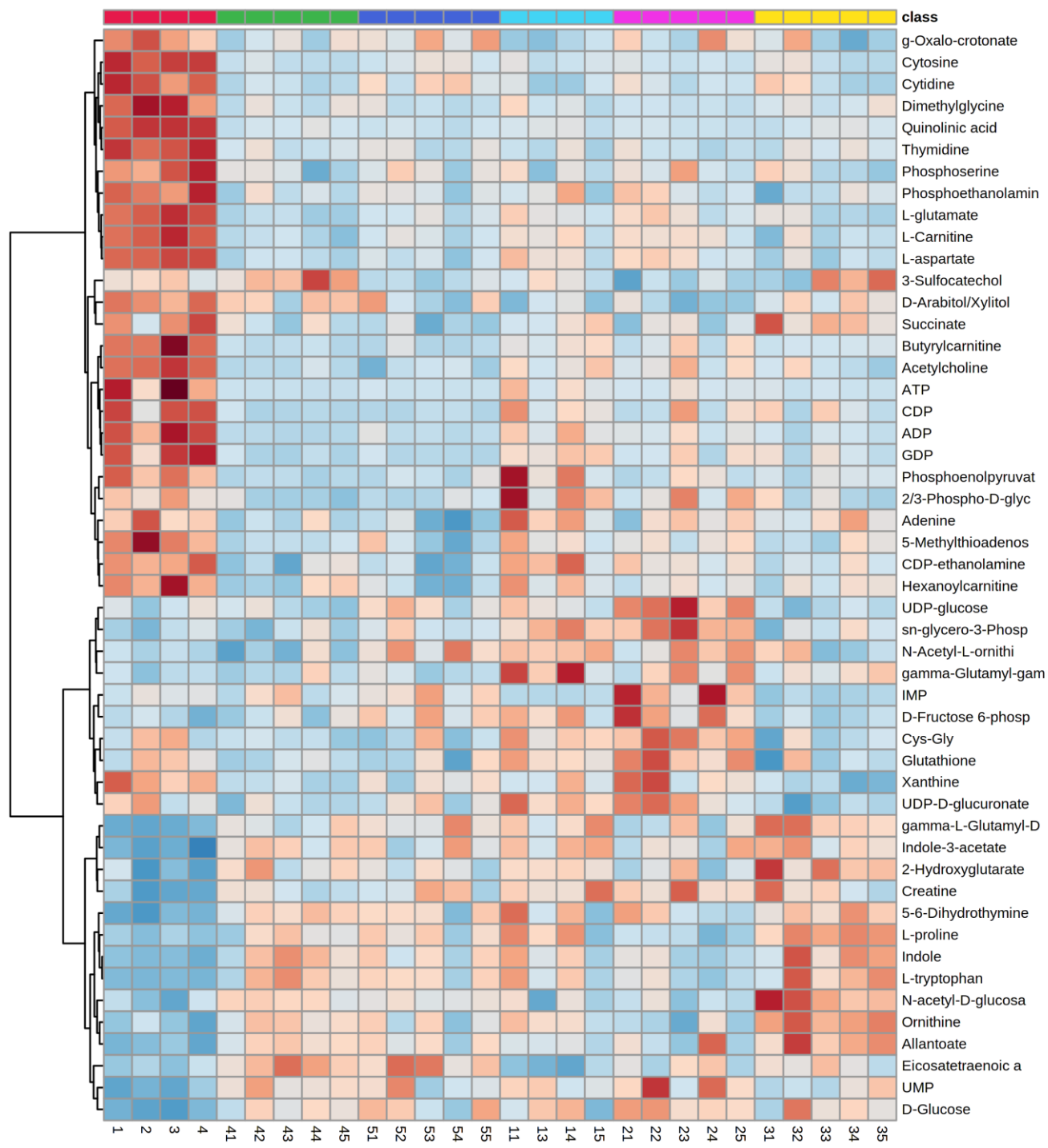


KIDNEY



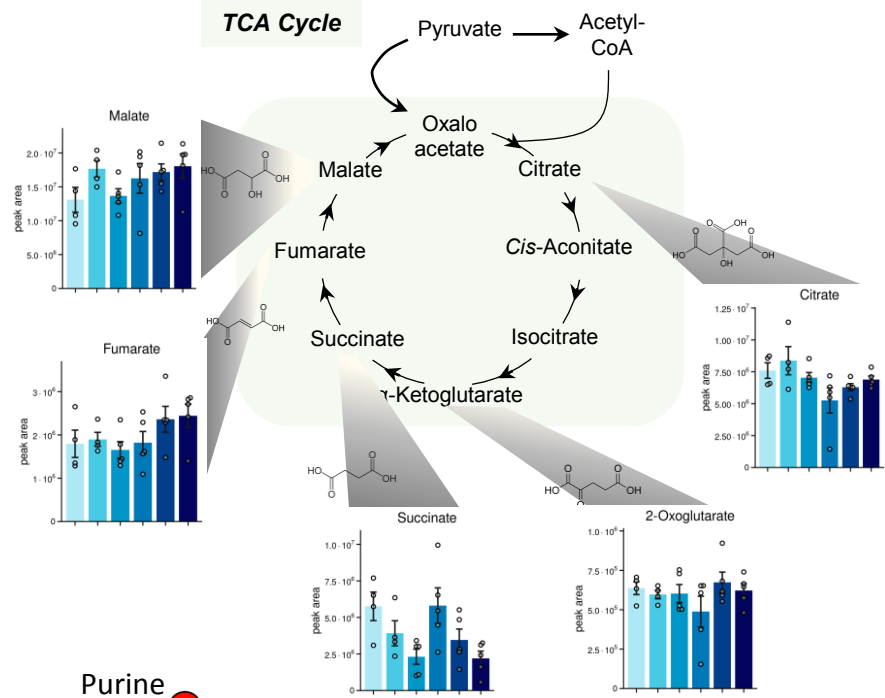
Supp Fig 1.C – Bar plots on the impact of radiation on protein damage and repair mechanisms in the kidneys.

SPLEEN

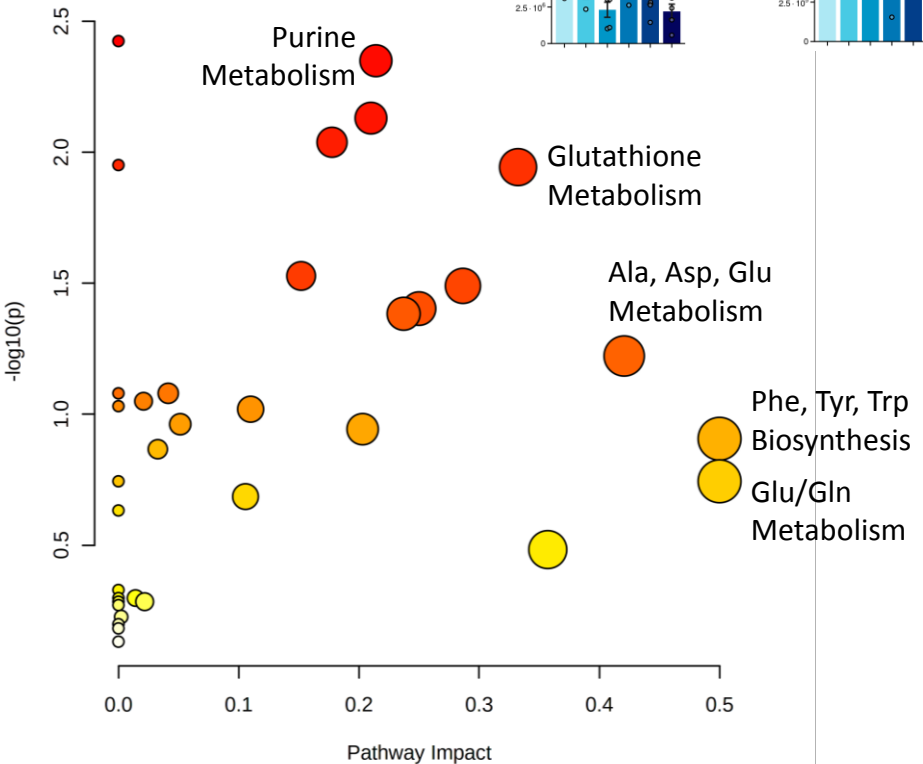
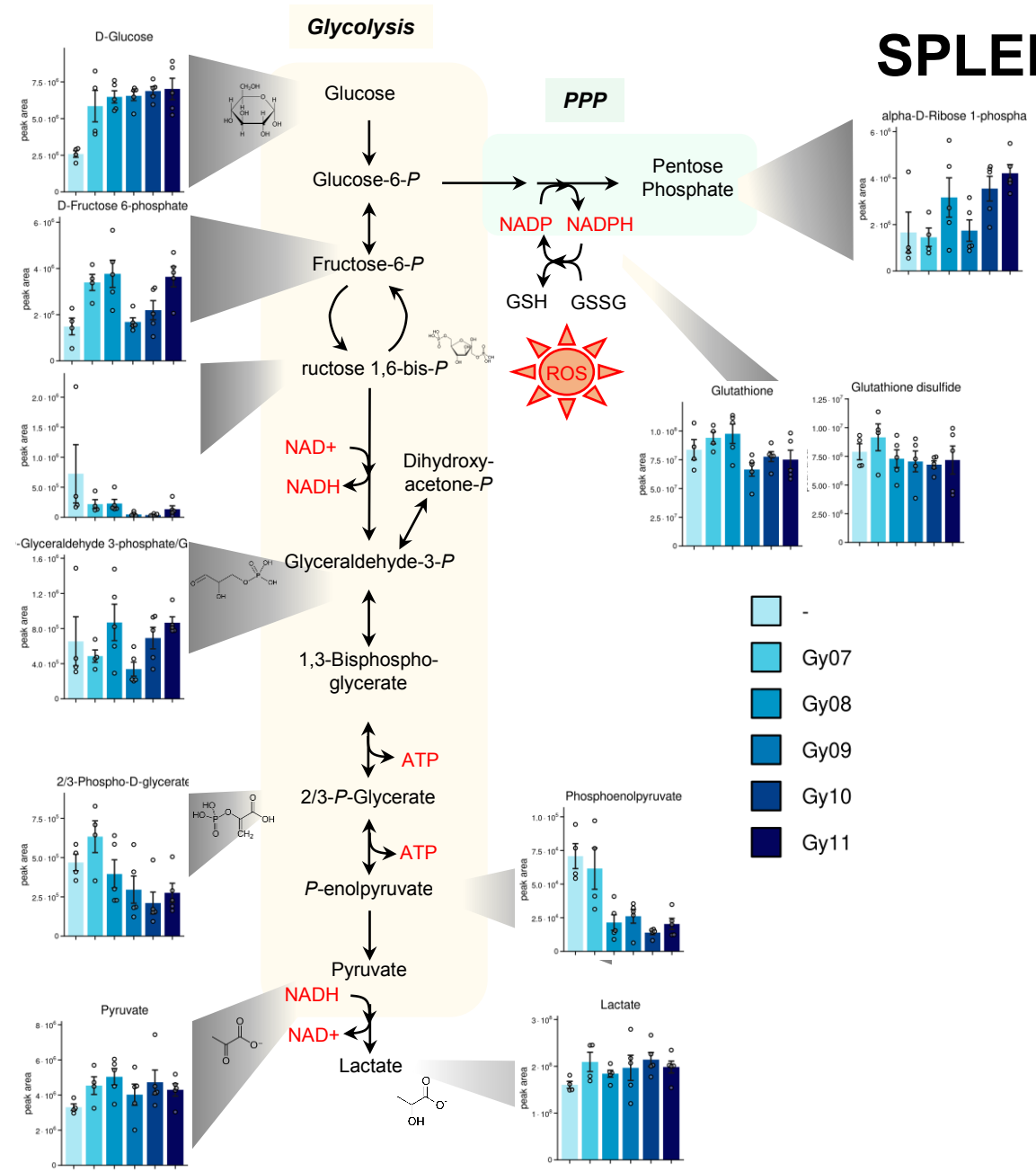


Supp Fig 1.D – Heat map (top 50 ANOVA), Principal Component Analysis and VIP Score plots for spleen metabolites in response to radiation.

TCA

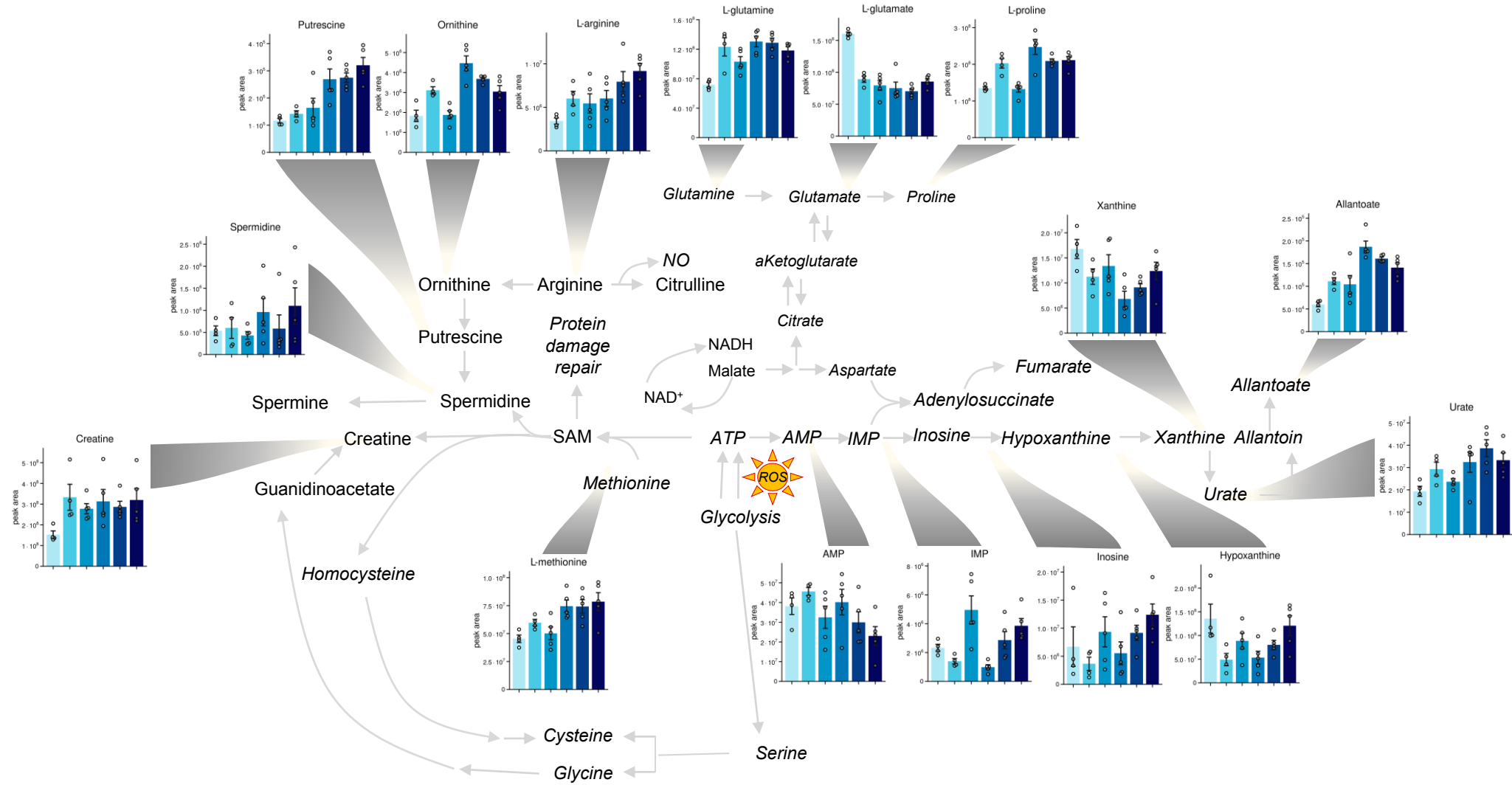


SPLEEN



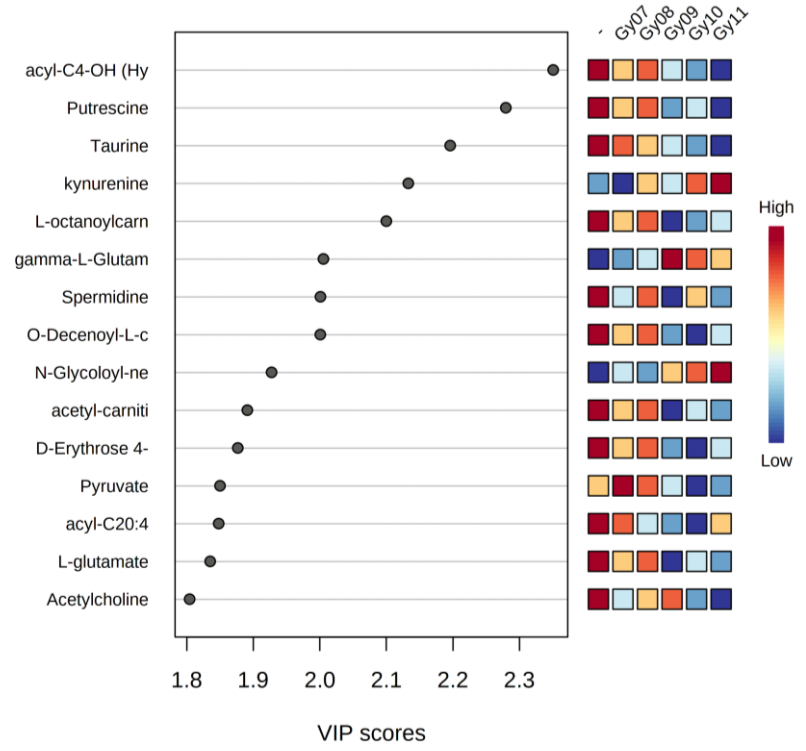
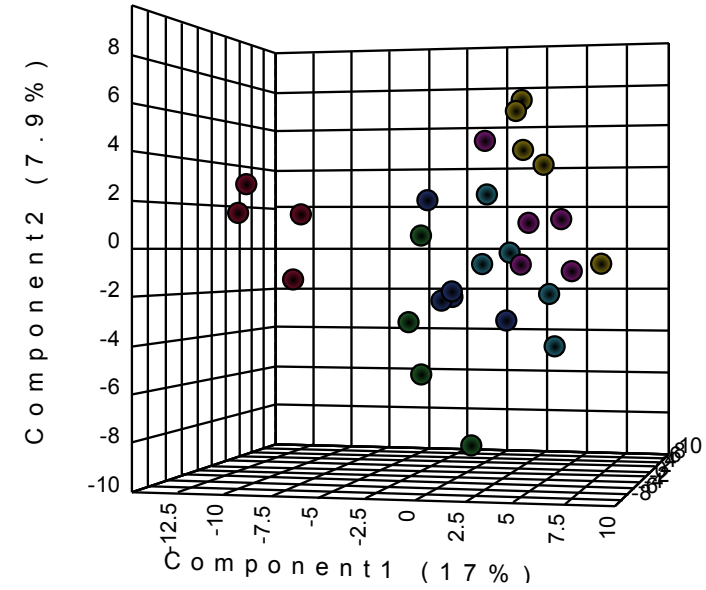
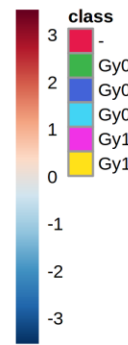
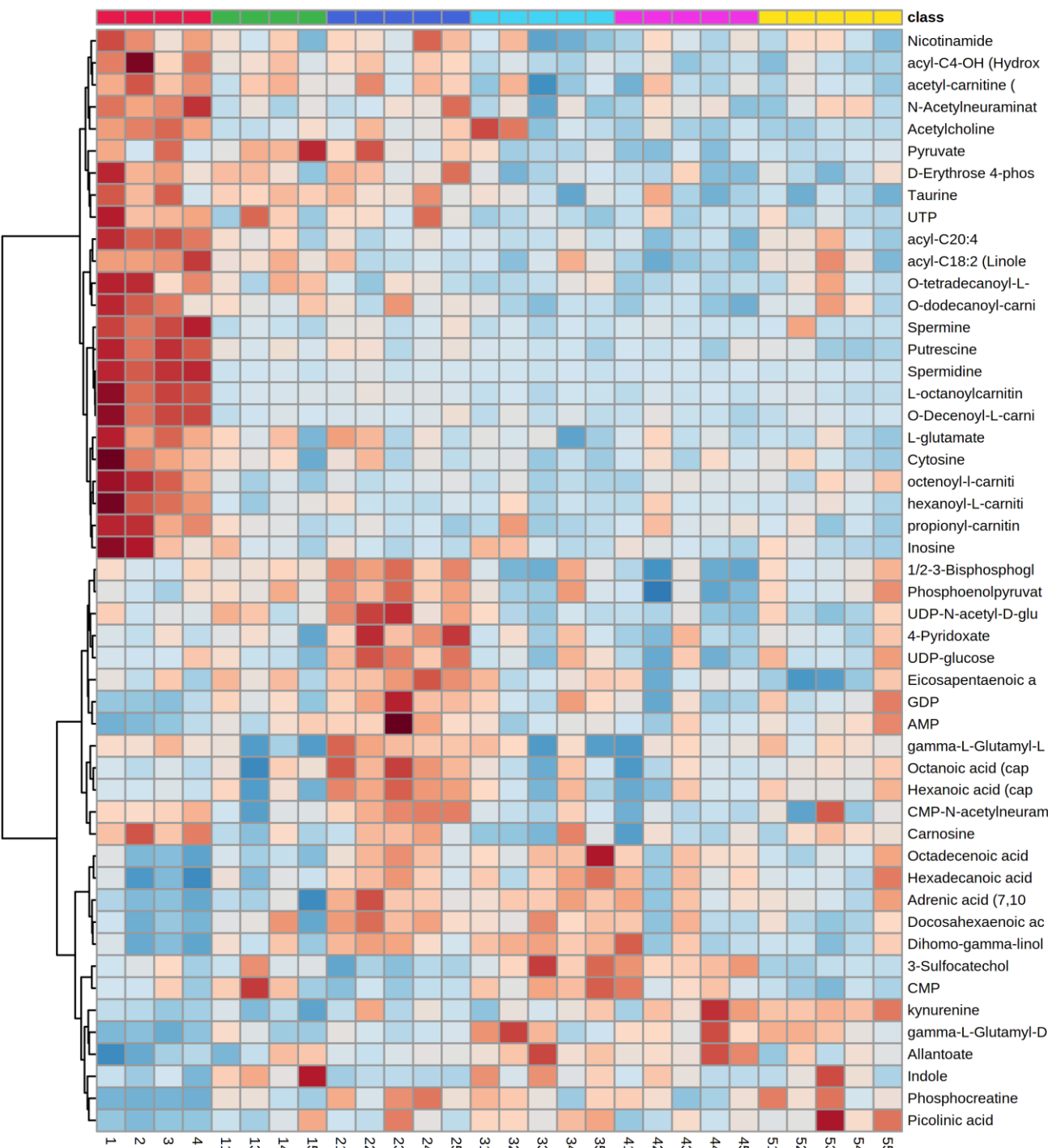
Supp Fig 1.E – Bar plots on the impact of radiation on the TCA cycle, glycolysis and pathway analysis of top metabolic effects in spleen.

SPLEEN

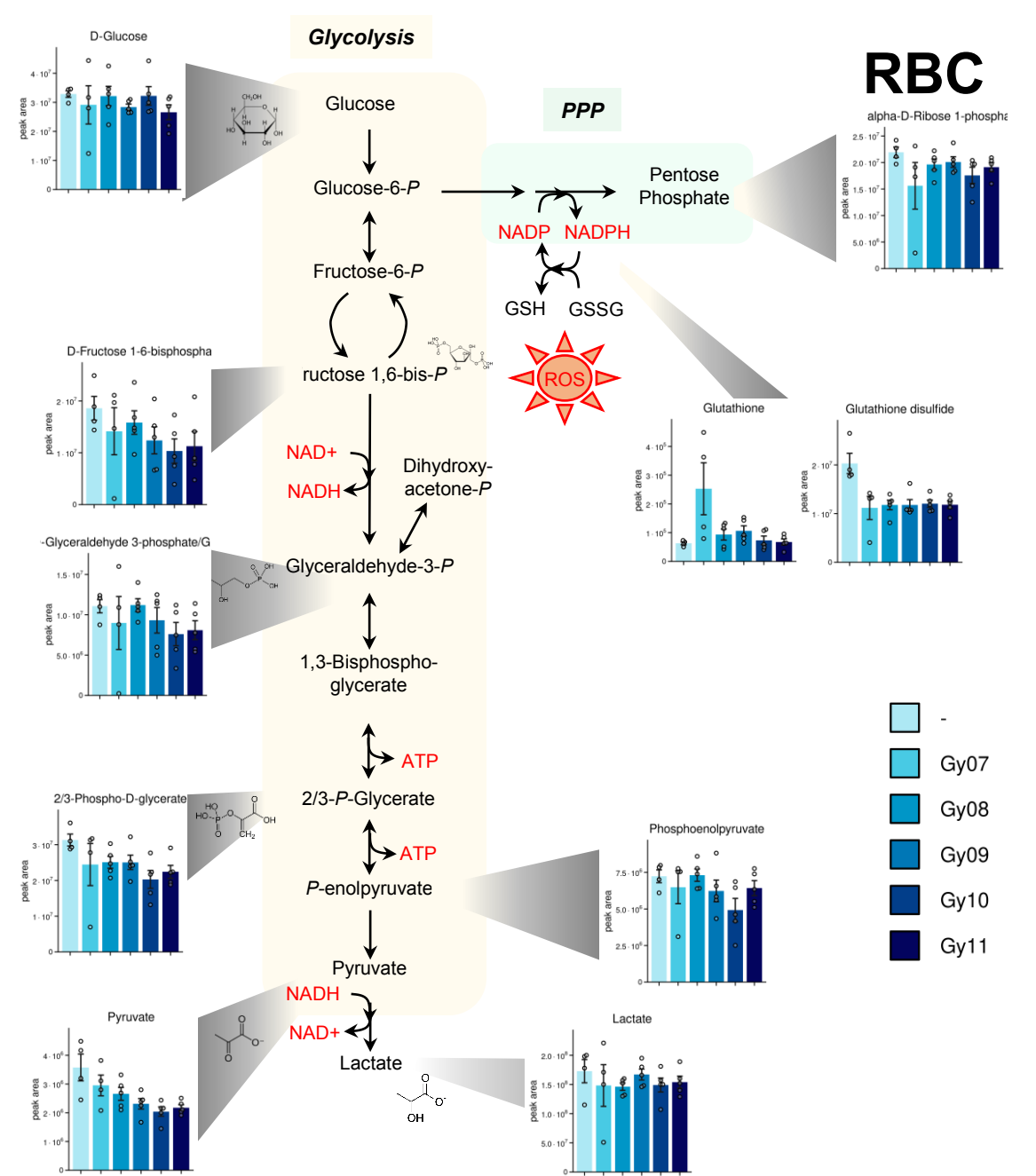
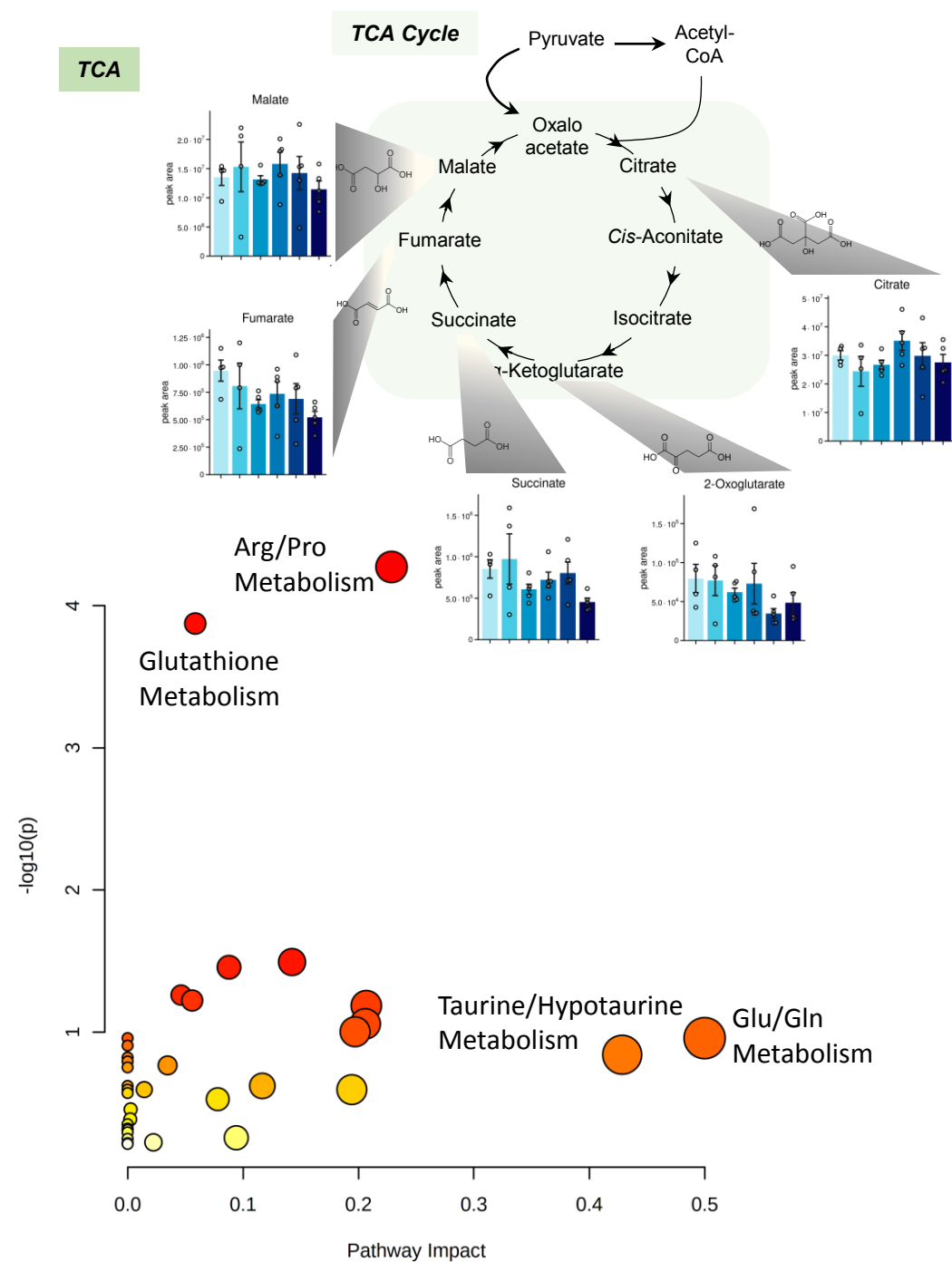


Supp Fig 1.F – Bar plots on the impact of radiation on protein damage and repair mechanisms in the spleen.

RBC

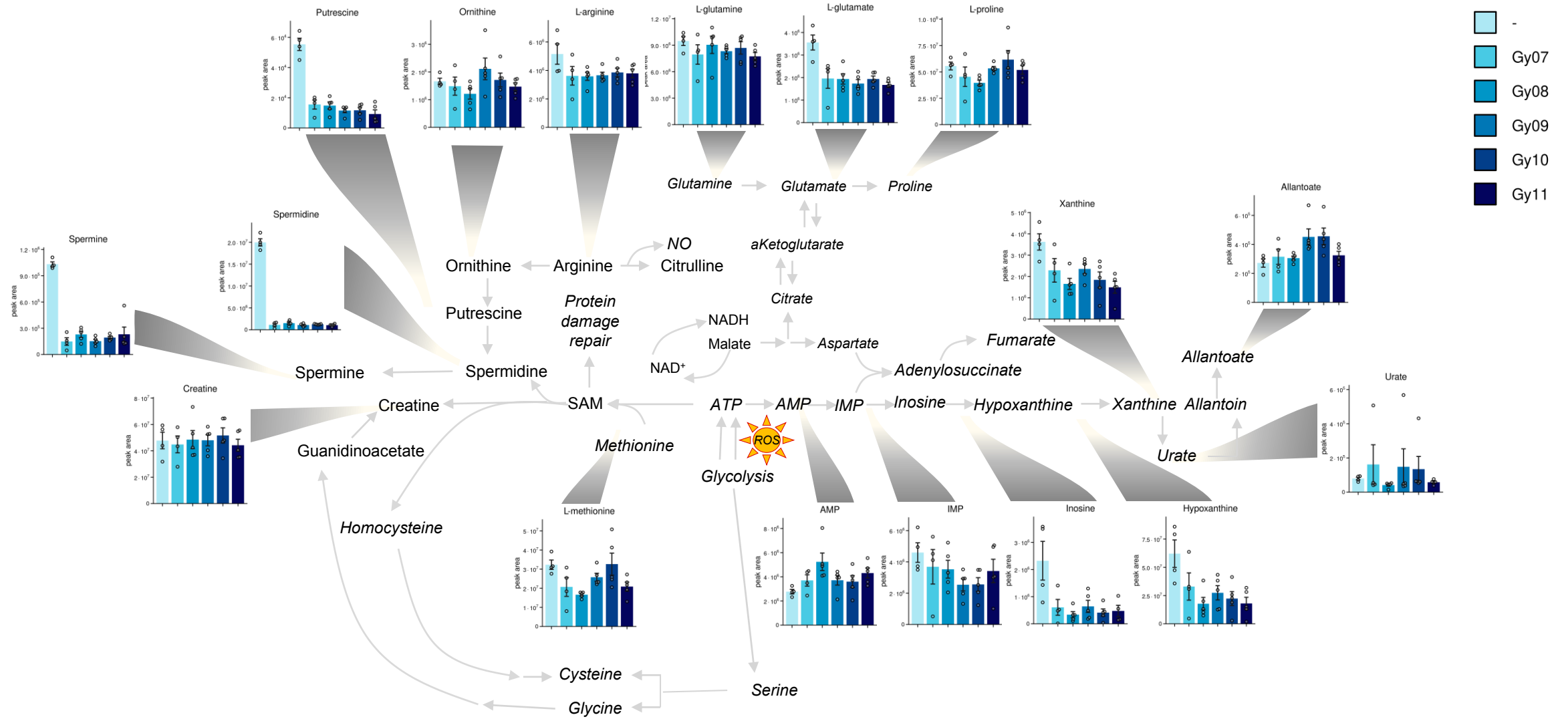


Supp Fig 1.G – Heat map (top 50 ANOVA), Principal Component Analysis and VIP Score plots for RBC metabolites in response to radiation.

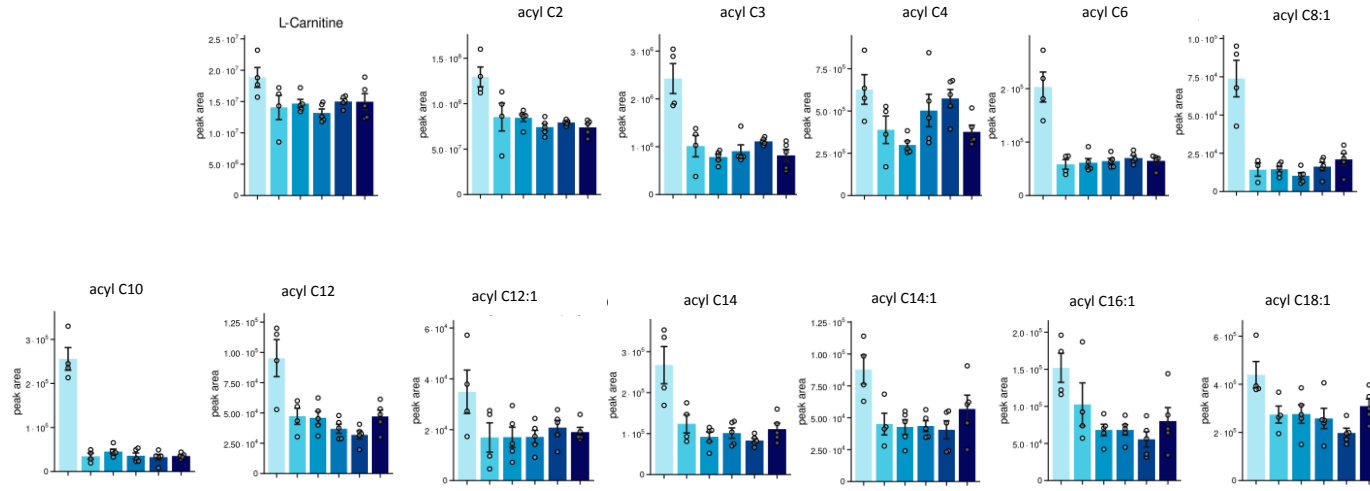
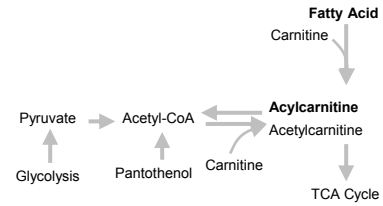


Supp Fig 1.H – Bar plots on the impact of radiation on the TCA cycle, glycolysis and pathway analysis of top metabolic effects in RBC.

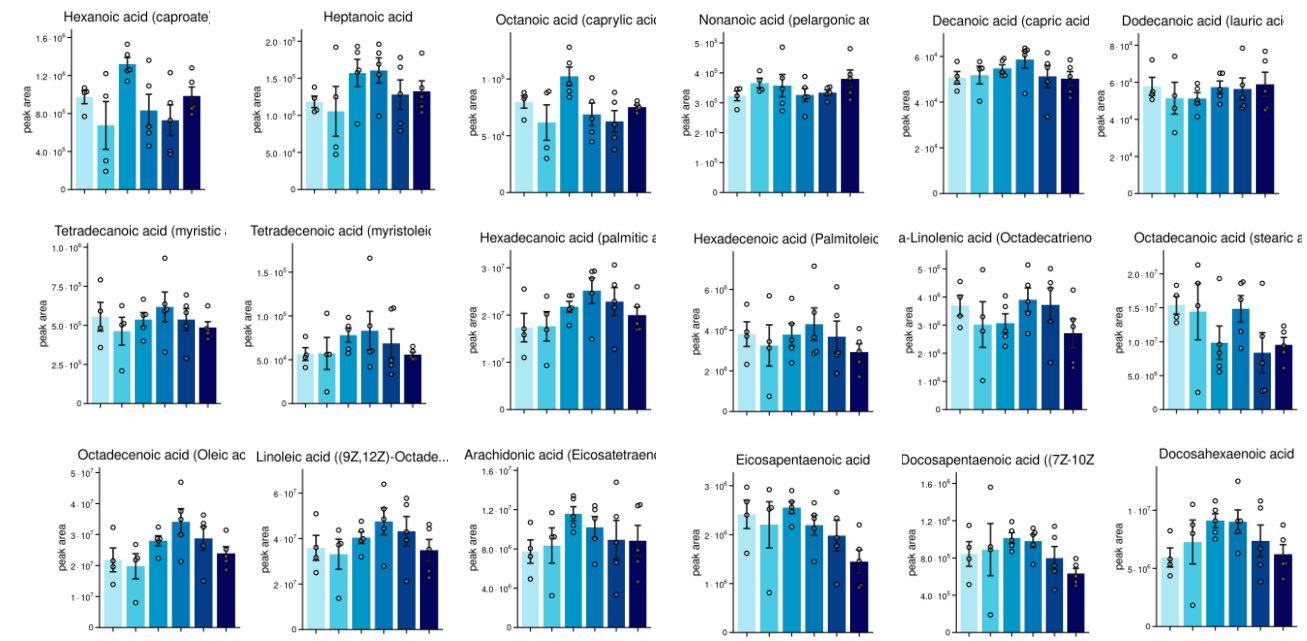
RBC



Supp Fig 1.I – Bar plots on the impact of radiation on protein damage and repair pathways in RBC.

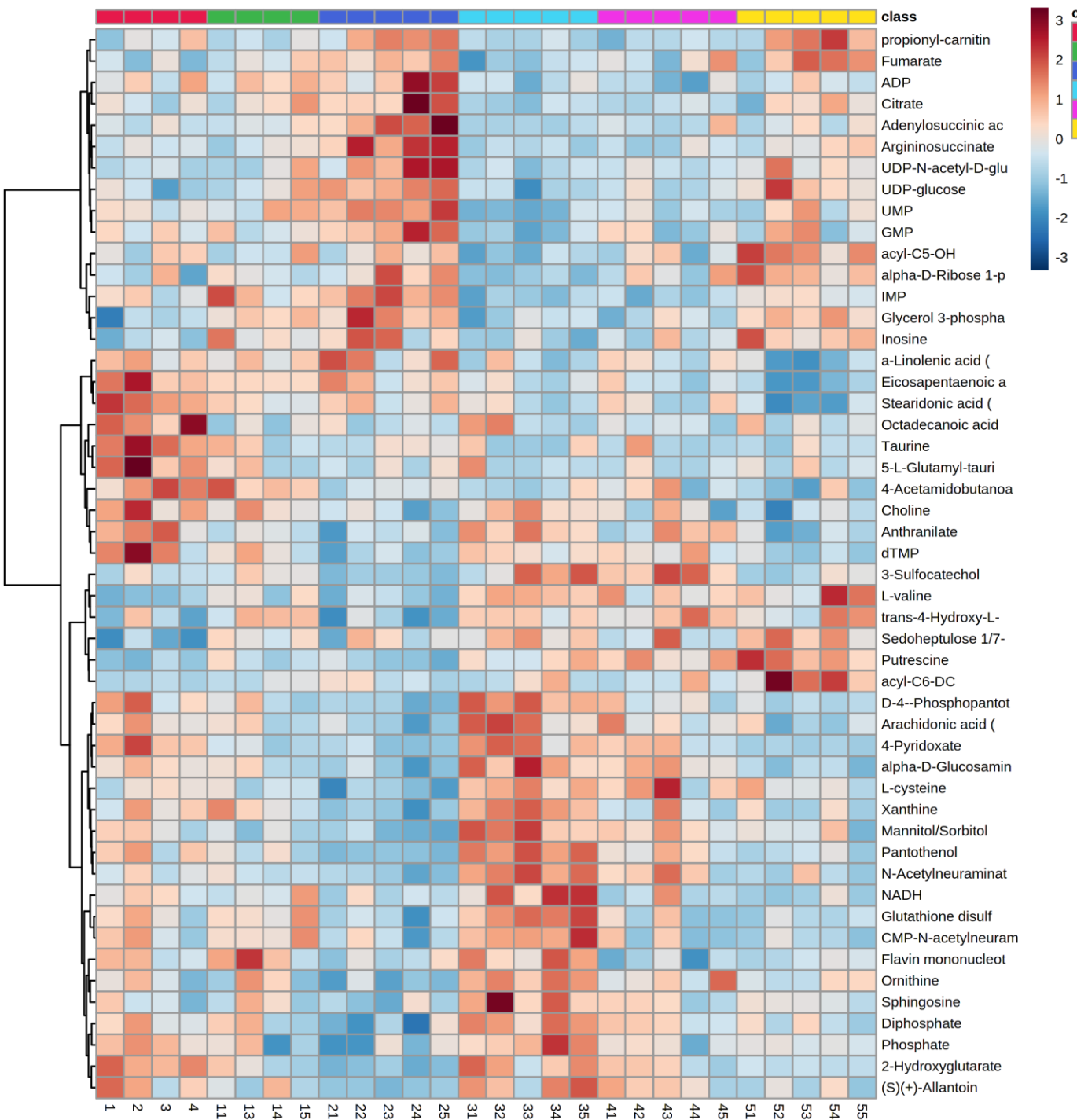


Acylcarnitines

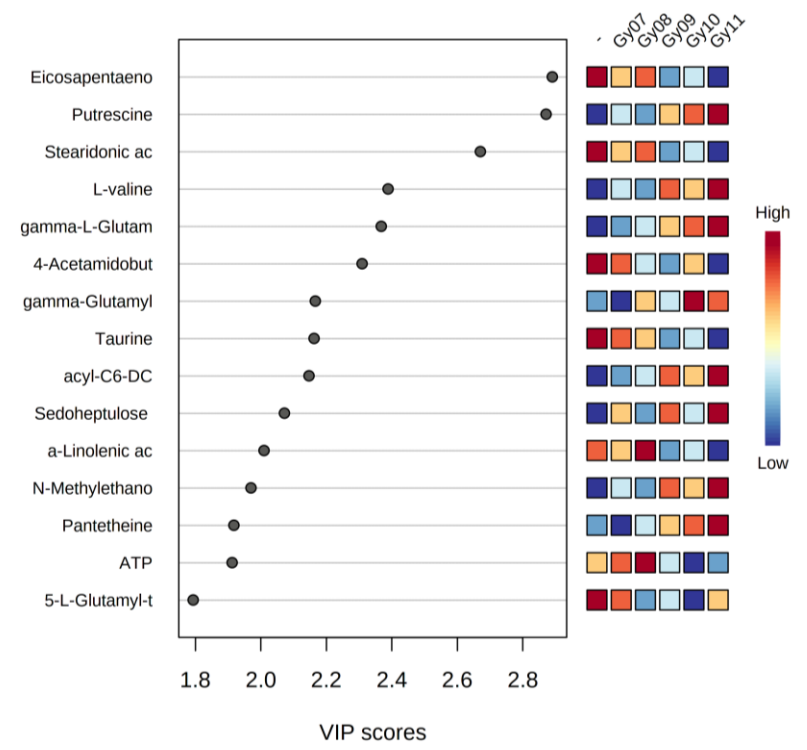
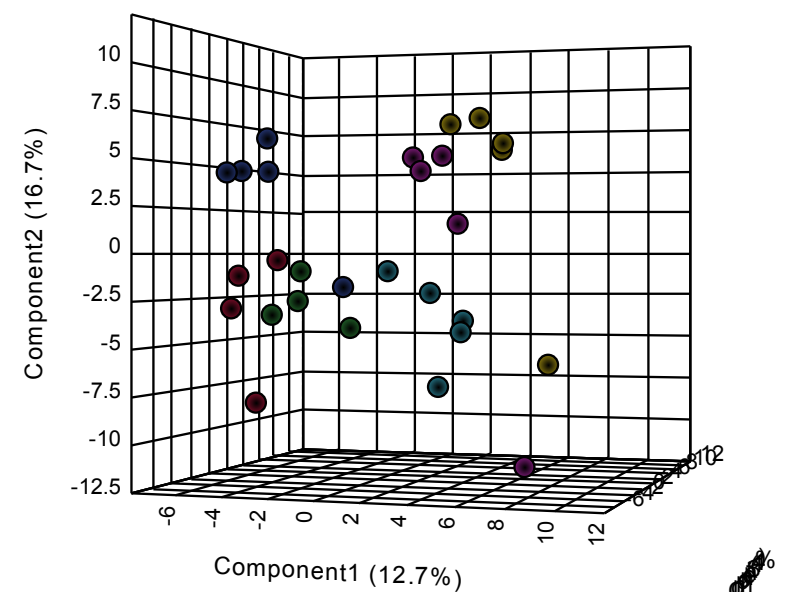


Fatty Acids

Supp Fig 1.J – Bar plots showing the impact of radiation on acyl-carnitines and fatty acids in RBC.

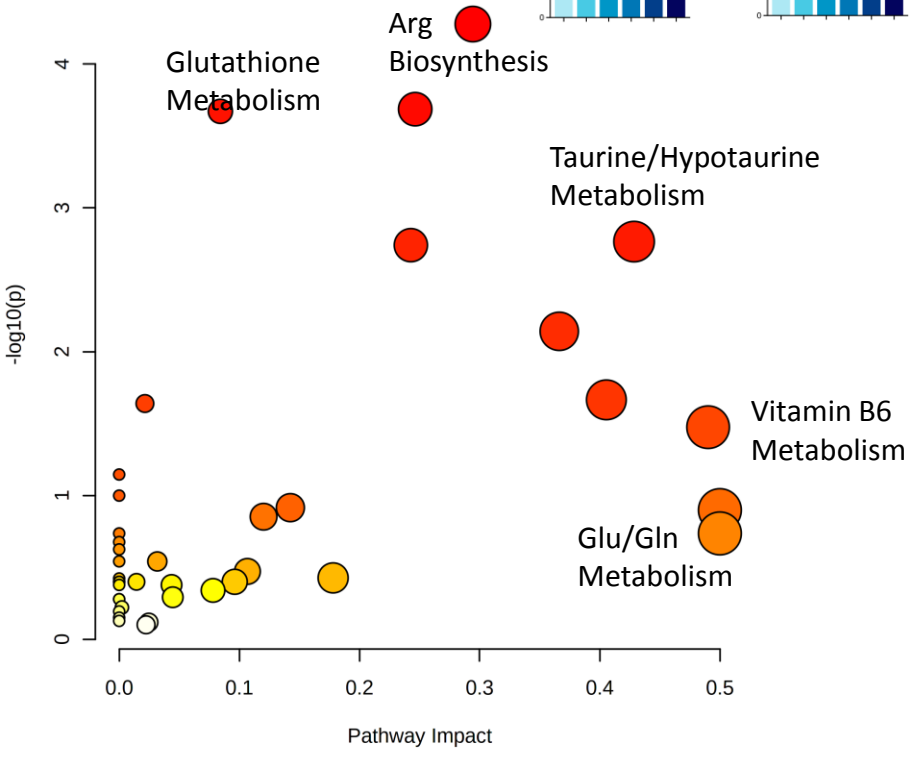
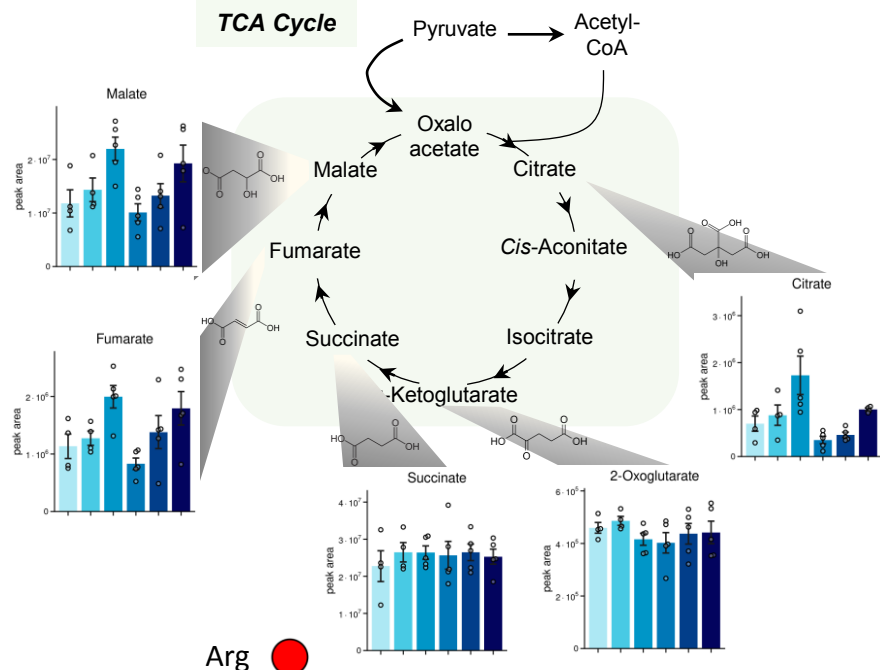


LIVER

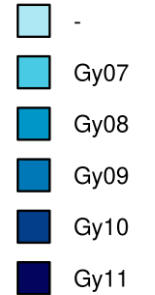
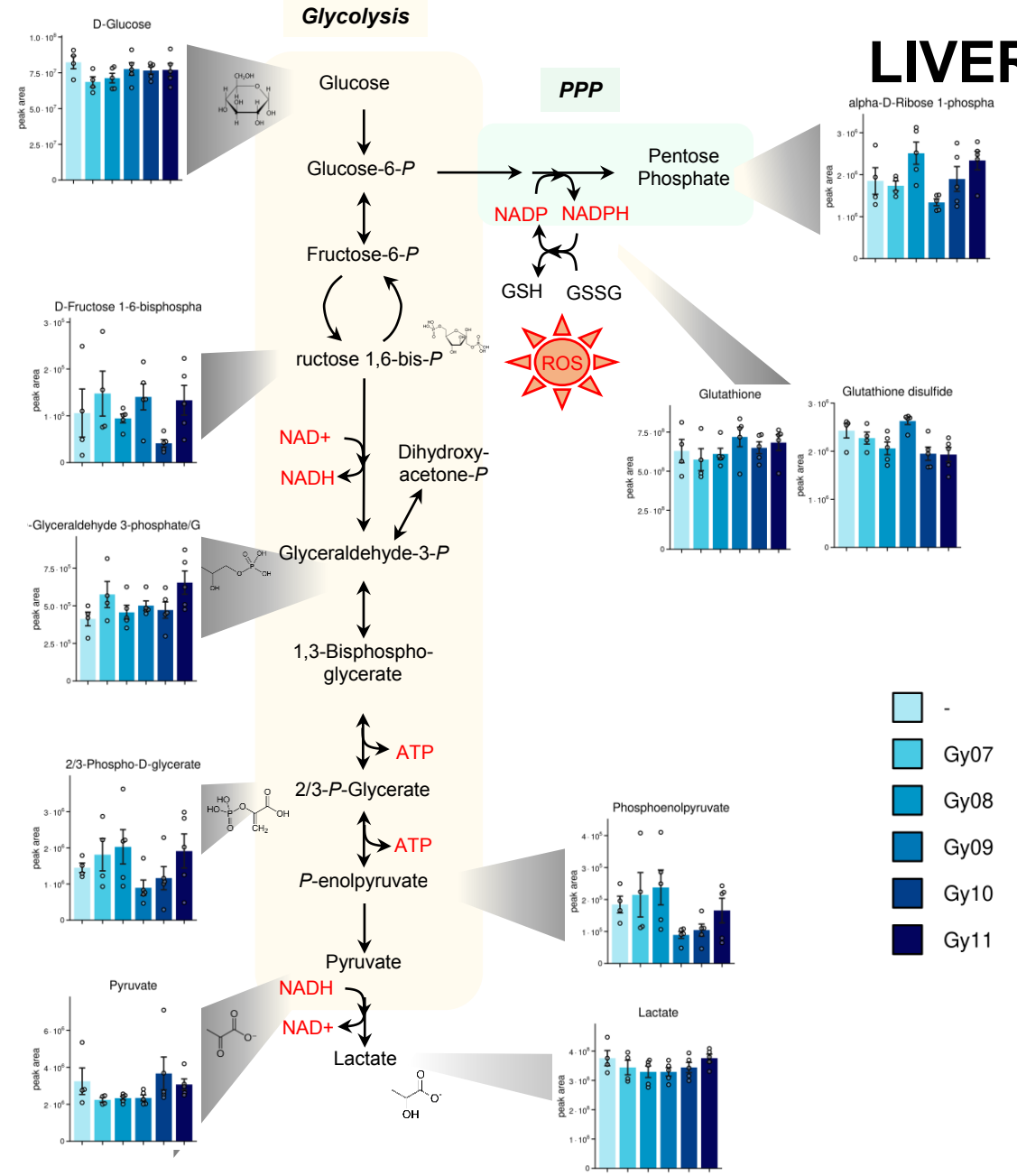


Supp Fig 1.K – Heat map (top 50 ANOVA), Principal Component Analysis and VIP Score plots for liver metabolites in response to radiation.

TCA

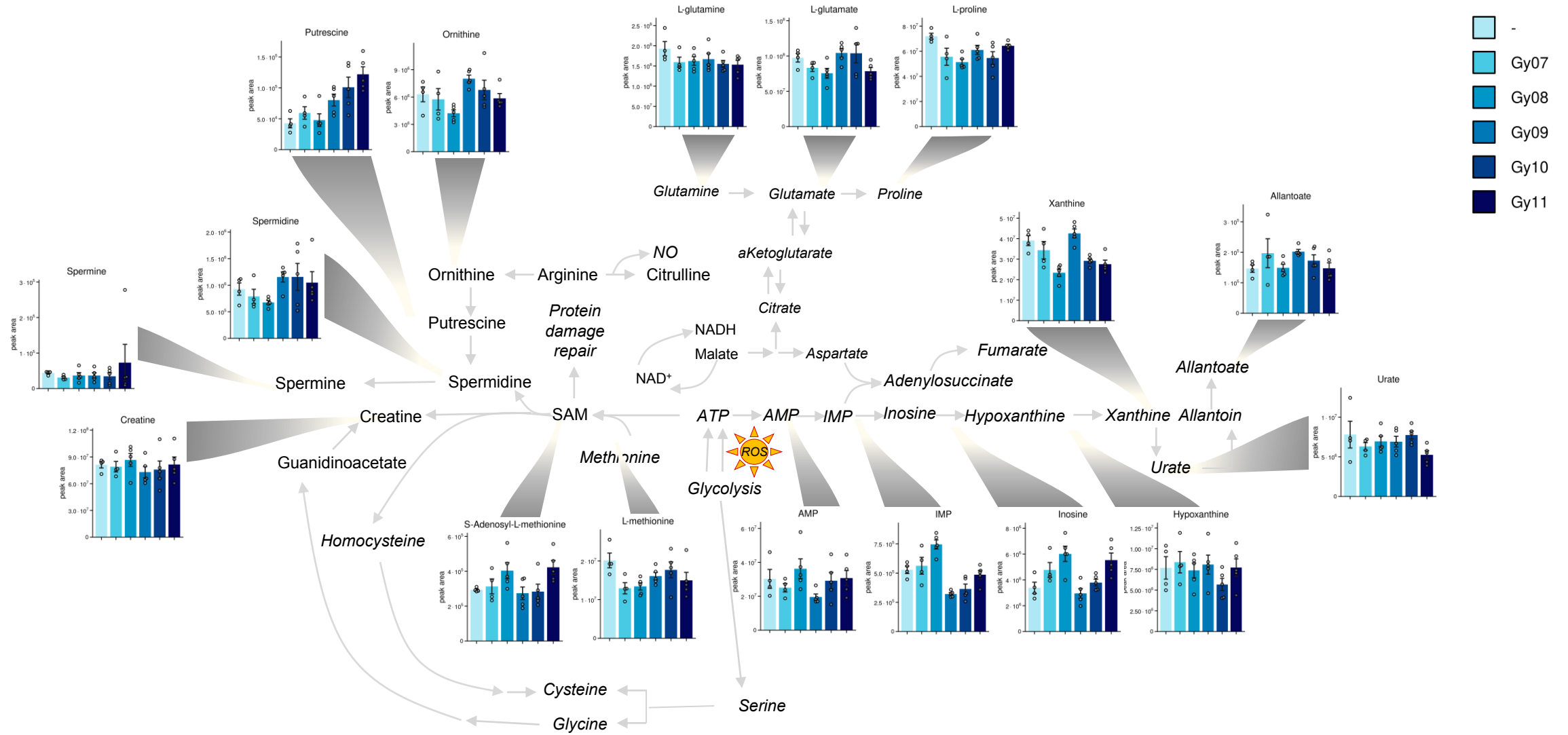


LIVER

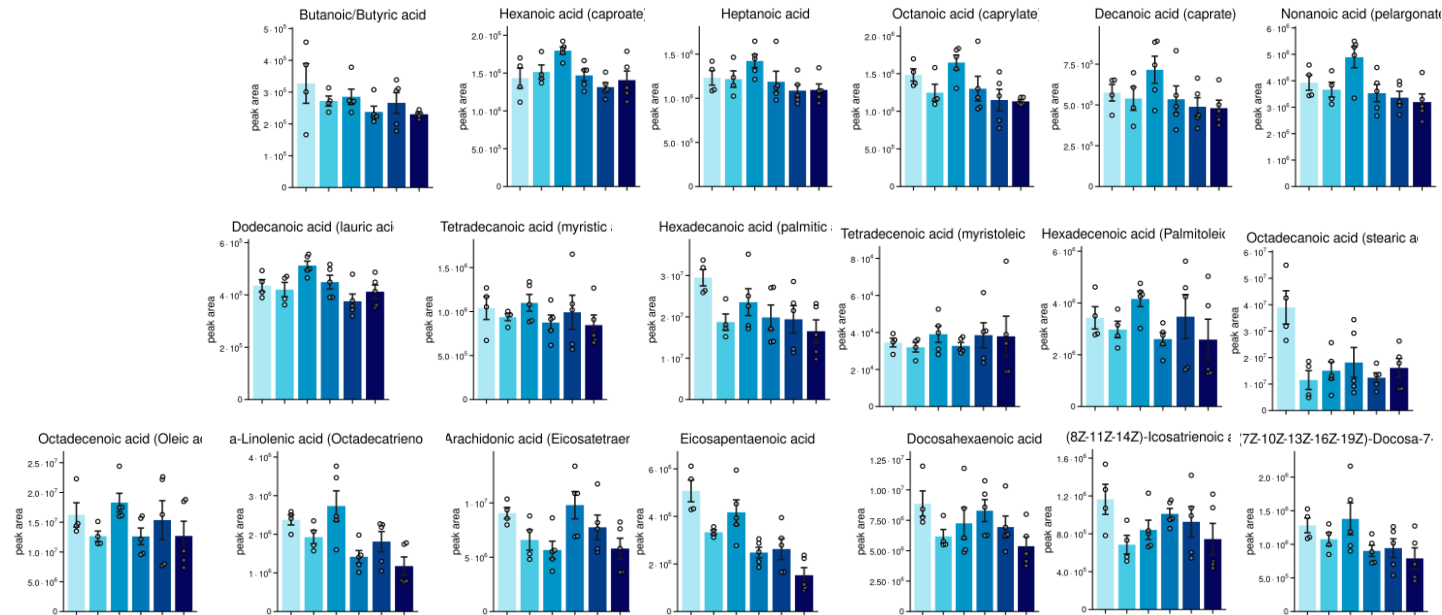
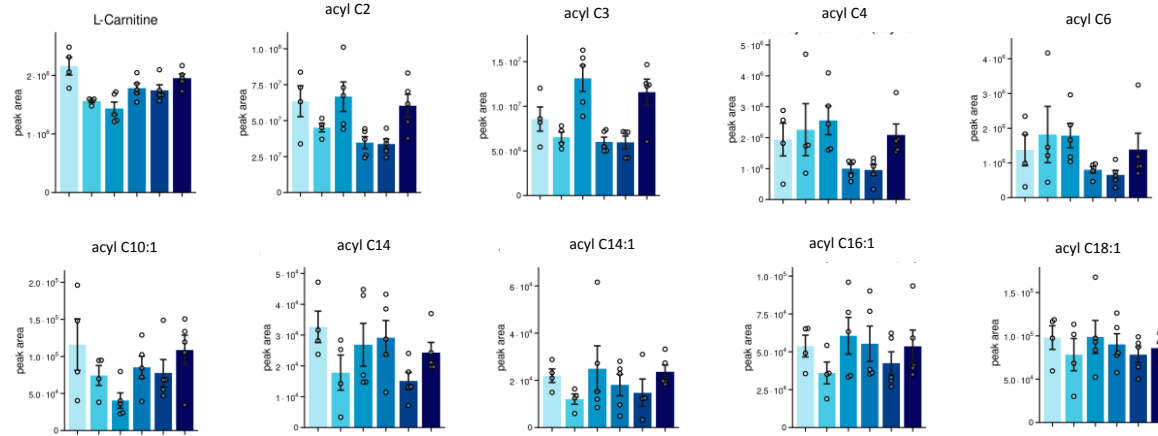
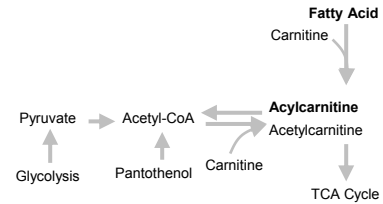


Supp Fig 1.L – Bar plots on the impact of radiation on the TCA cycle, glycolysis and pathway analysis of top metabolic effects in the liver.

LIVER



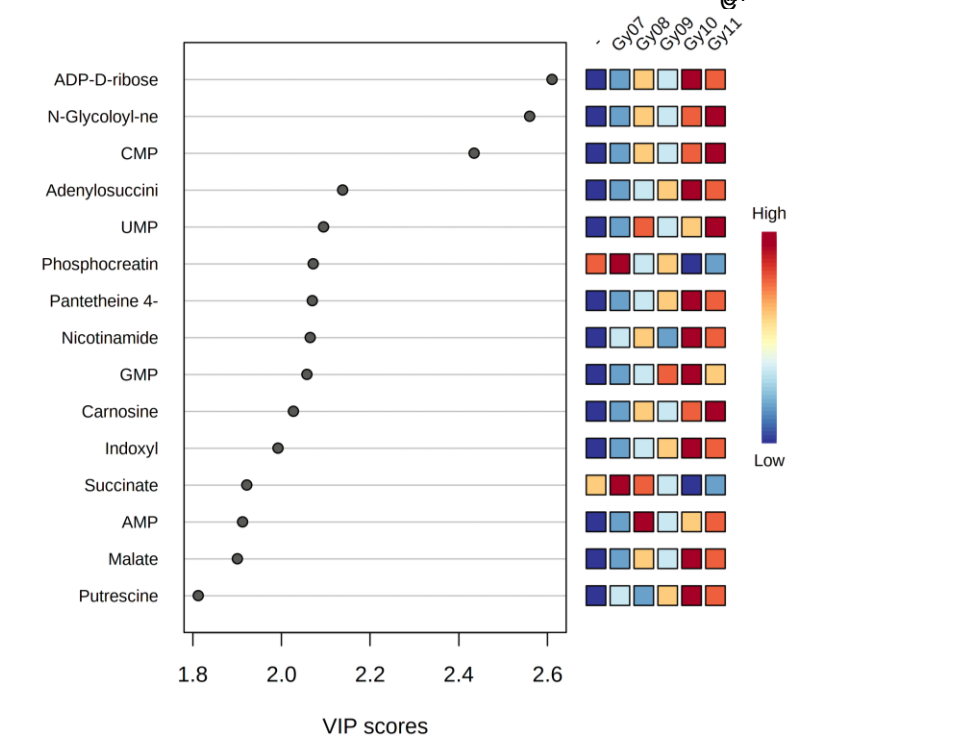
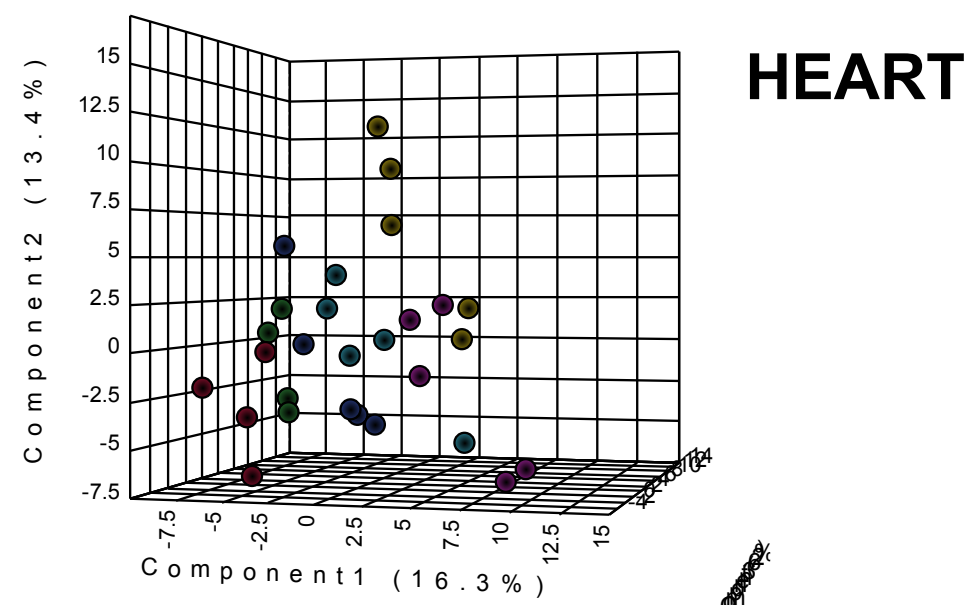
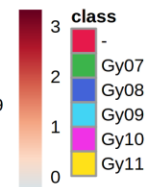
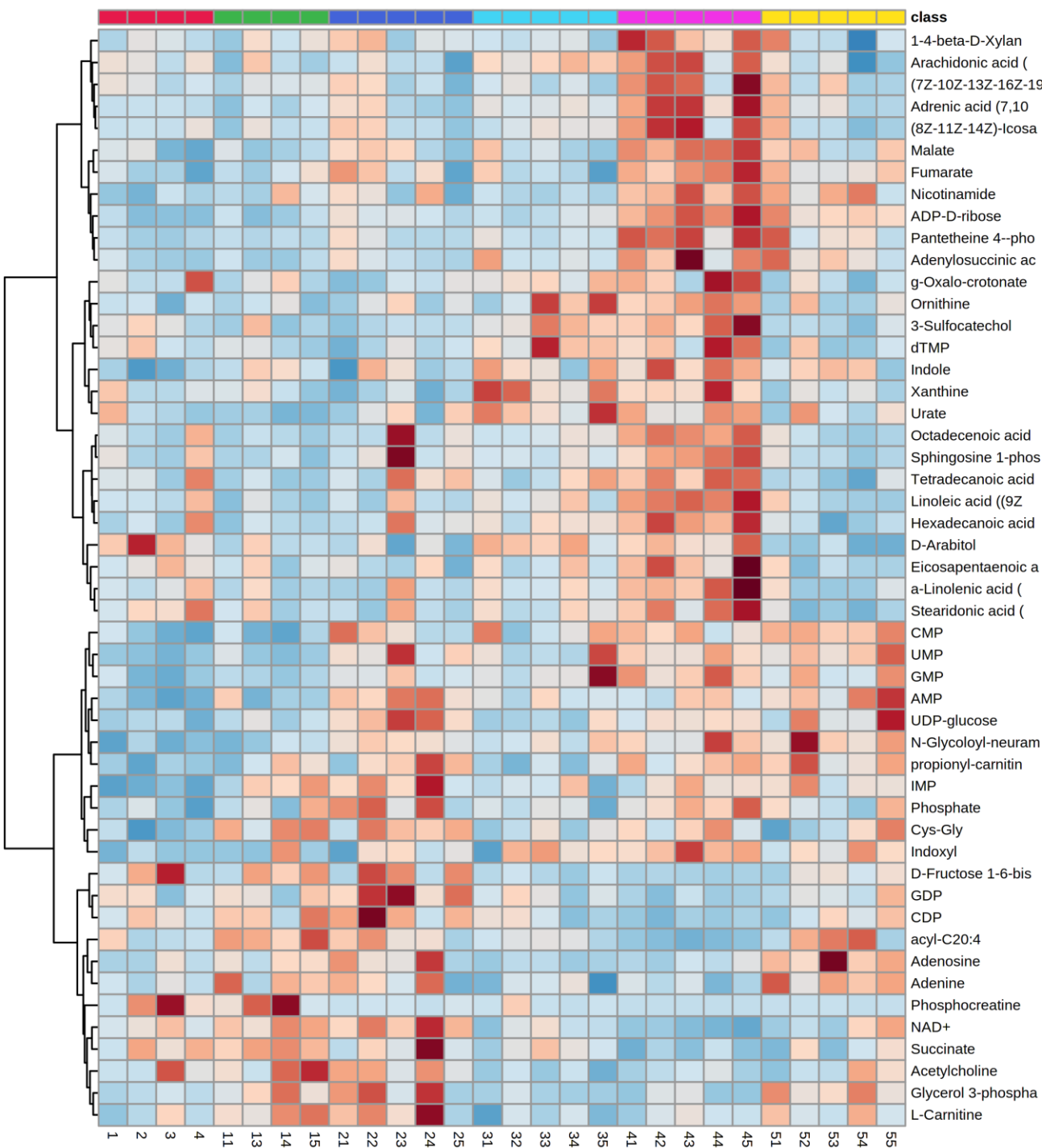
Supp Fig 1.M – Bar plots on the impact of radiation on protein damage and repair pathways in the liver.



Acylcarnitines

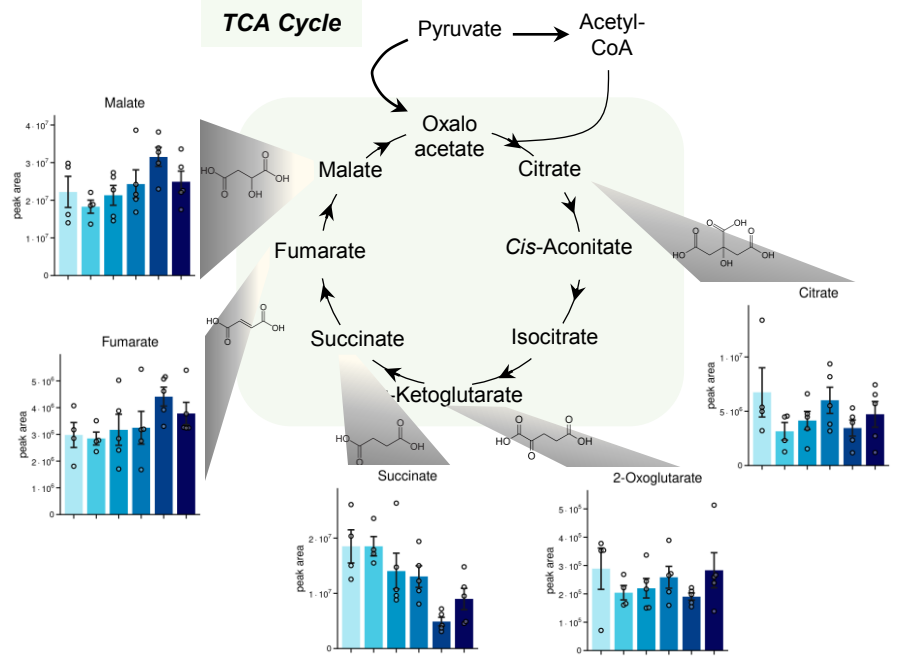
Fatty Acids

Supp Fig 1.N – Bar plots showing the impact of radiation on acyl-carnitines and fatty acids in the liver.

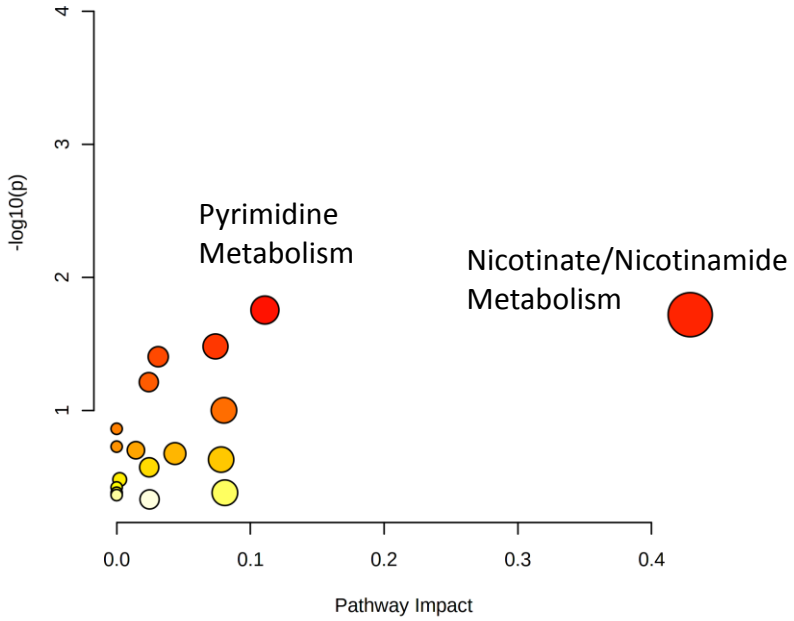


Supp Fig 1.O – Heat map (top 50 ANOVA), Principal Component Analysis and VIP Score plots for heart metabolites in response to radiation.

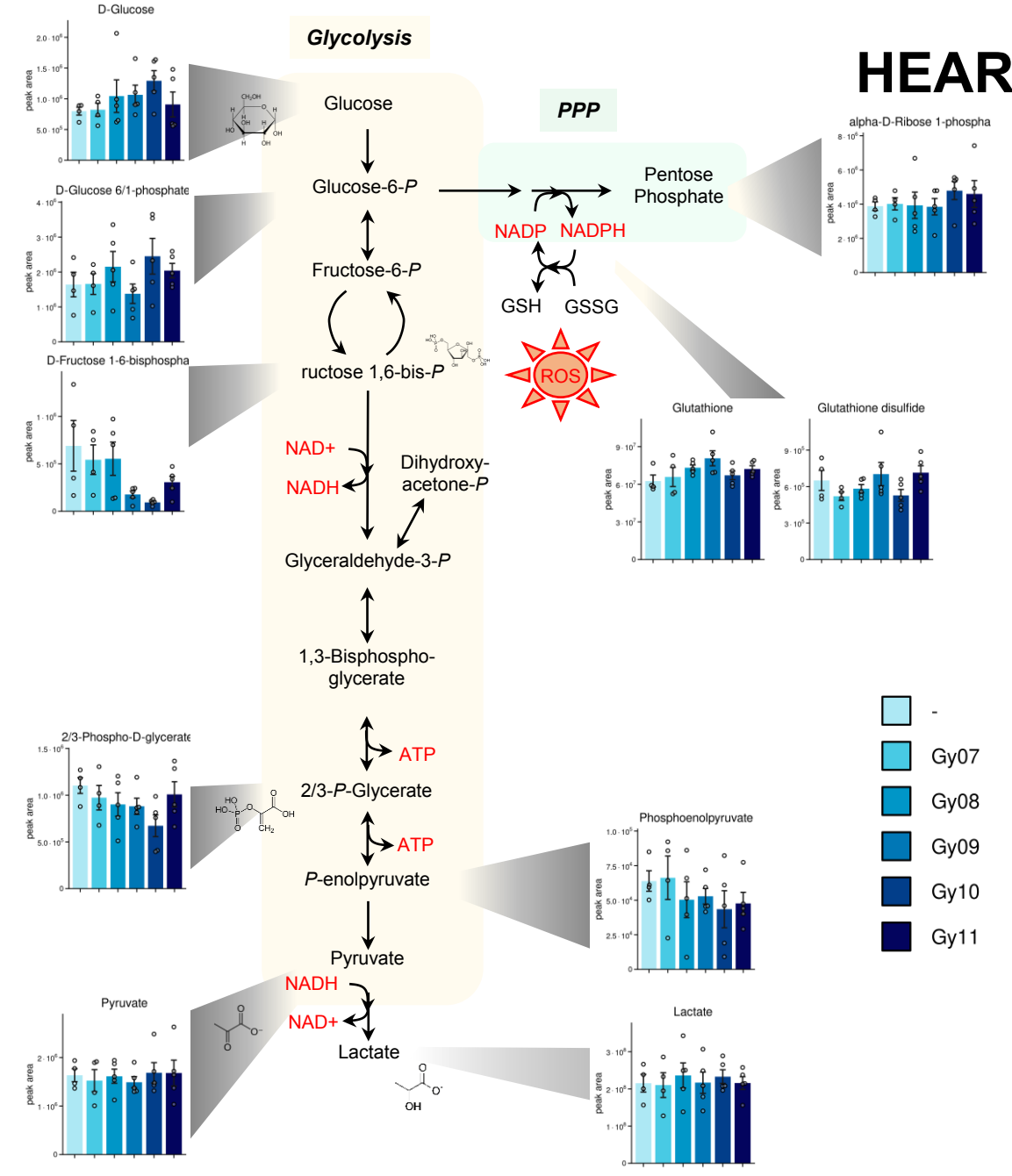
TCA



Purine ●
Metabolism

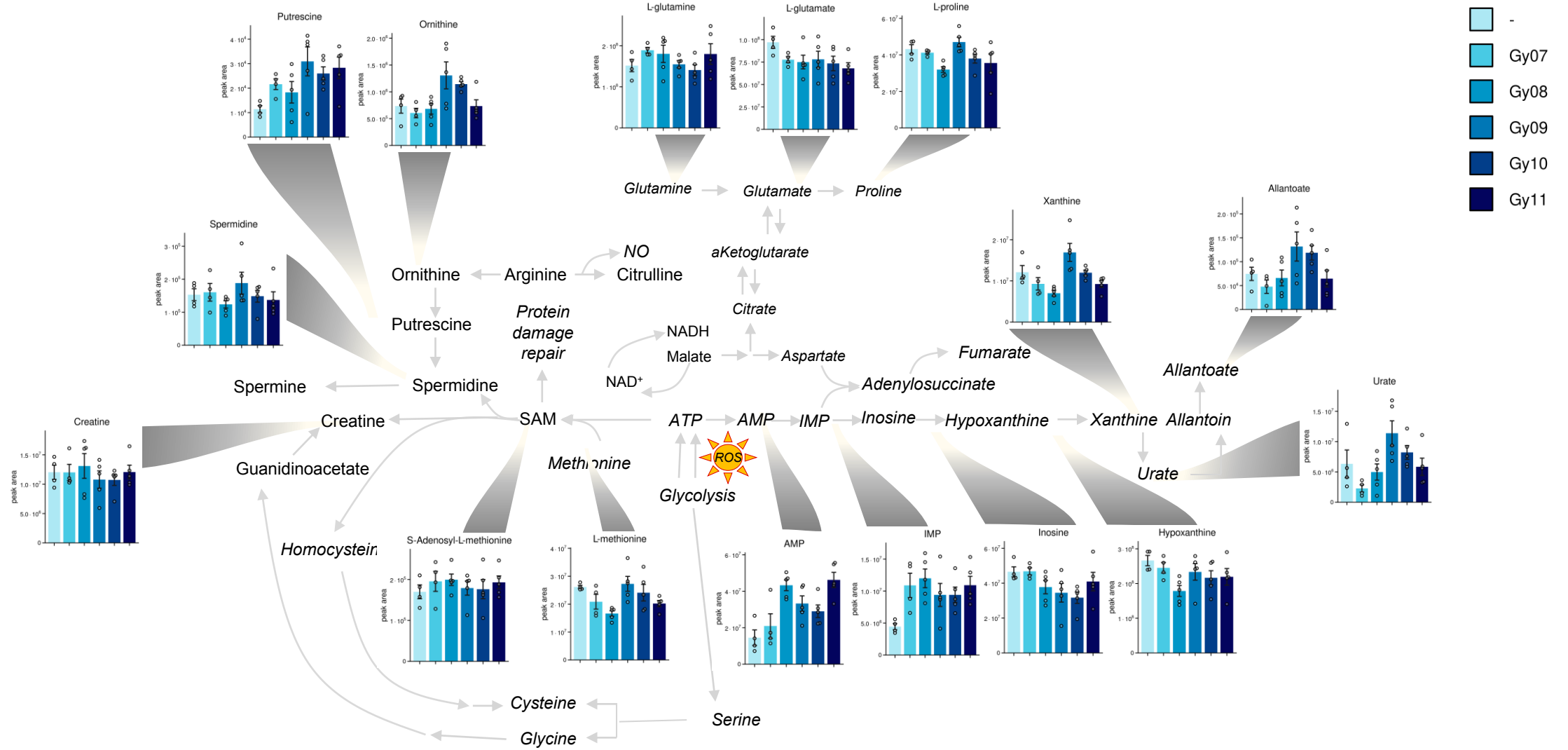


HEART

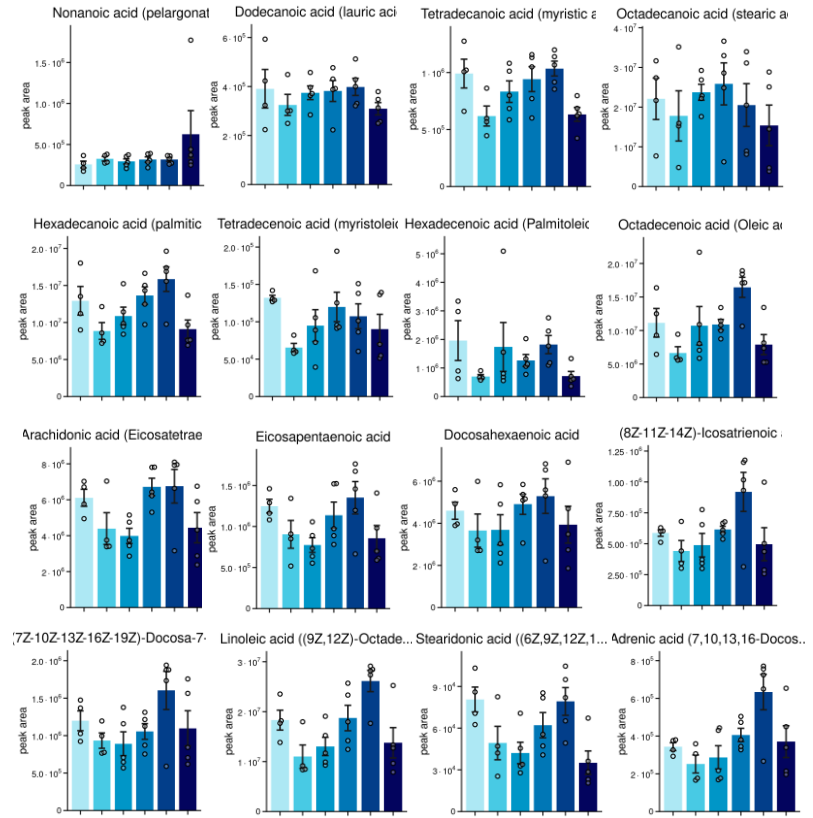
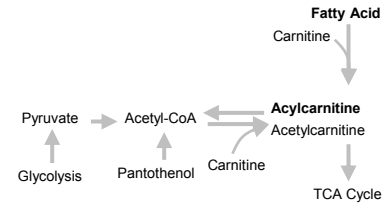


Supp Fig 1.P – Bar plots on the impact of radiation on the TCA cycle, glycolysis and pathway analysis of top metabolic effects in the heart.

HEART



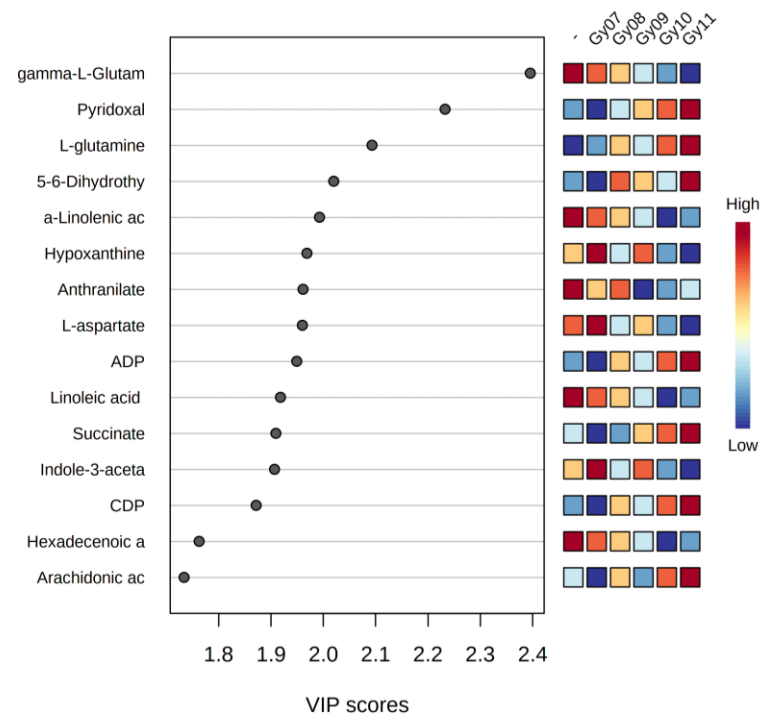
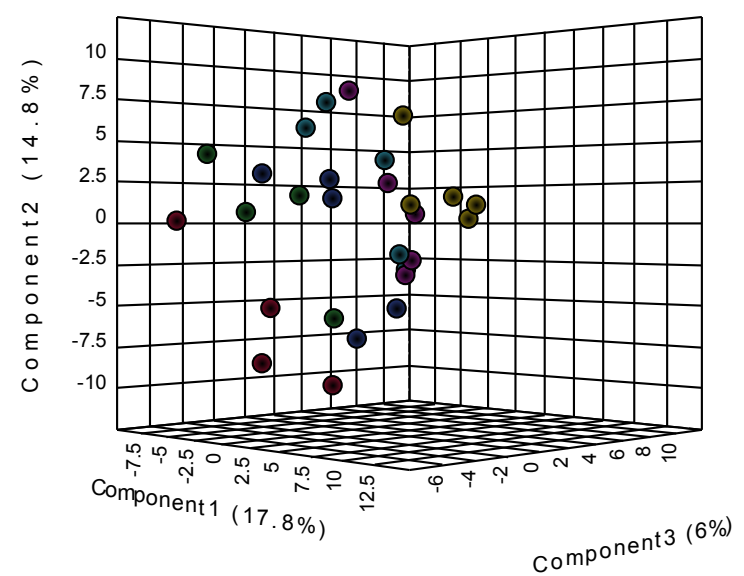
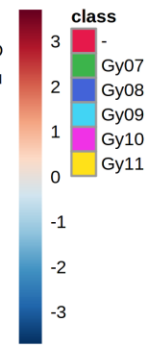
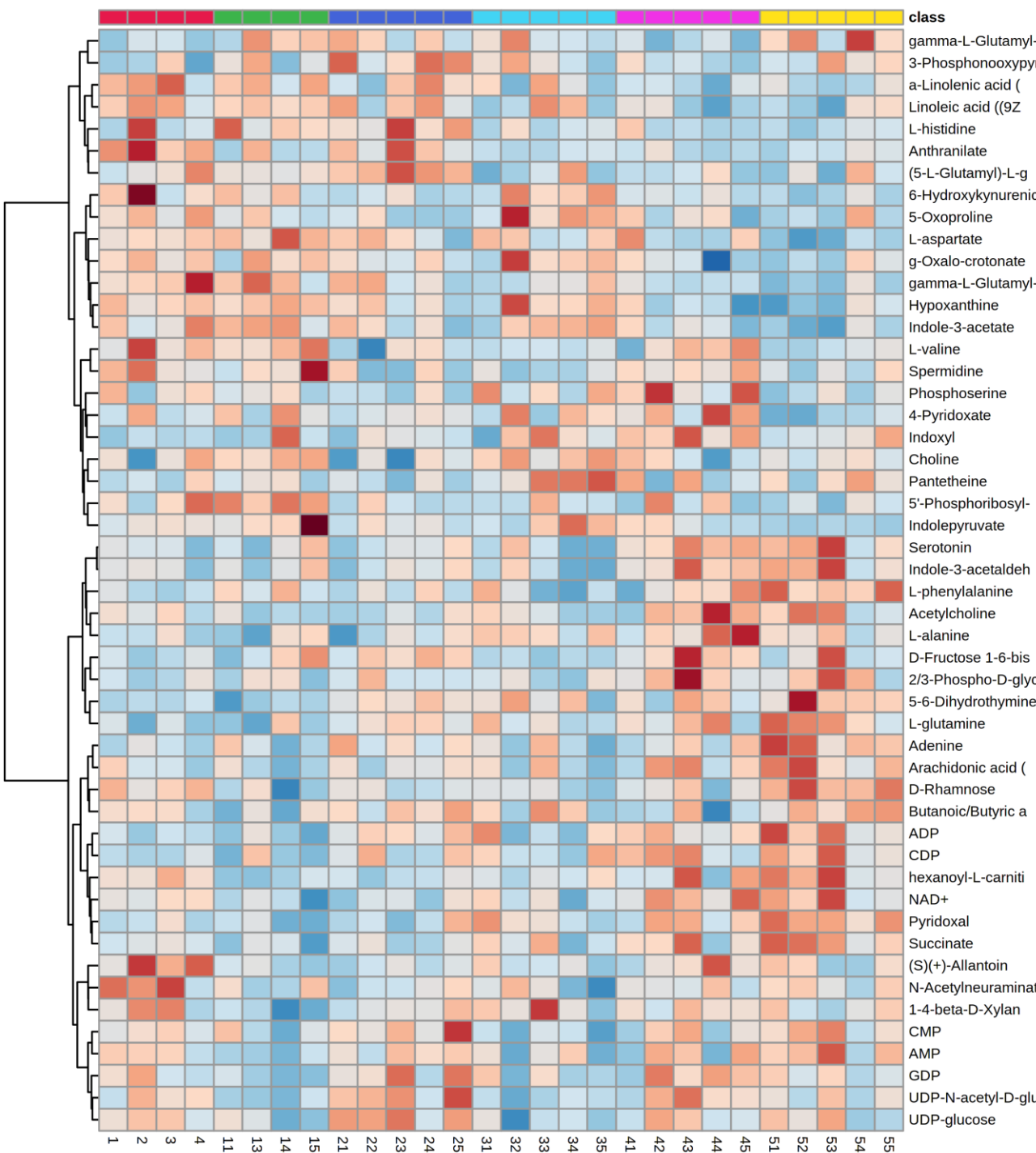
Supp Fig 1.Q – Bar plots on the impact of radiation on protein damage and repair pathways in the heart.



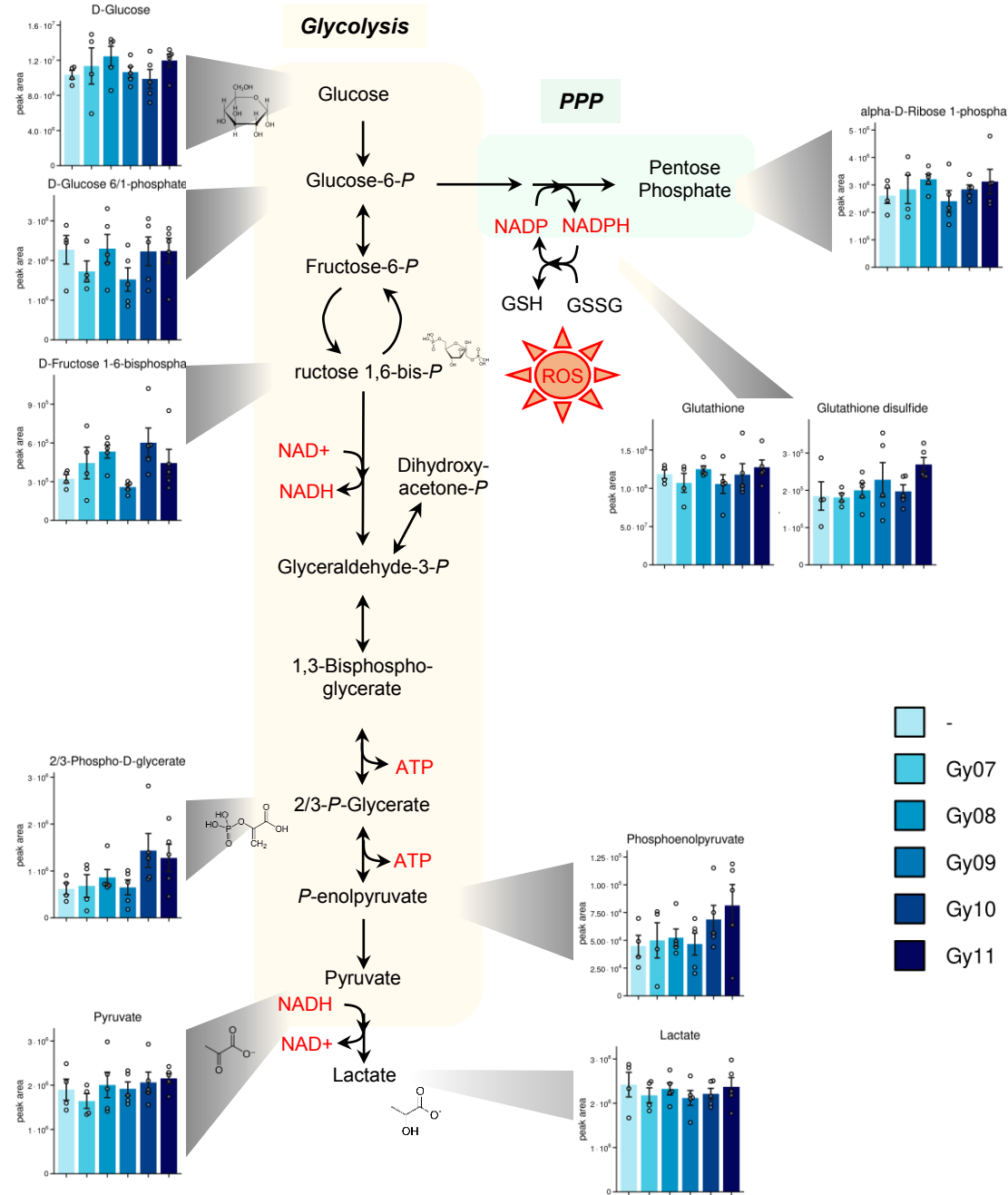
Fatty Acids

Supp Fig 1.R – Bar plots showing the impact of radiation on fatty acids in the heart.

BRAIN

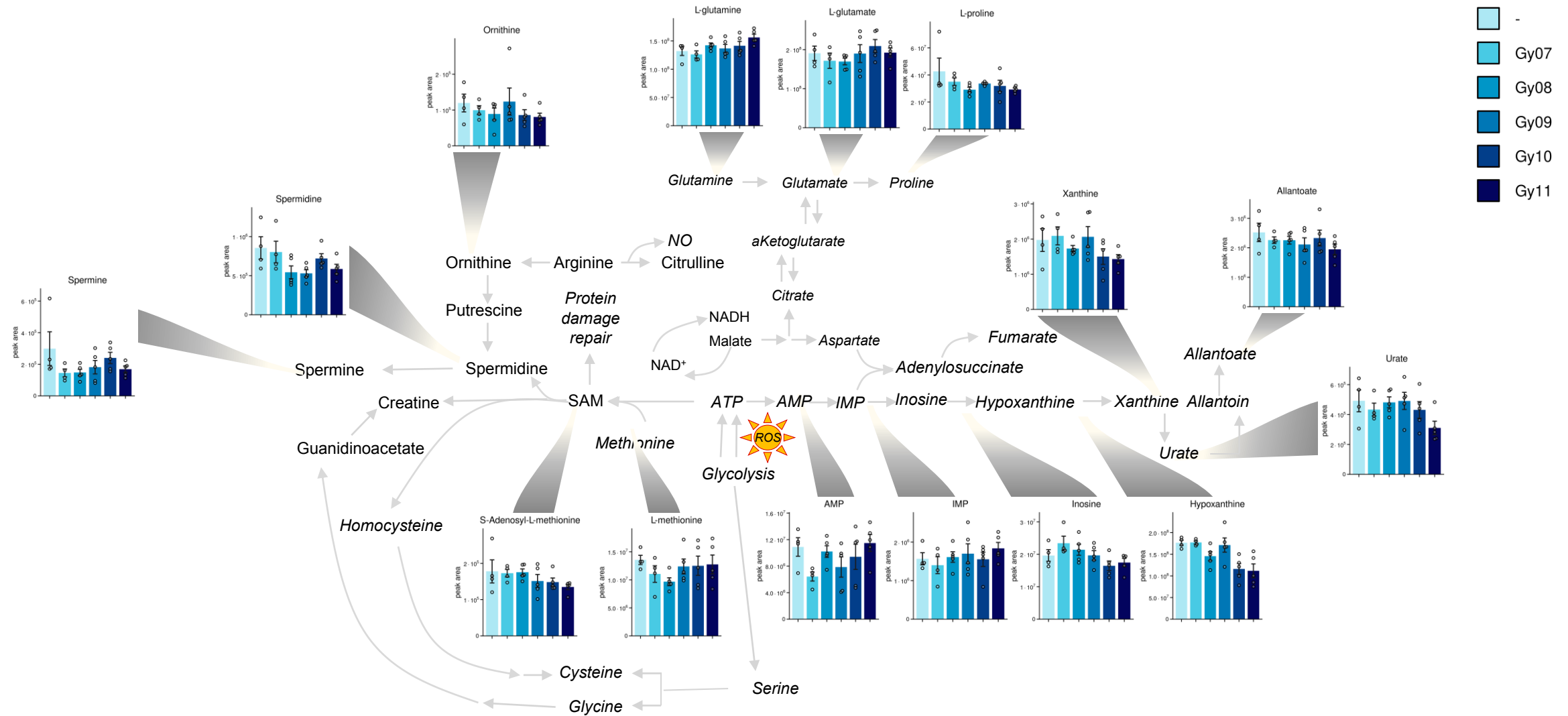


Supp Fig 1.S – Heat map (top 50 ANOVA), Principal Component Analysis and VIP Score plots for brain metabolites in response to radiation.



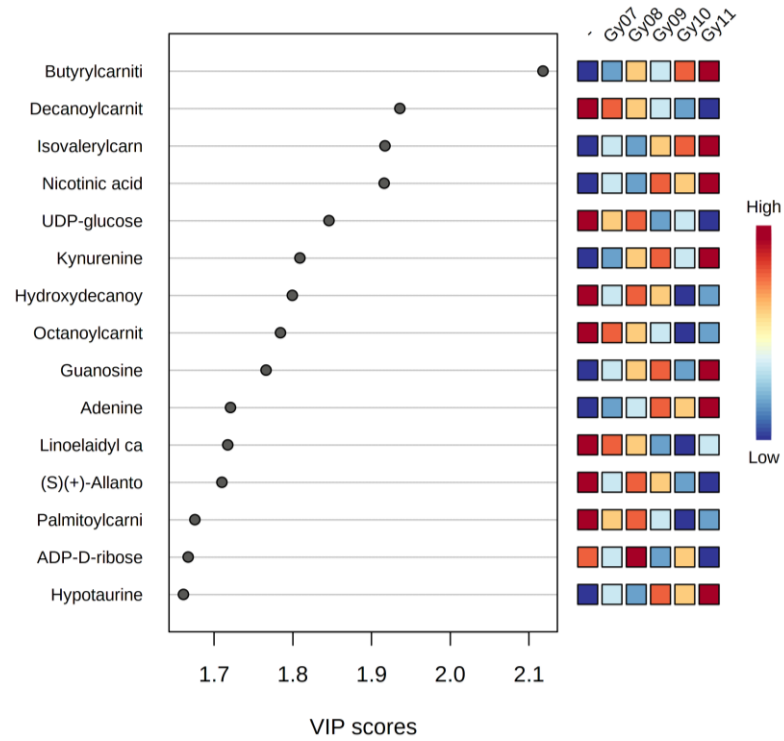
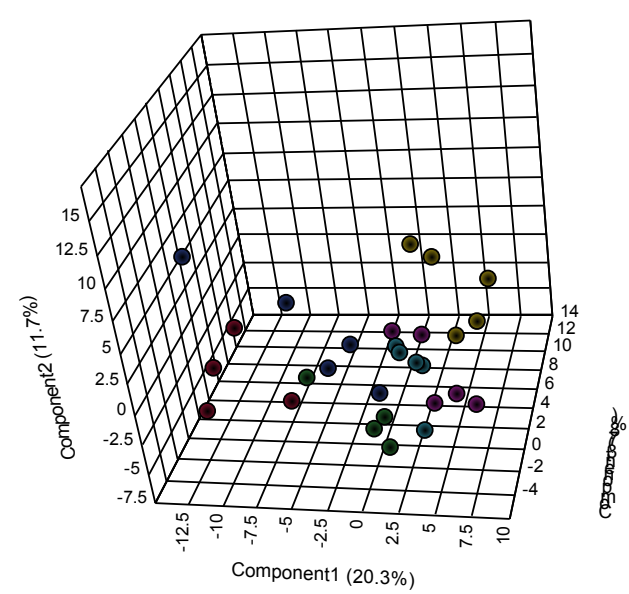
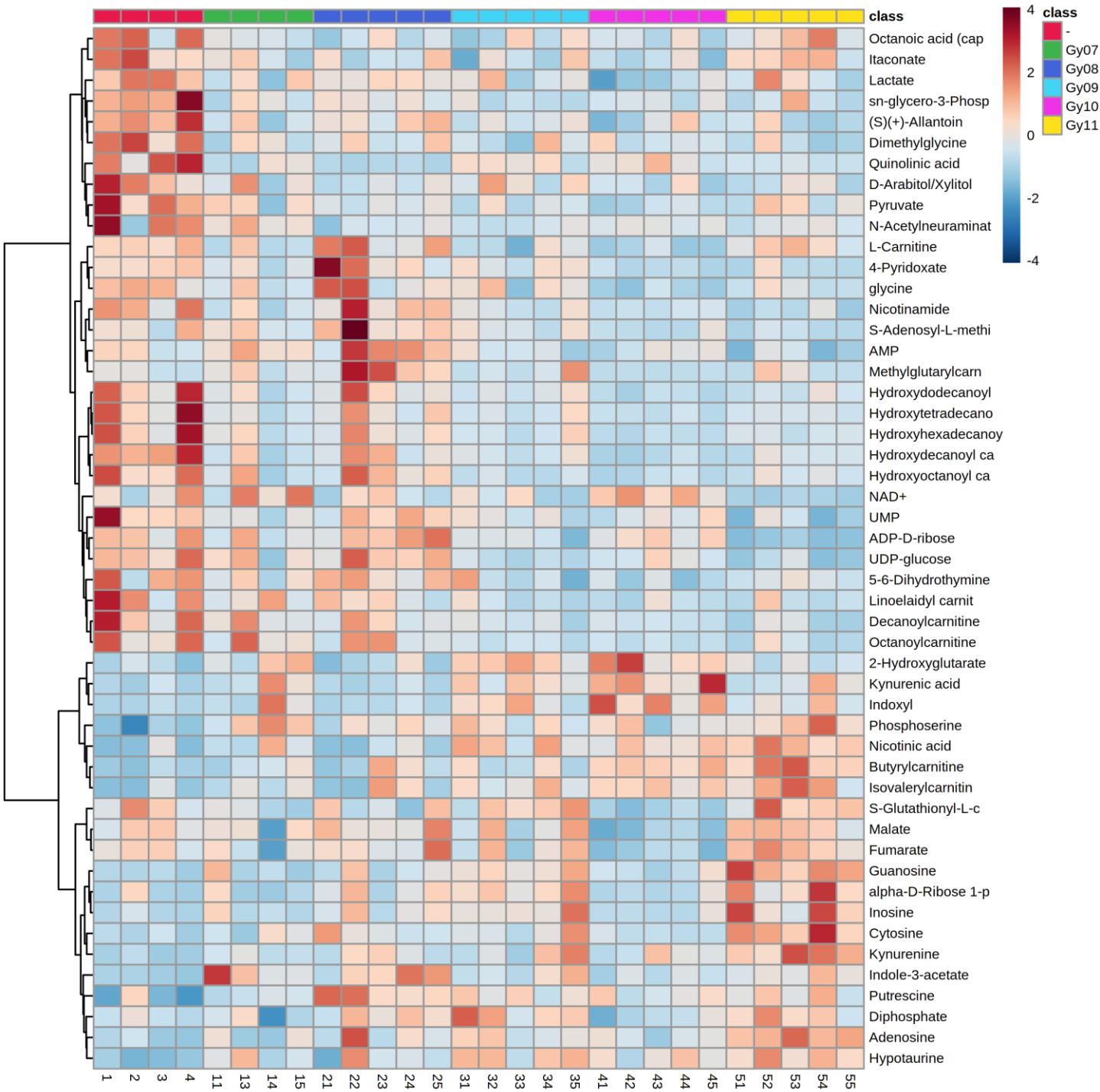
Supp Fig 1.T – Bar plots on the impact of radiation on glycolysis in the brain.

BRAIN



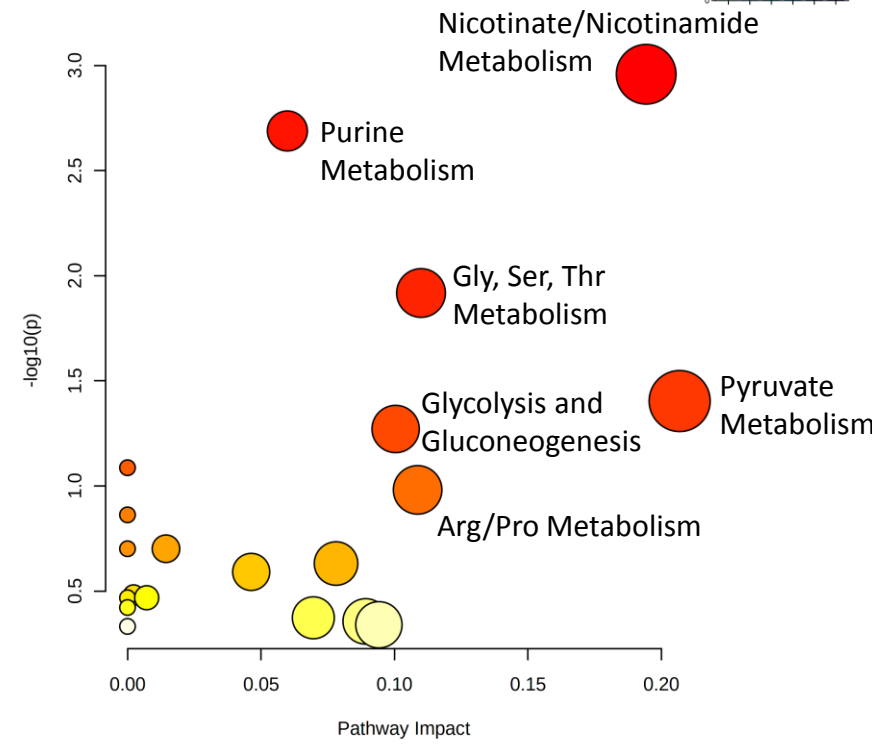
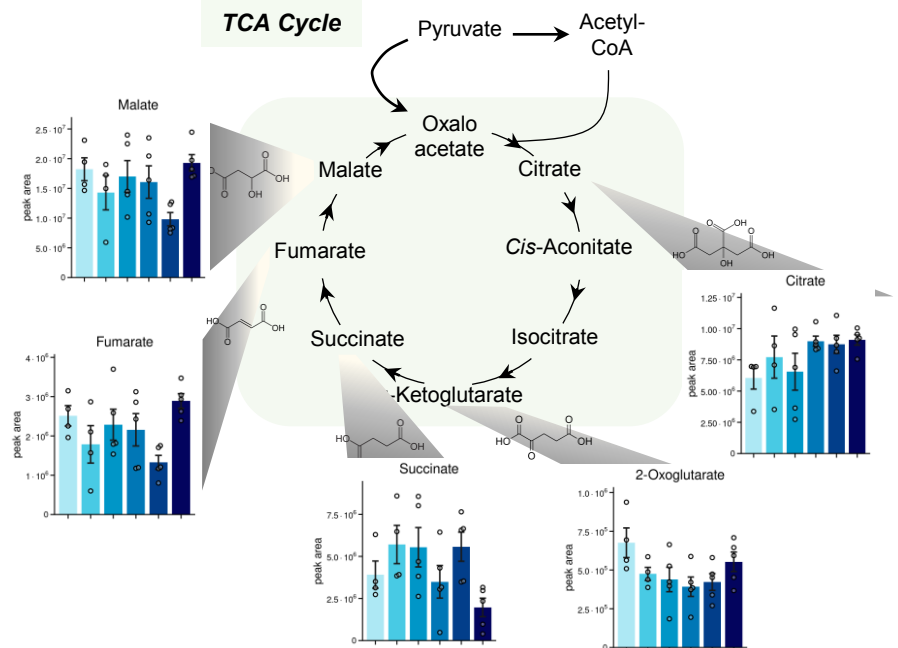
Supp Fig 1.U – Bar plots on the impact of radiation on protein damage and repair pathways in the brain.

COLON

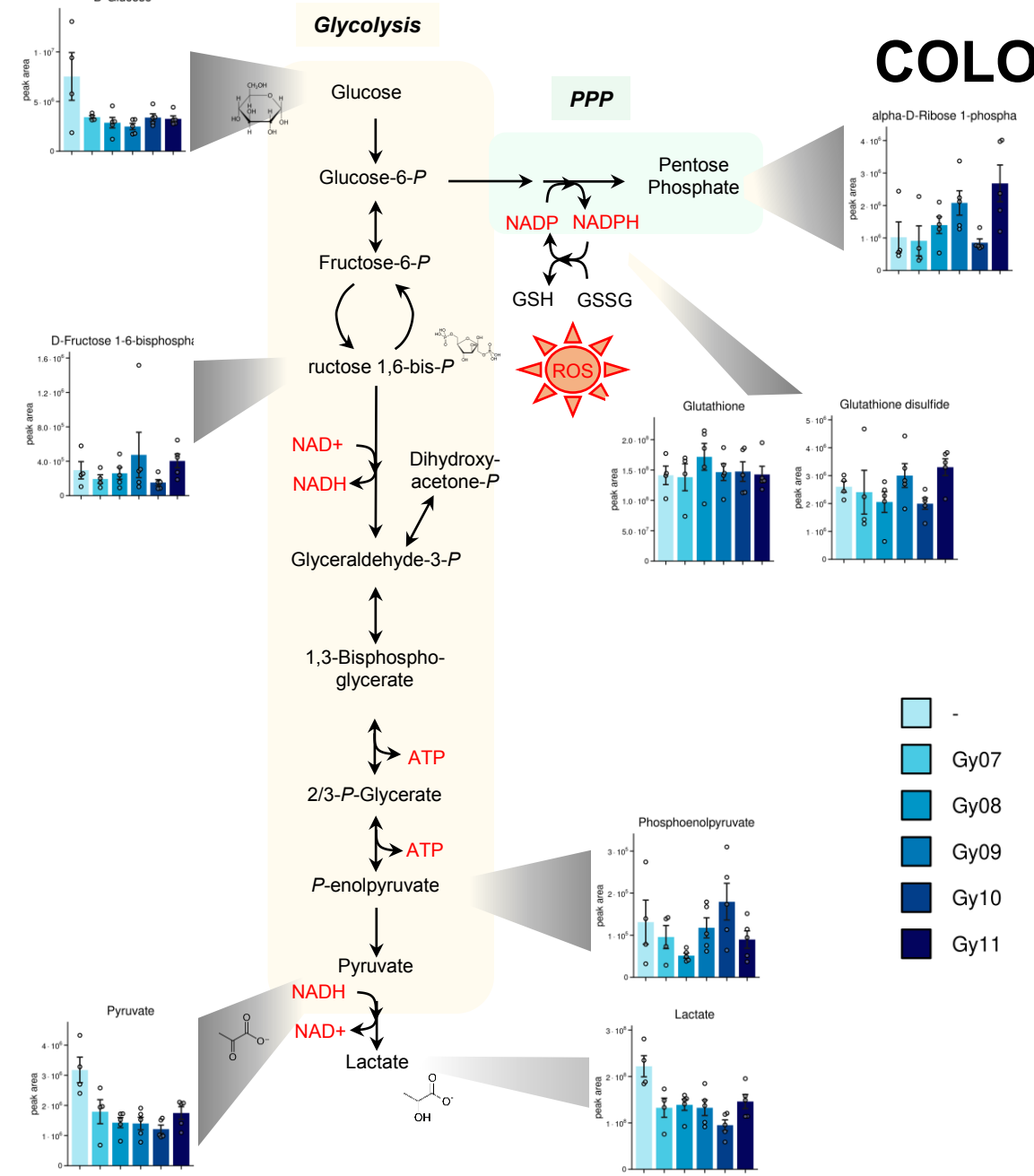


Supp Fig 1.V– Heat map (top 50 ANOVA), Principal Component Analysis and VIP Score plots for colon metabolites in response to radiation.

TCA

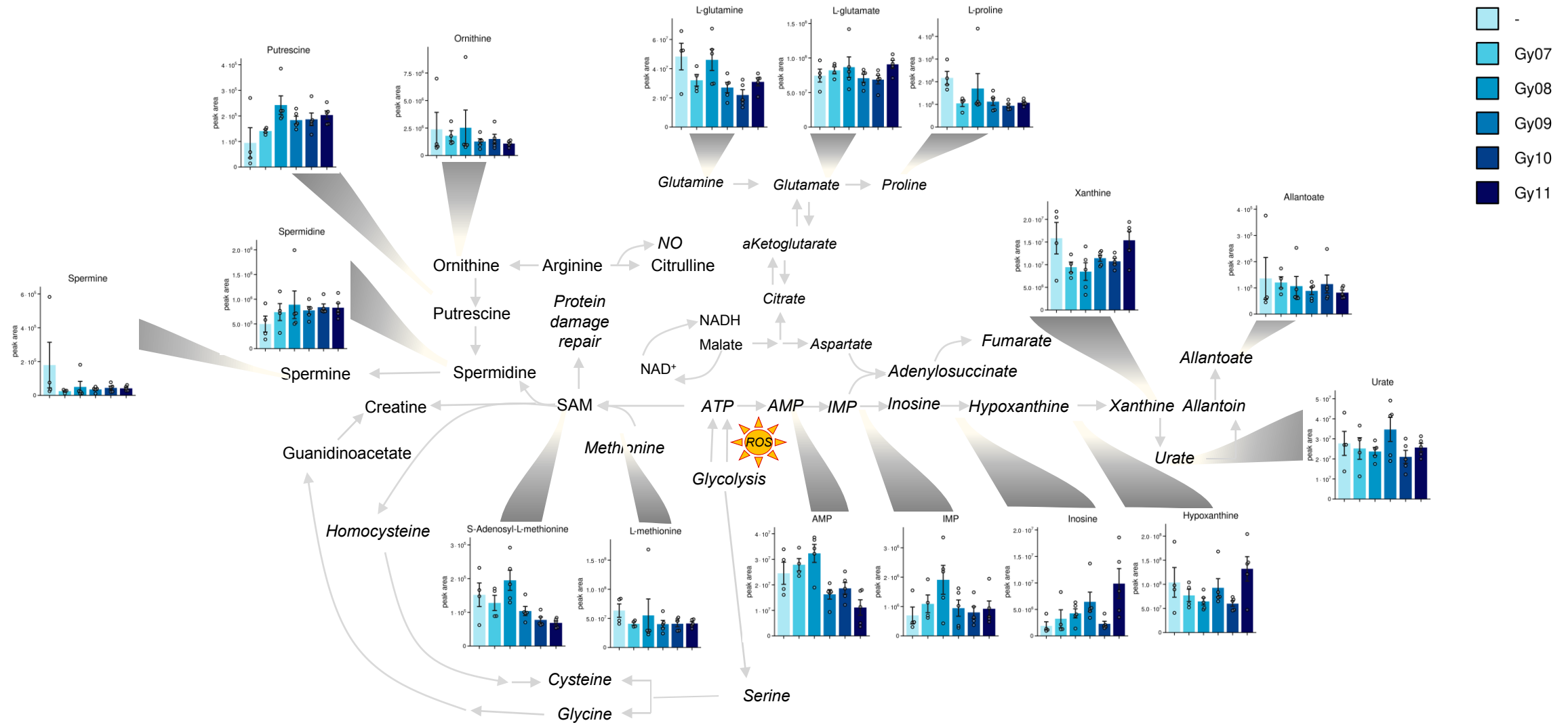


COLON

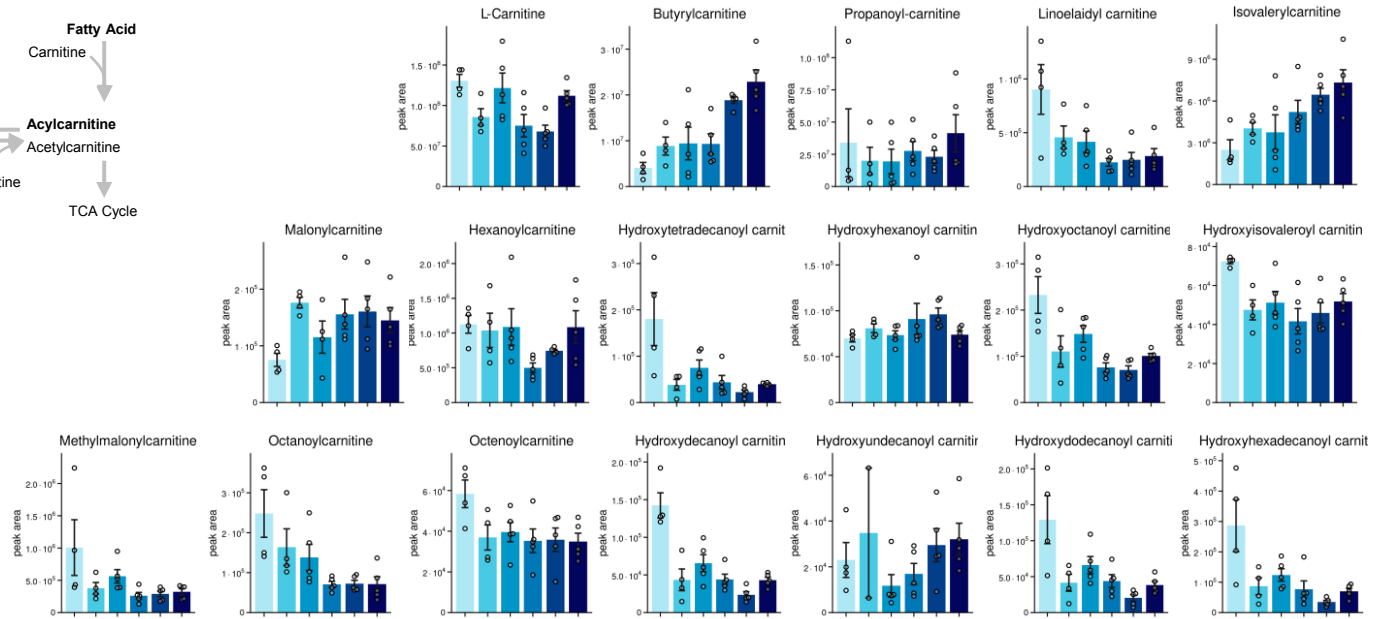
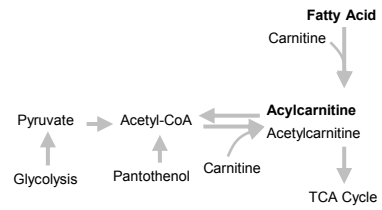


Supp Fig 1.W – Bar plots on the impact of radiation on the TCA cycle, glycolysis and pathway analysis of top metabolic effects in the colon.

COLON

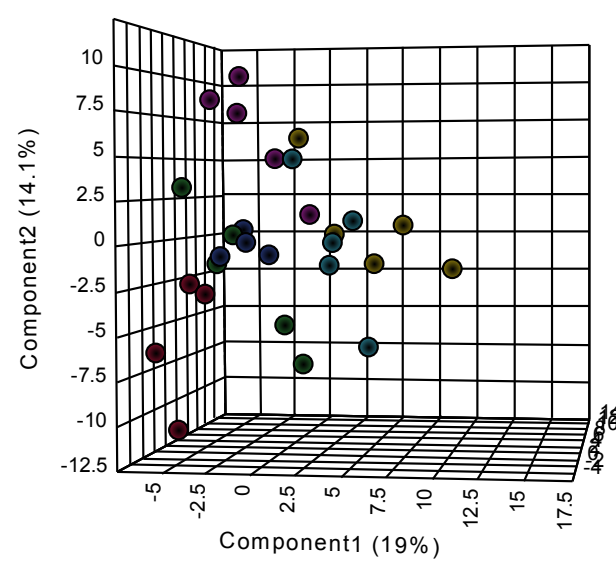
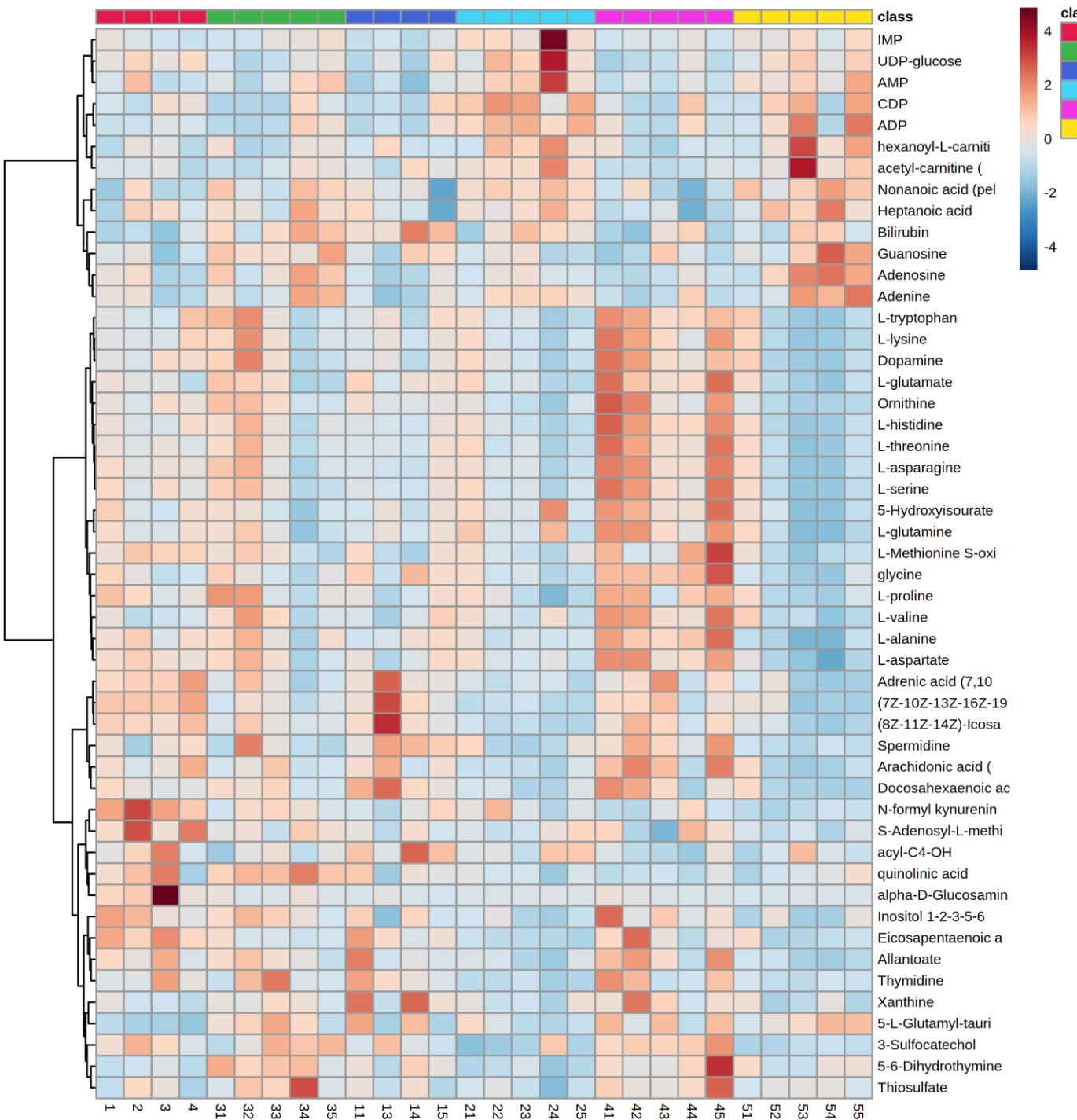


Supp Fig 1.X – Bar plots on the impact of radiation on protein damage and repair pathways in the colon.

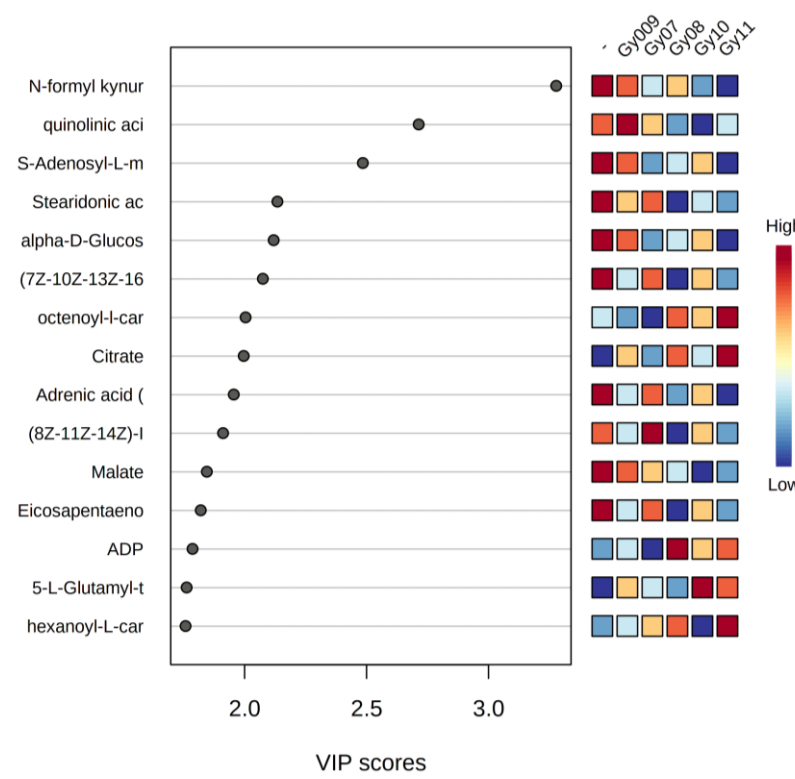


Acylcarnitines

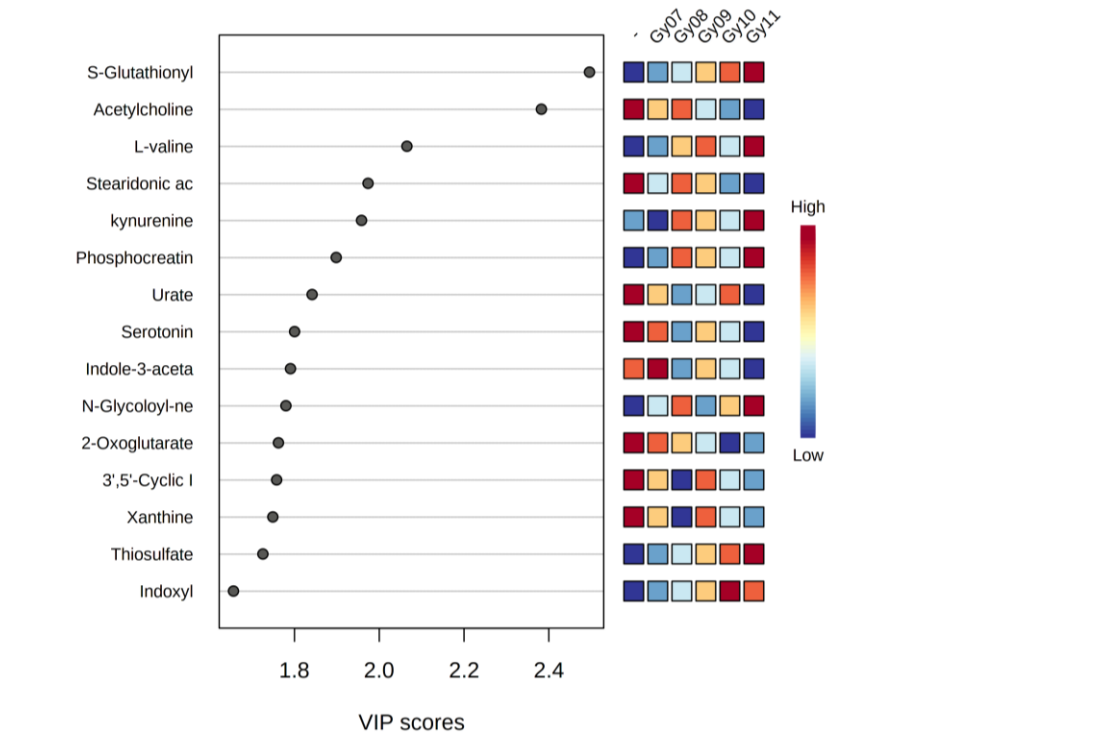
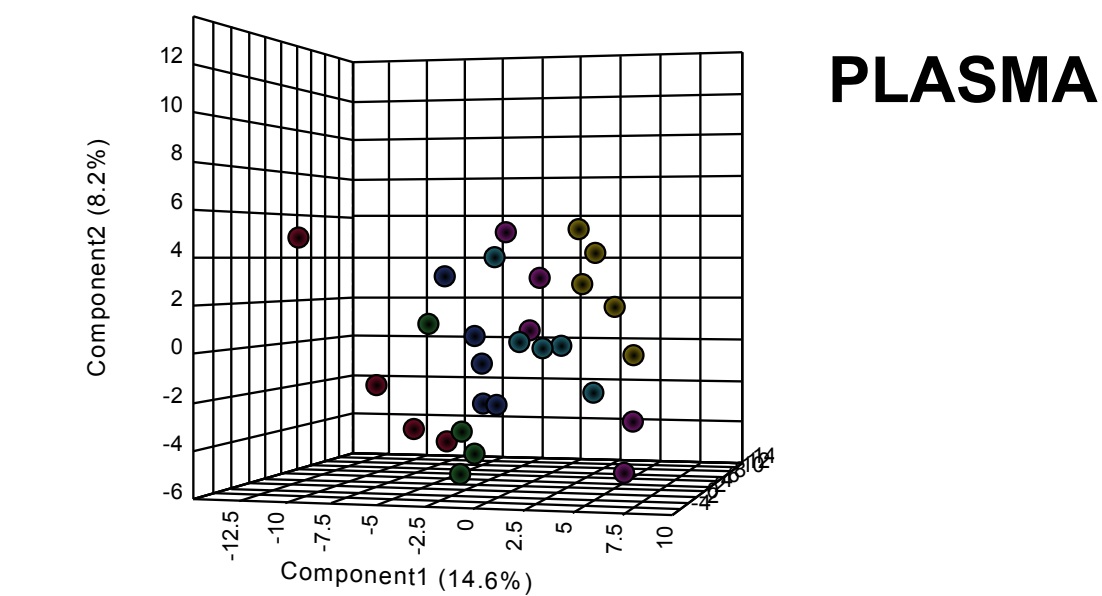
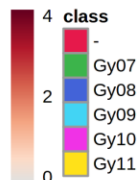
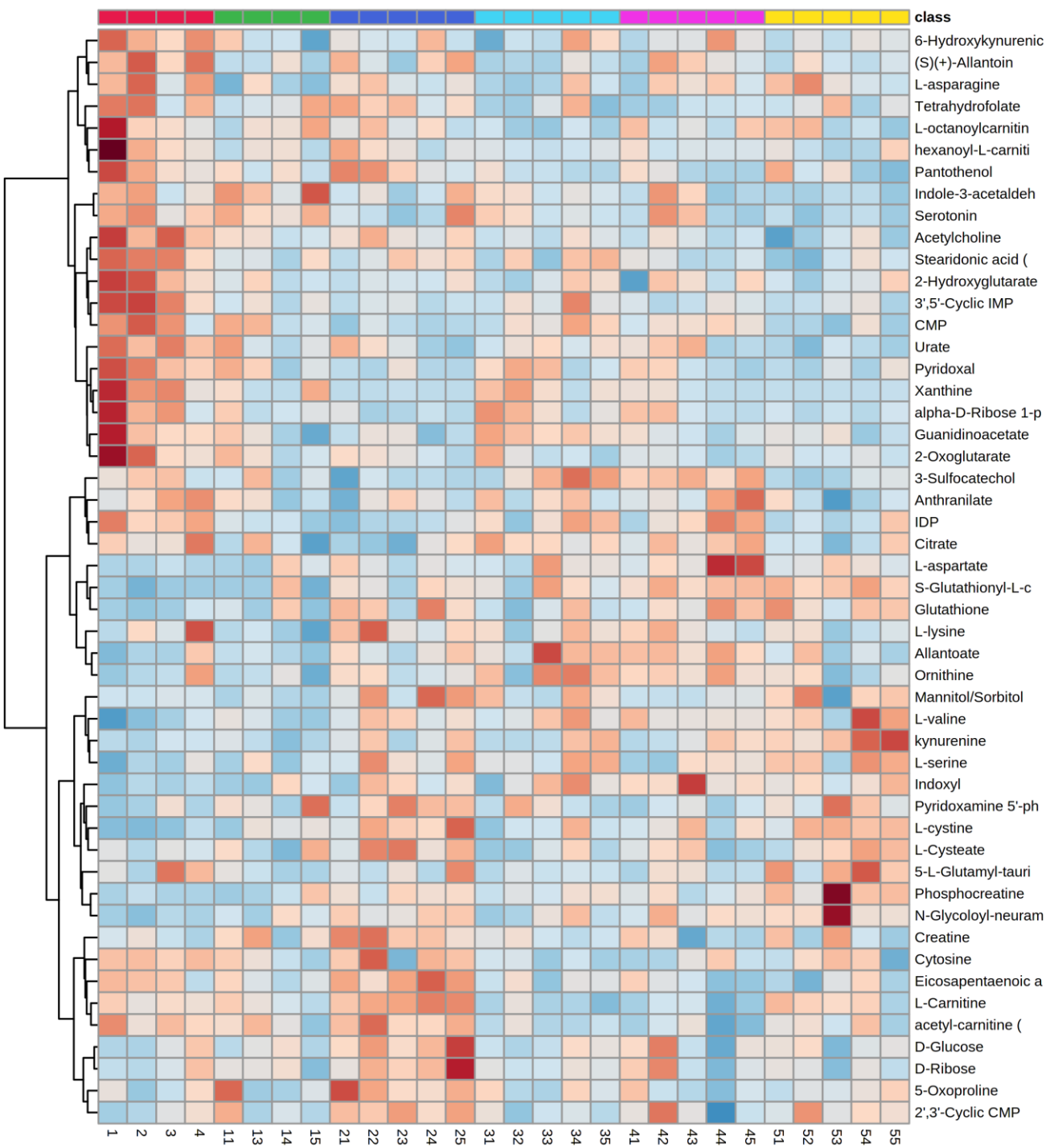
Supp Fig 1.Y – Bar plots showing the impact of radiation on acylcarnitines in the colon.



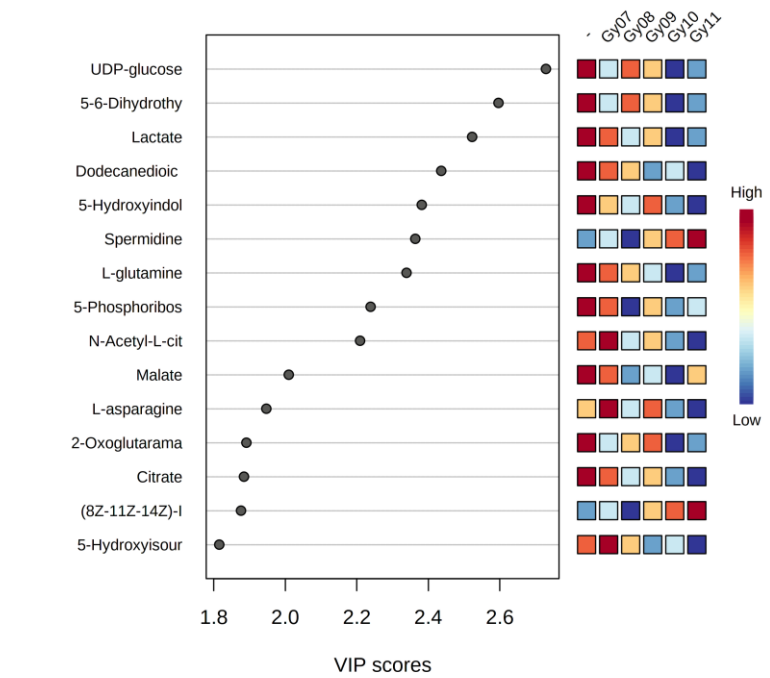
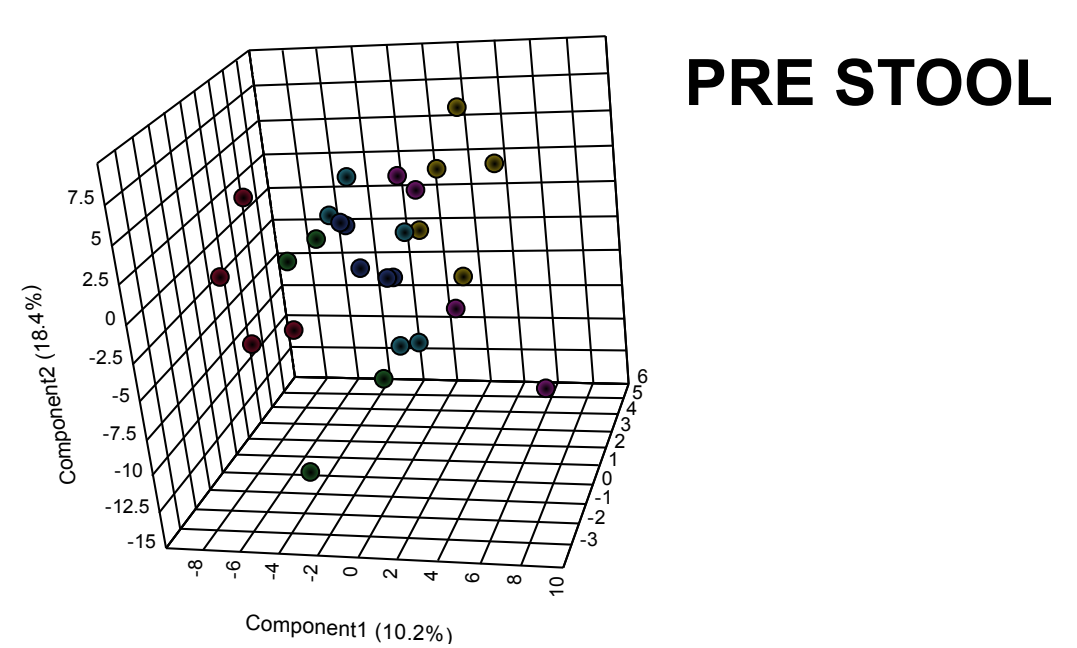
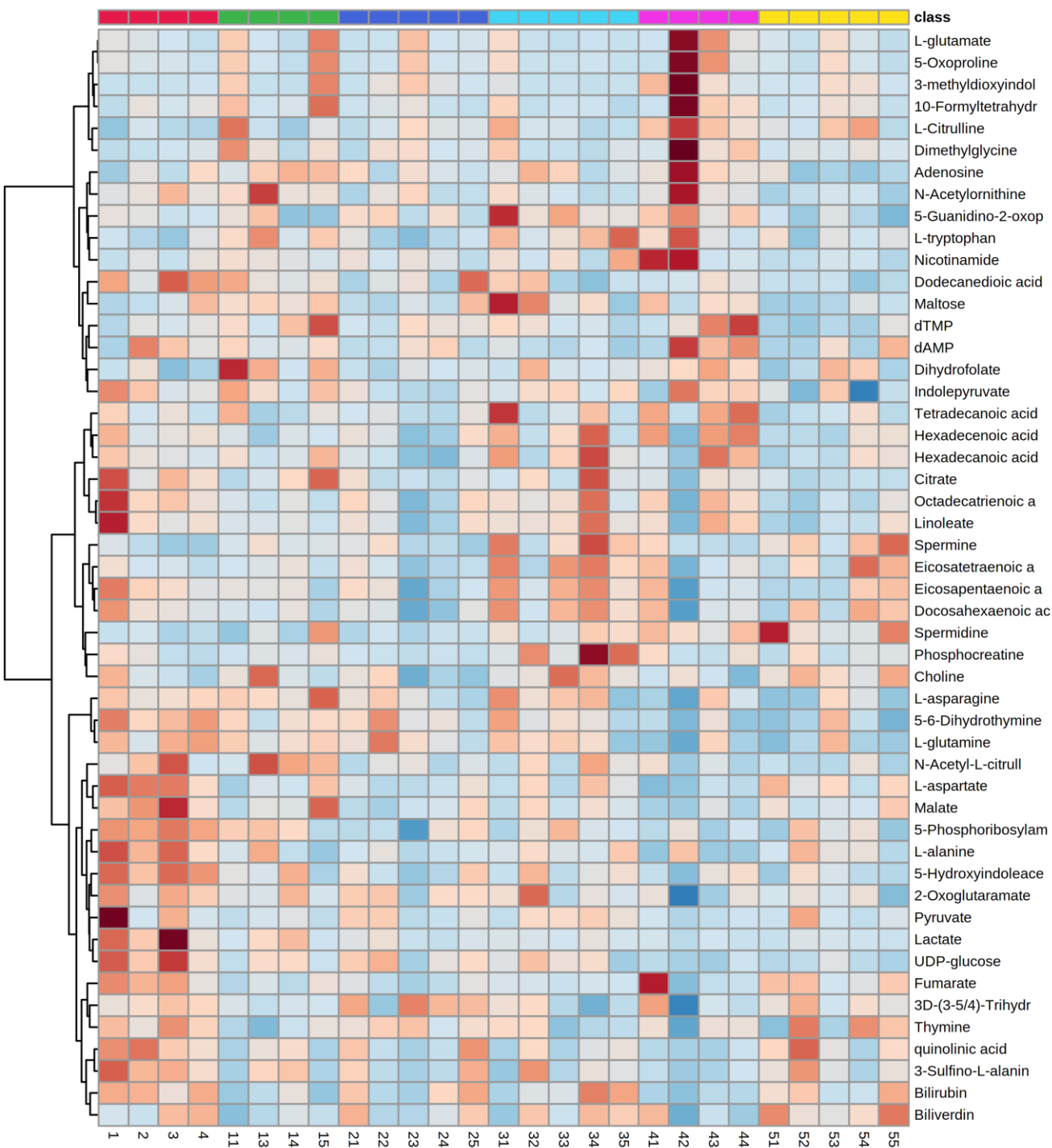
DUODENUM



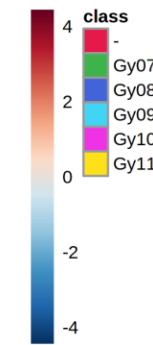
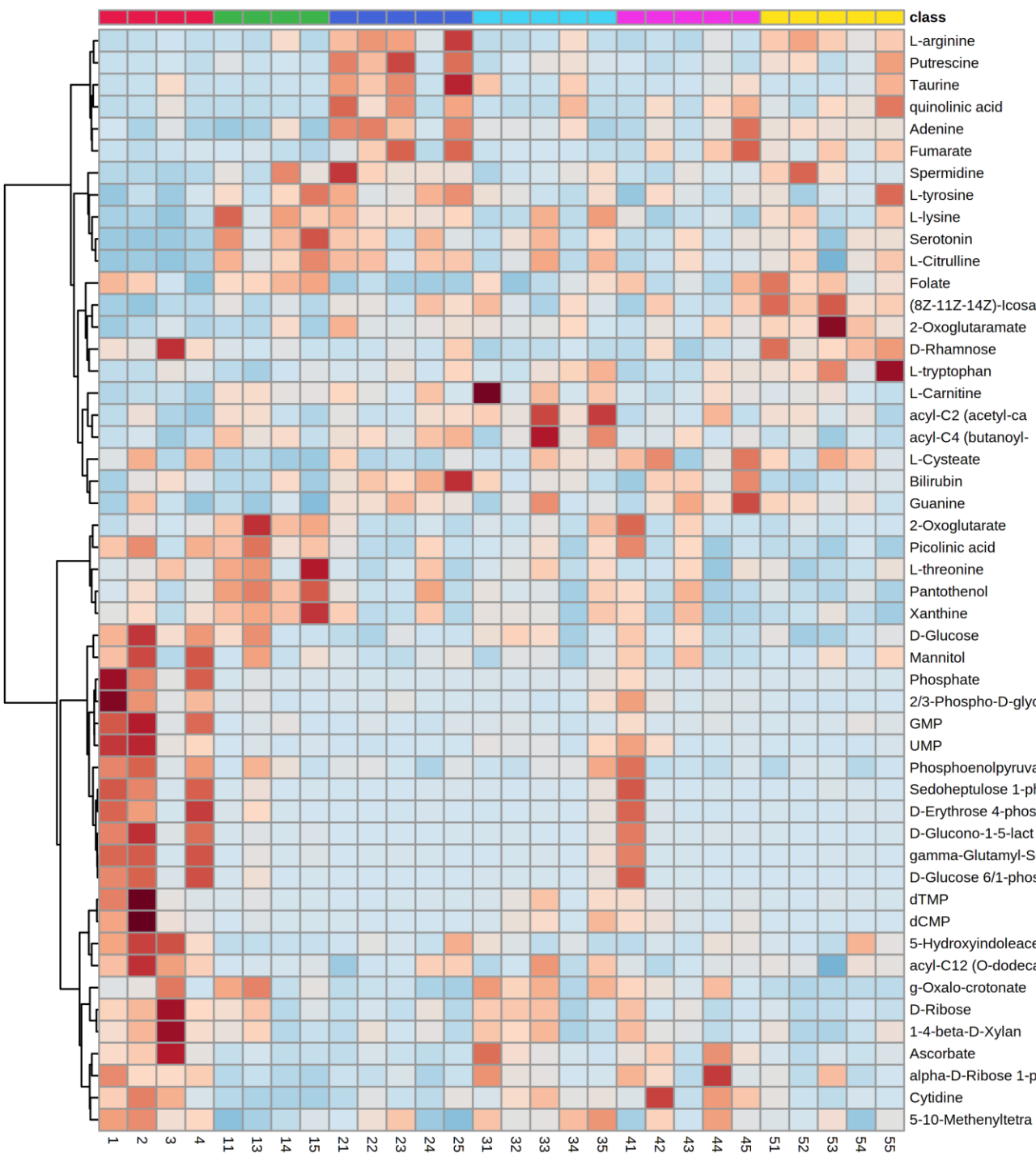
Supp Fig 1.Z– Heat map (top 50 ANOVA), Principal Component Analysis and VIP Score plots for duodenum metabolites in response to radiation.



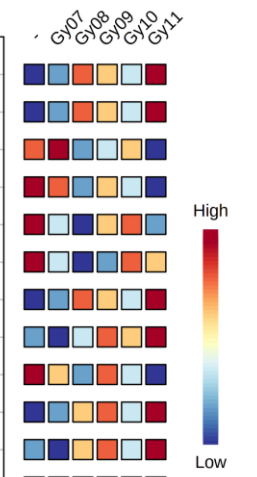
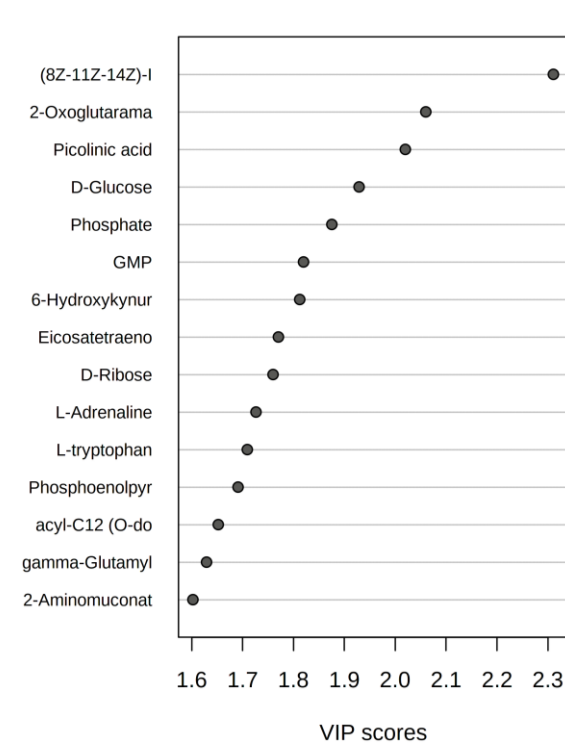
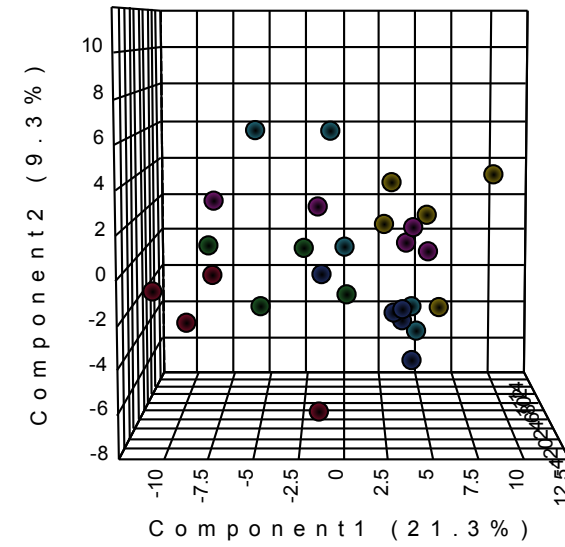
Supp Fig 1.AA– Heat map (top 50 ANOVA), Principal Component Analysis and VIP Score plots for plasma metabolites in response to radiation.



Supp Fig 1.BB– Heat map (top 50 ANOVA), Principal Component Analysis and VIP Score plots for stool metabolites prior to radiation (pre-stool).

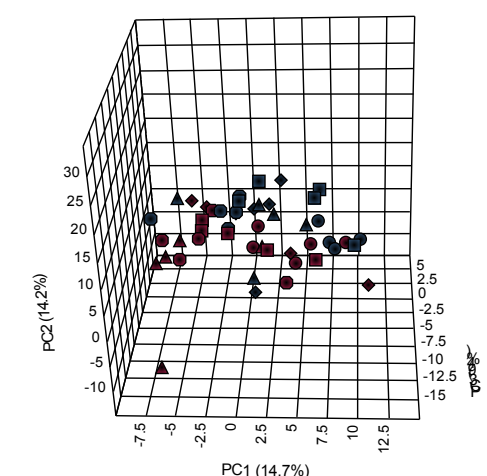
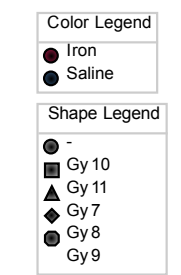
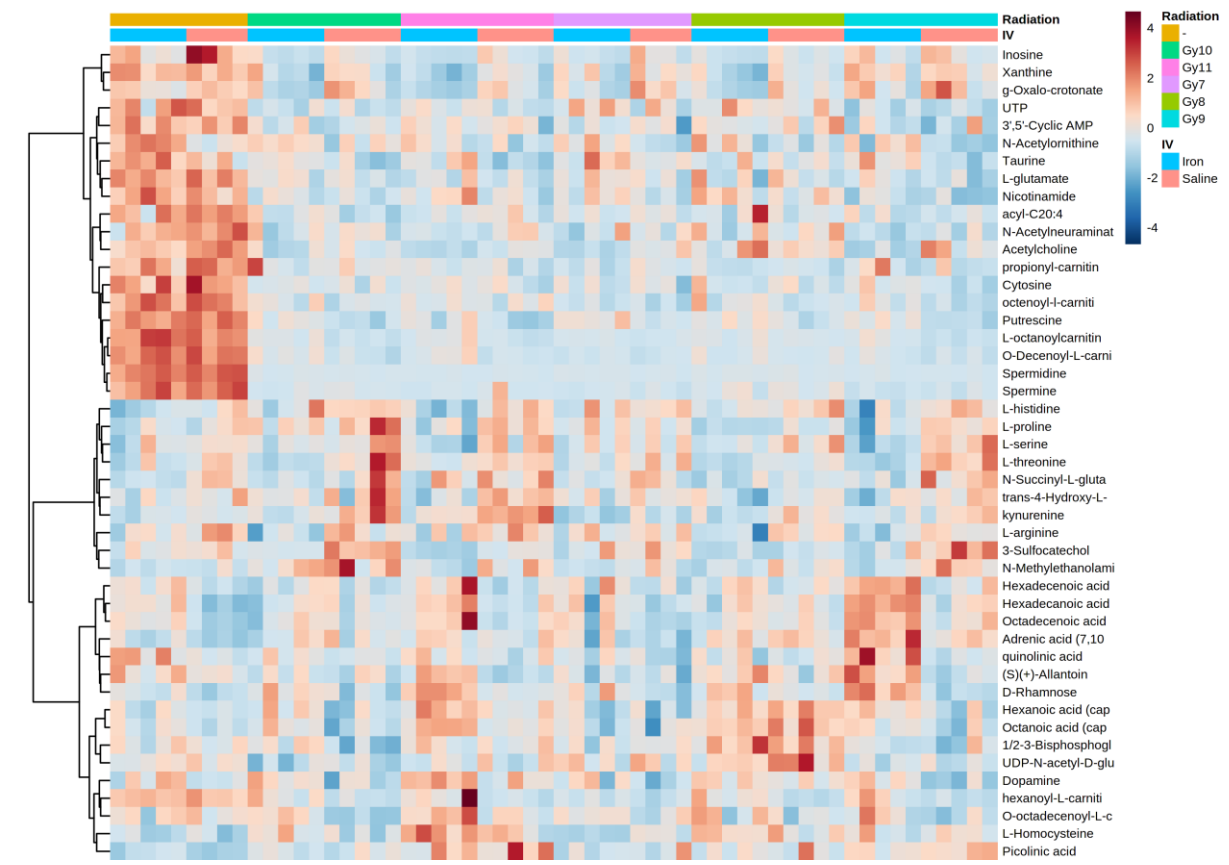
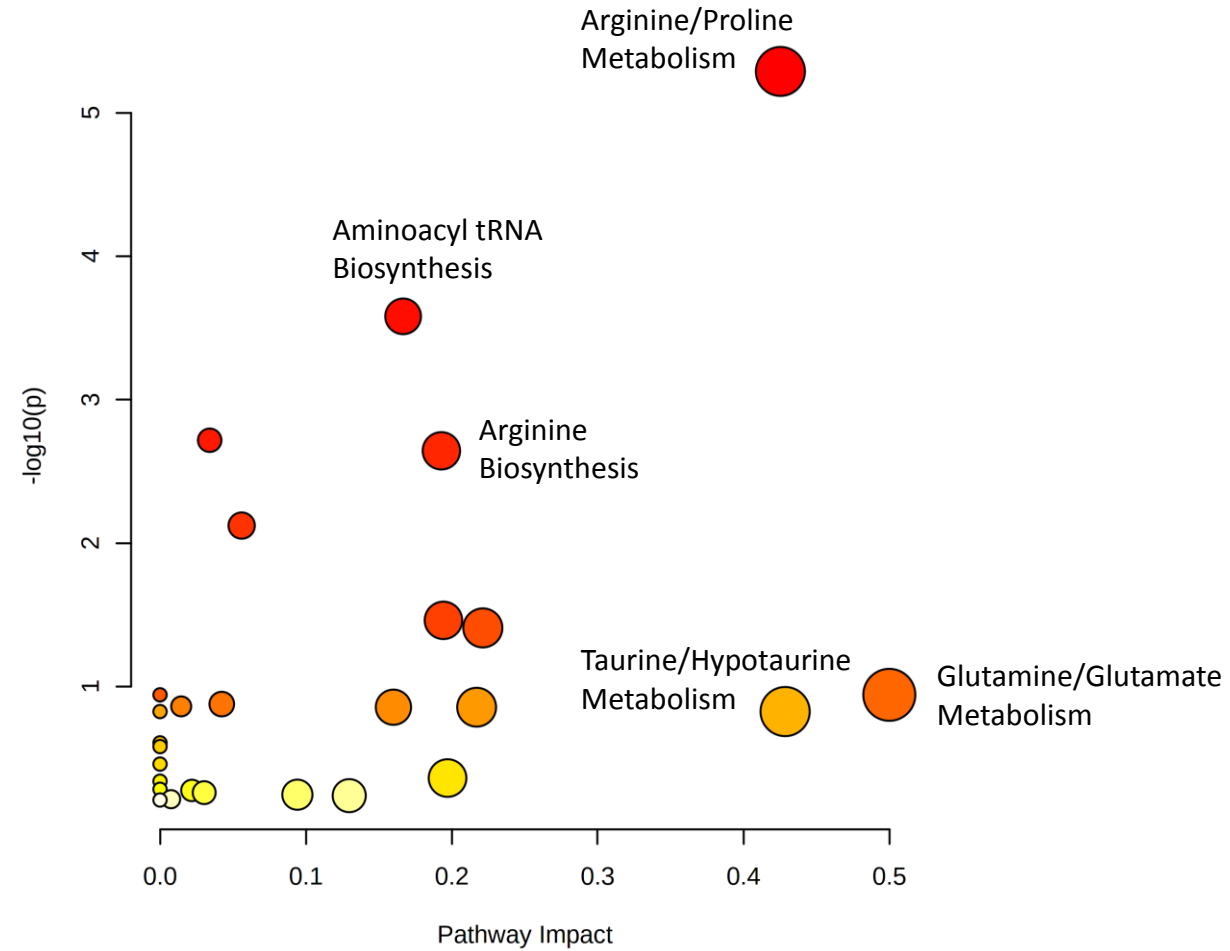


POST STOOL



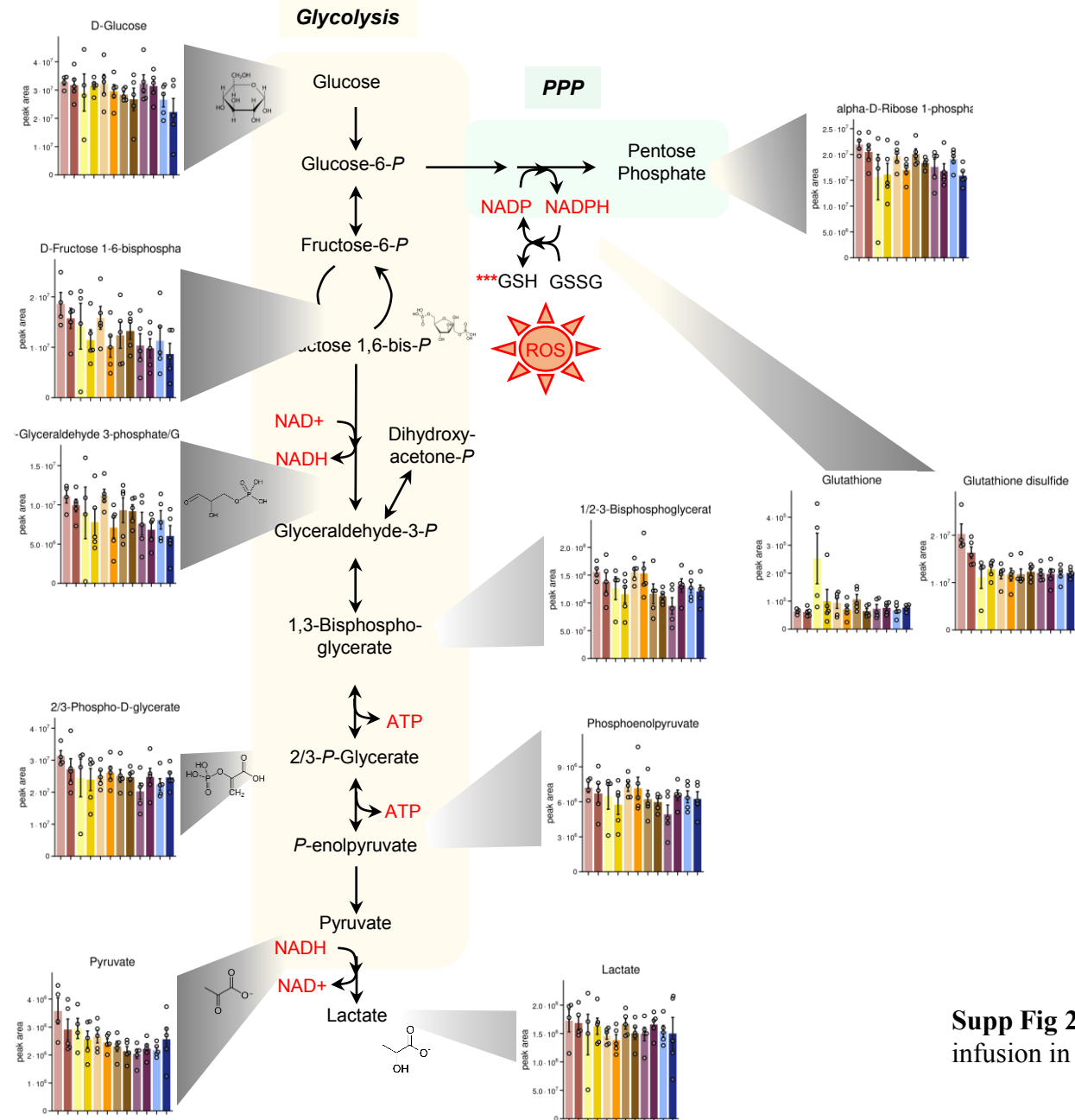
Supp Fig 1.CC– Heat map (top 50 ANOVA), Principal Component Analysis and VIP Score plots for stool metabolites in response to radiation (post-stool).

RBC

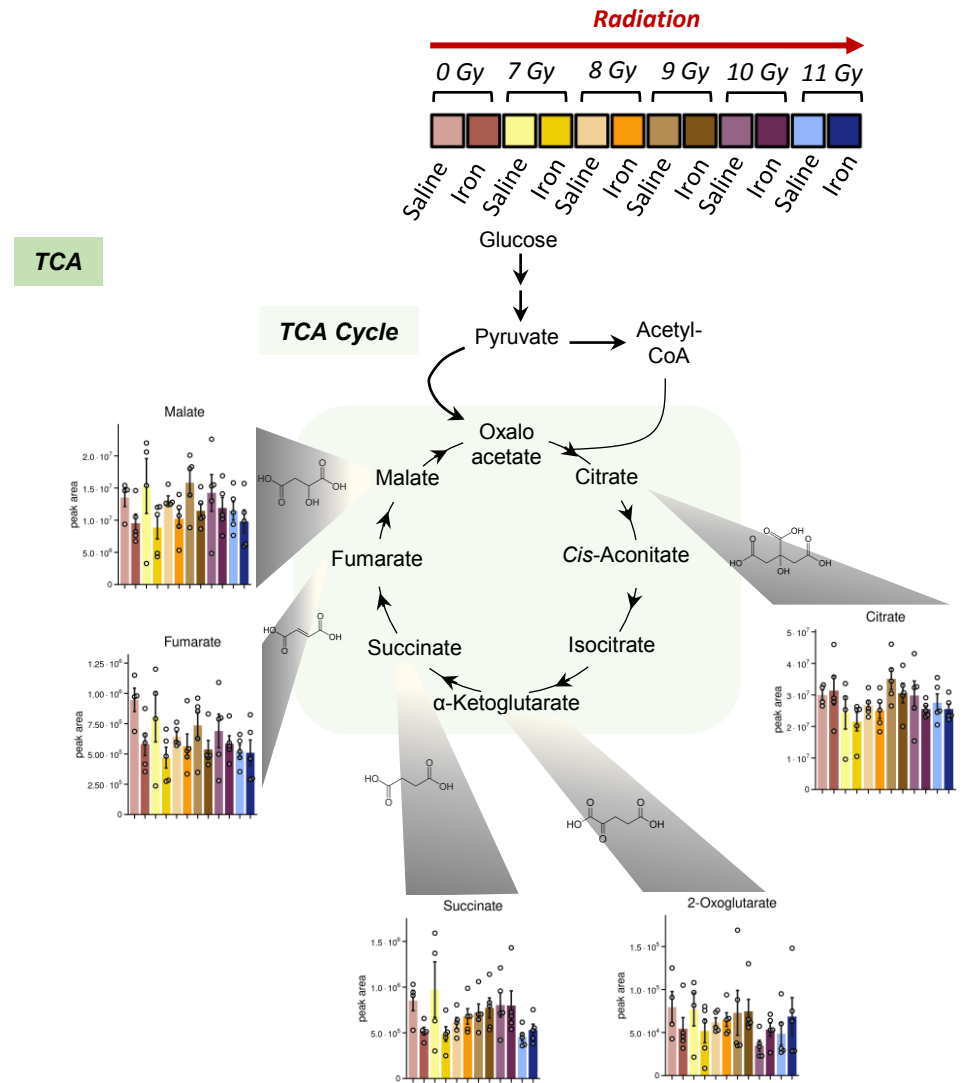


Supp Fig 2.A – Heat map (features significant by ANOVA), Principal Component Analysis, and Pathway Analysis of top metabolic effects for RBC metabolites in response to radiation with and without iron infusion.

Glycolysis

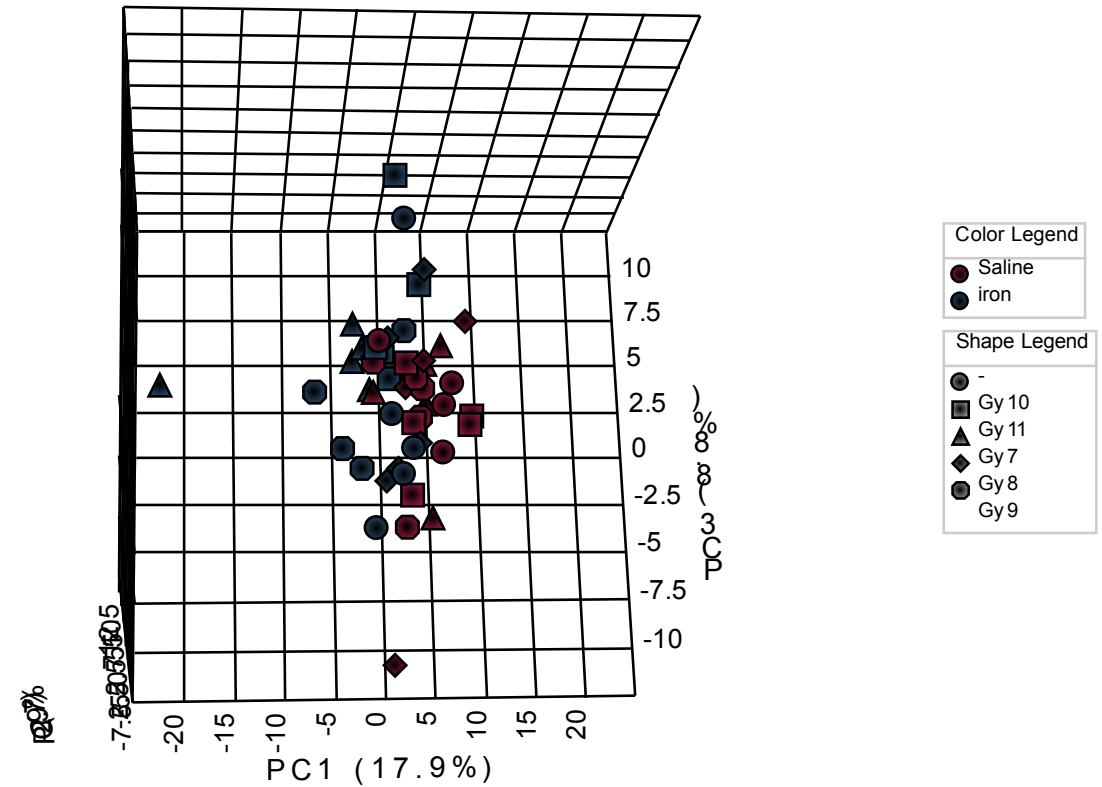
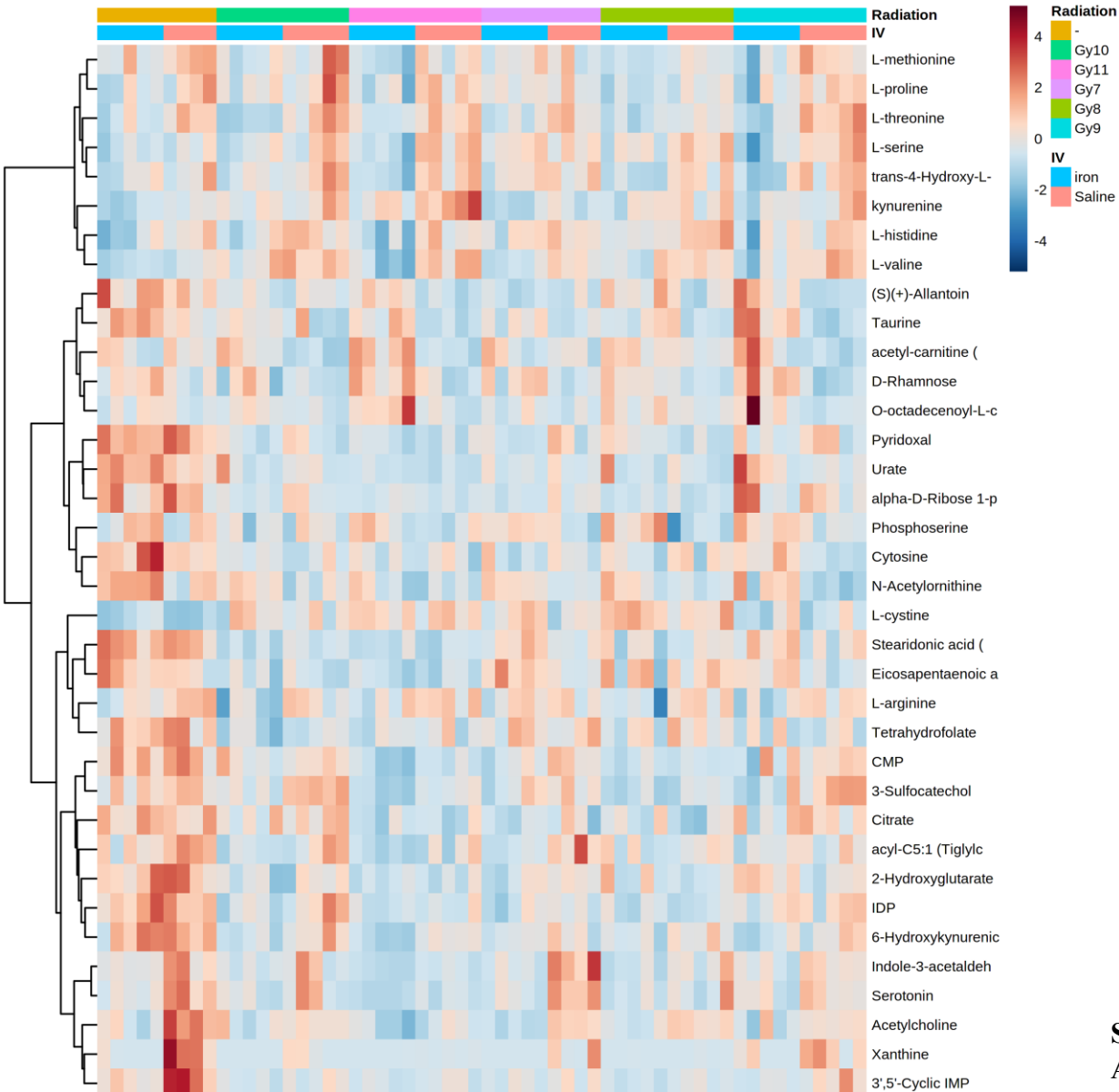


RBC



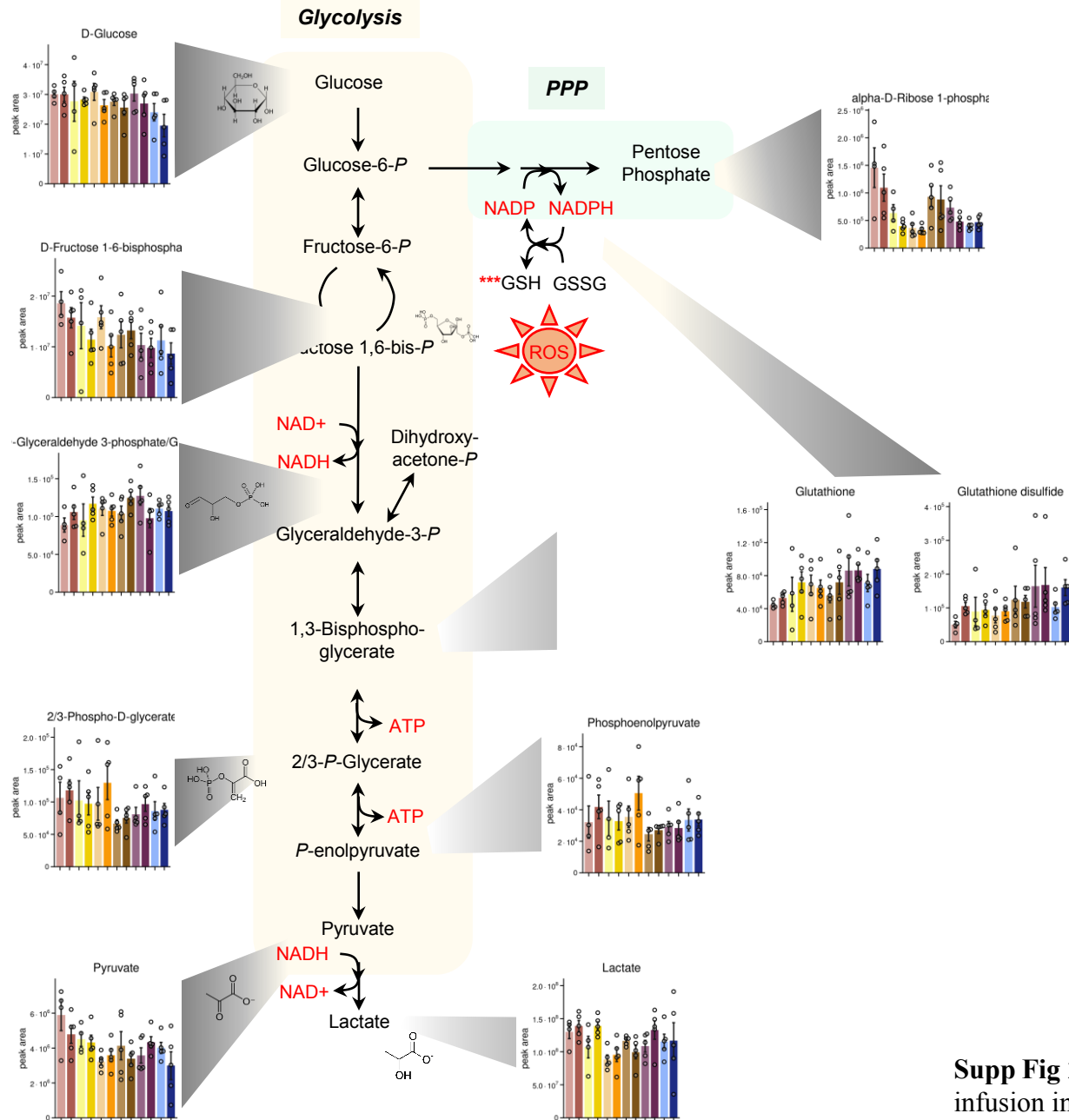
Supp Fig 2.B – Bar plots on the impact of radiation with and without iron infusion in the RBC TCA cycle and glycolysis pathway.

PLASMA

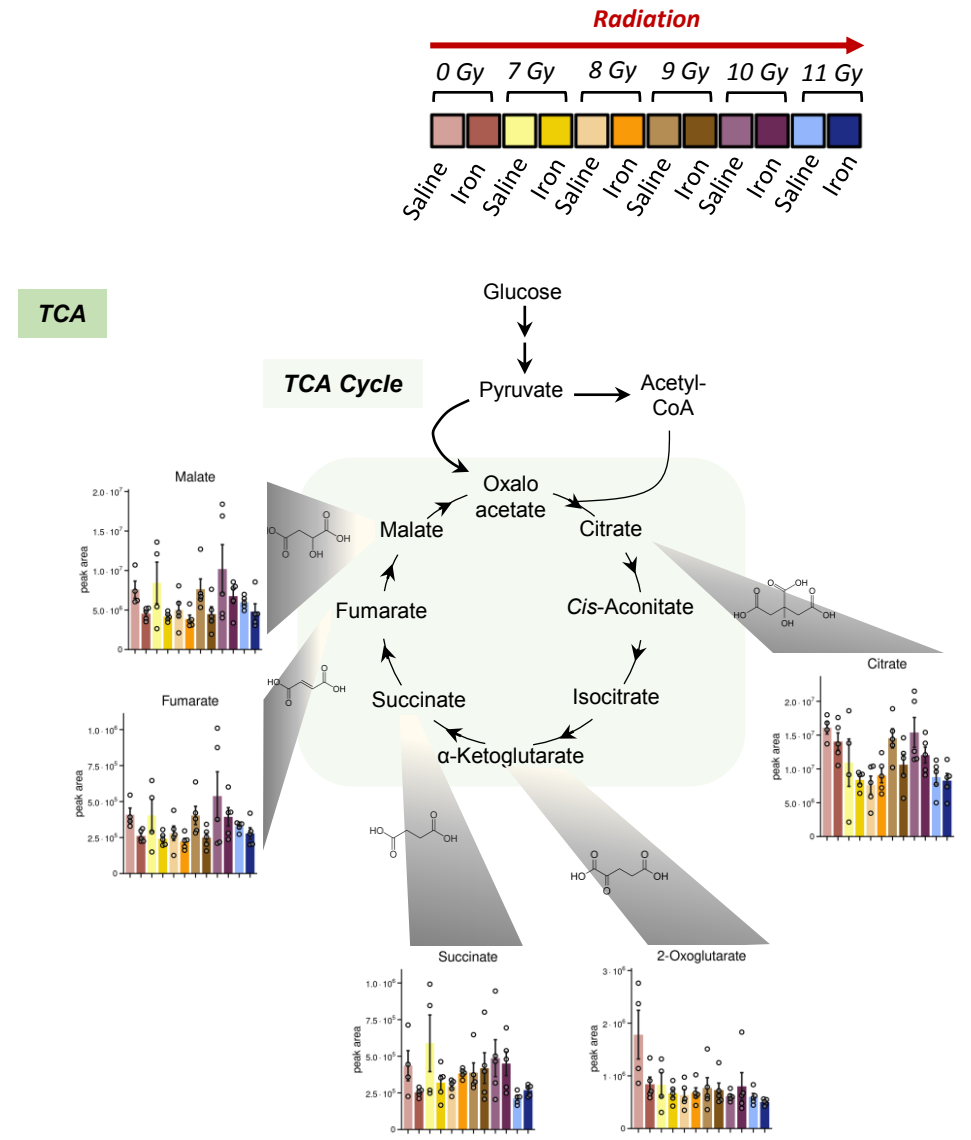


Supp Fig 2.D – Heat map (features significant by ANOVA) and Principal Component Analysis for plasma metabolites in response to radiation with and without iron infusion.

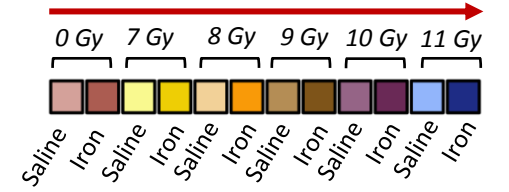
Glycolysis



Plasma

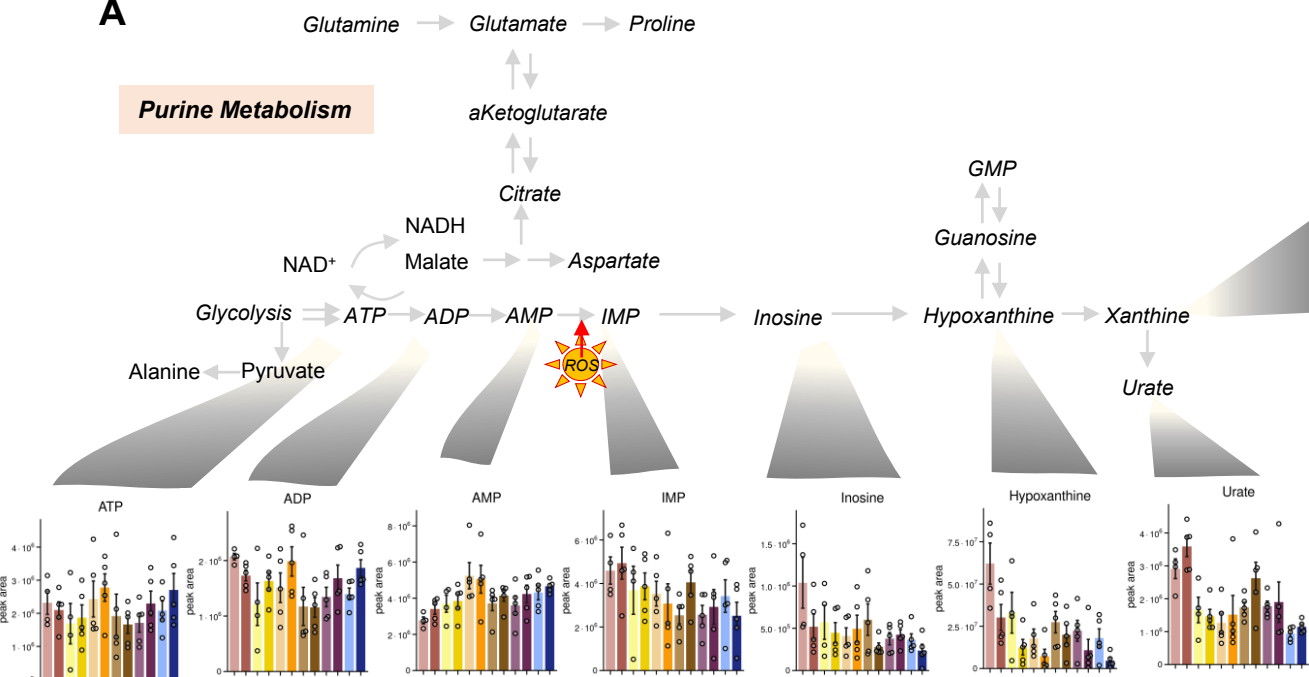


Radiation

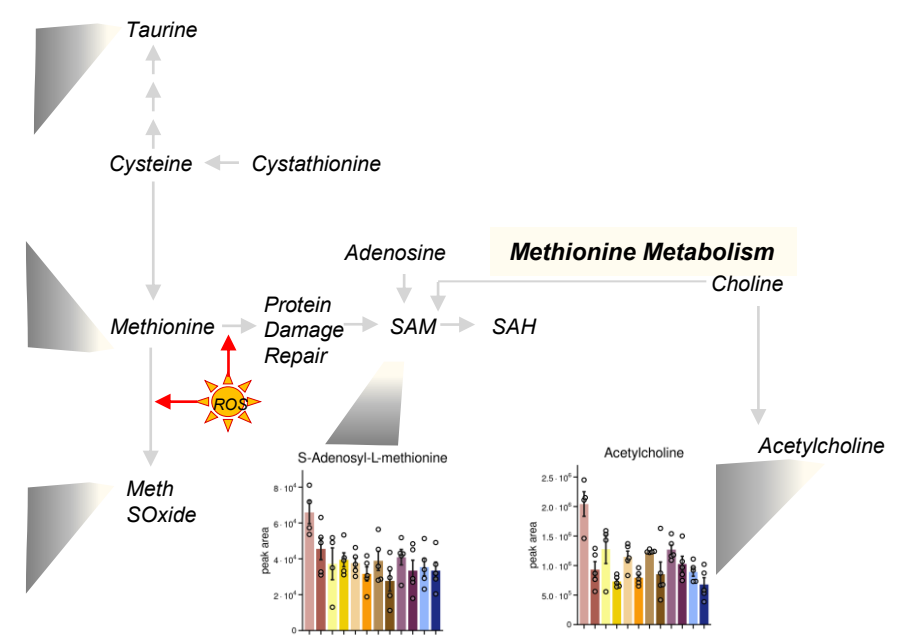
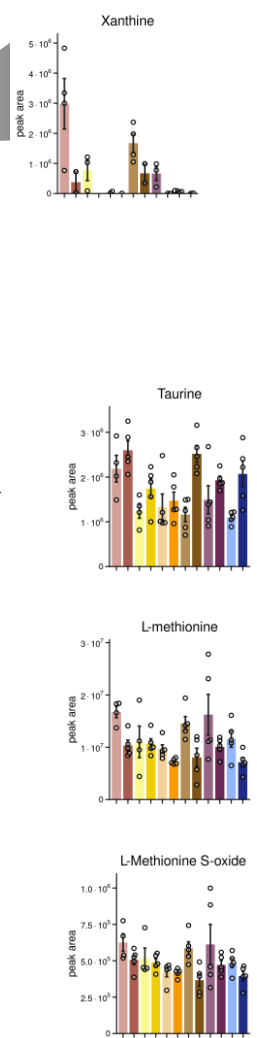
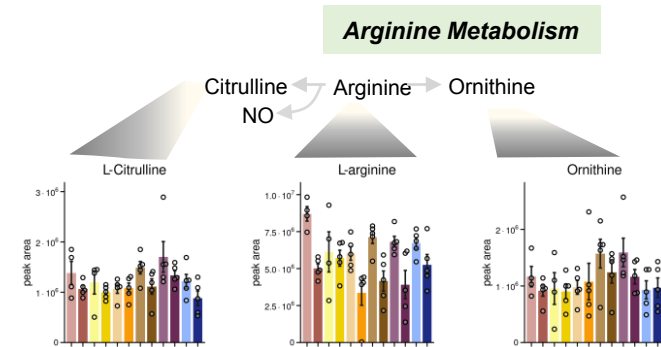
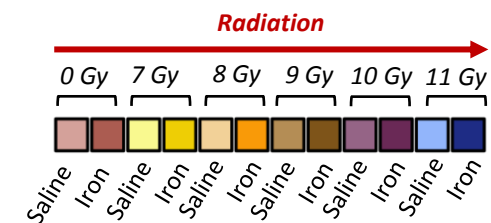


Supp Fig 2.E– Bar plots on the impact of radiation with and without iron infusion in the Plasma TCA cycle and glycolysis pathway.

A

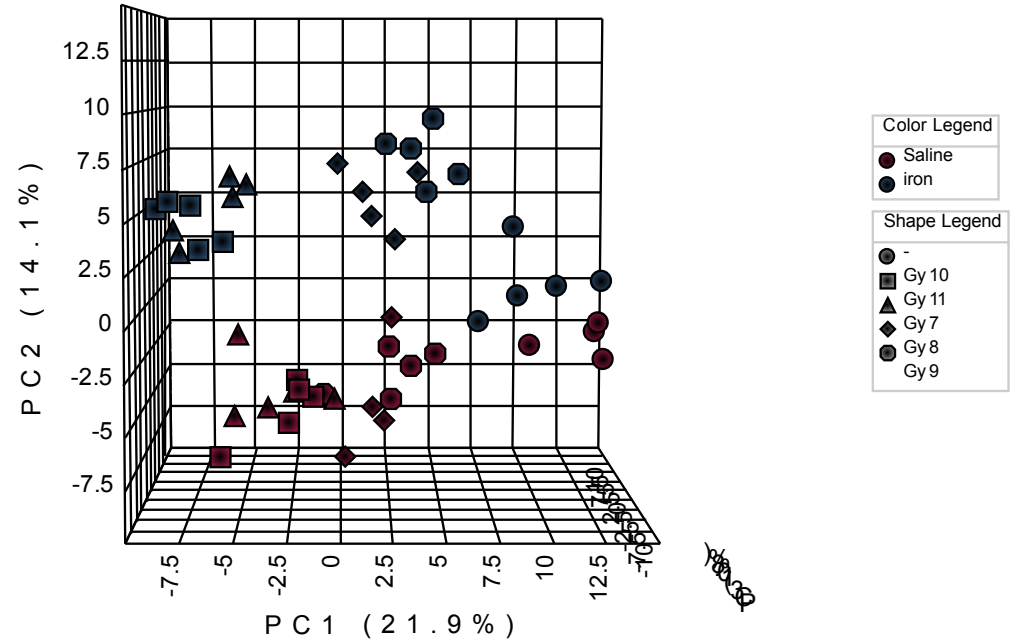
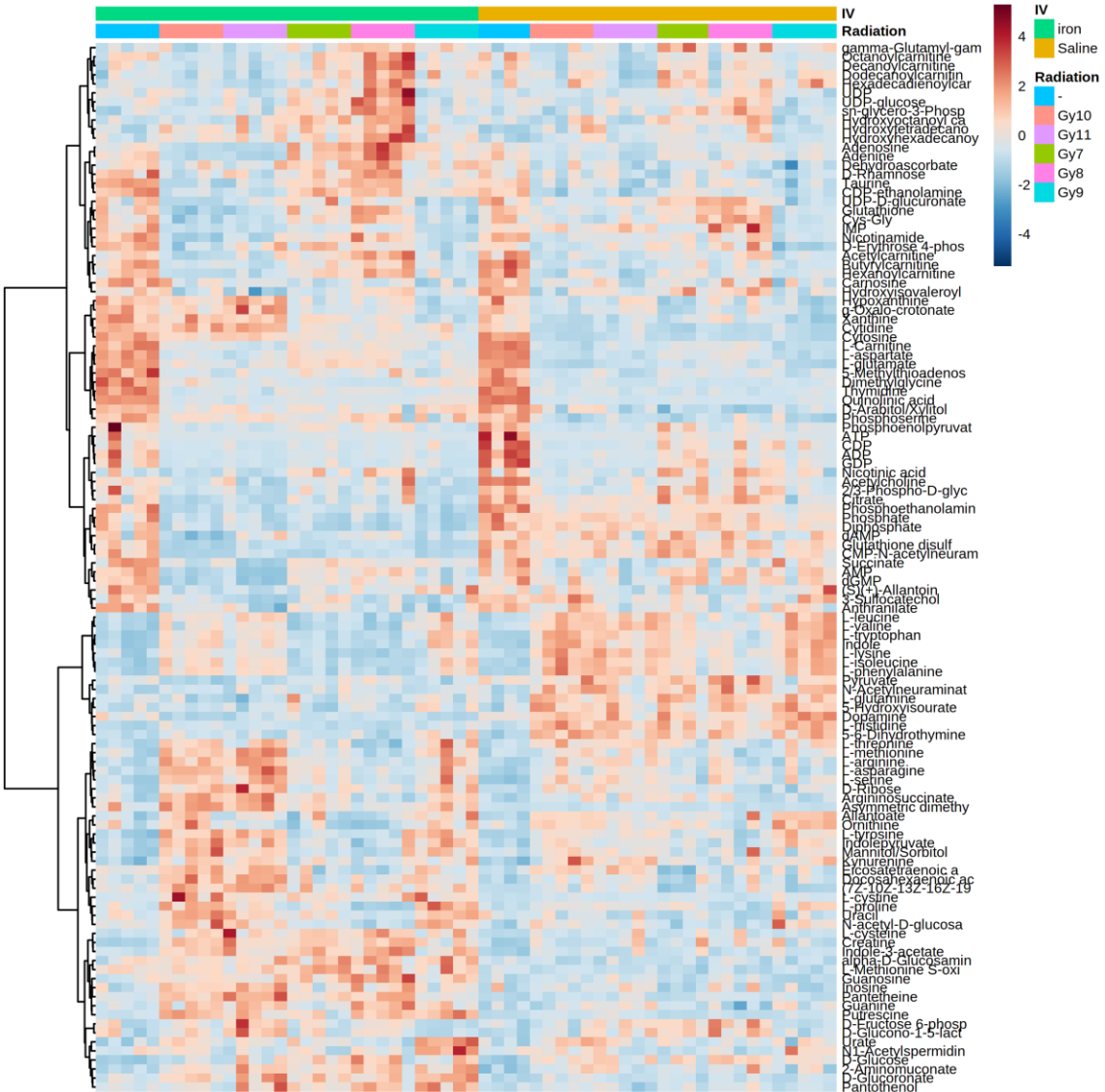


PLASMA



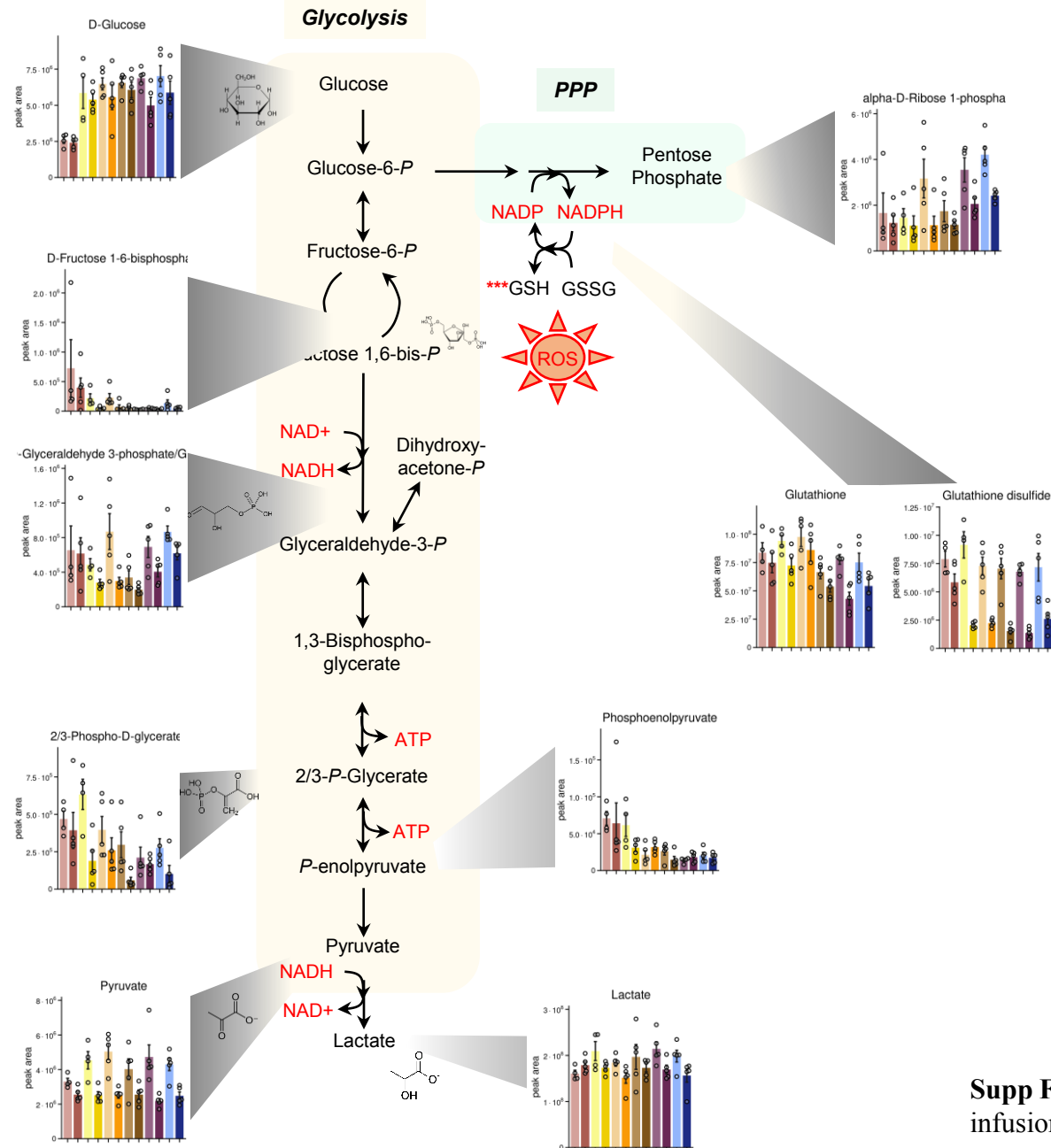
Supp Fig 2.F– Bar plots on the impact of radiation with and without iron infusion in plasma purine, arginine, and methionine metabolism.

SPLEEN

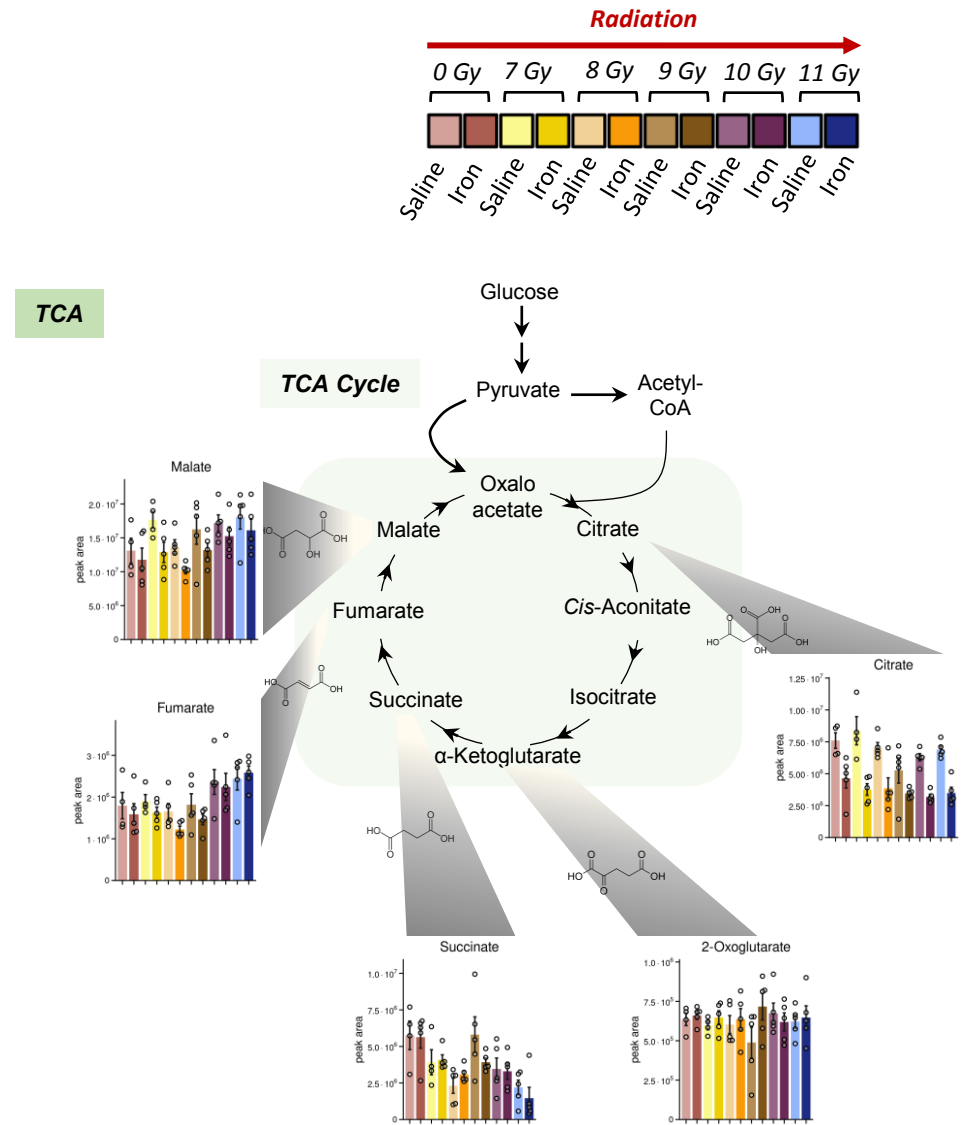


Supp Fig 2.G – Heat map (features significant by ANOVA) and Principal Component Analysis of top metabolic effects for spleen metabolites in response to radiation with and without iron infusion.

Glycolysis

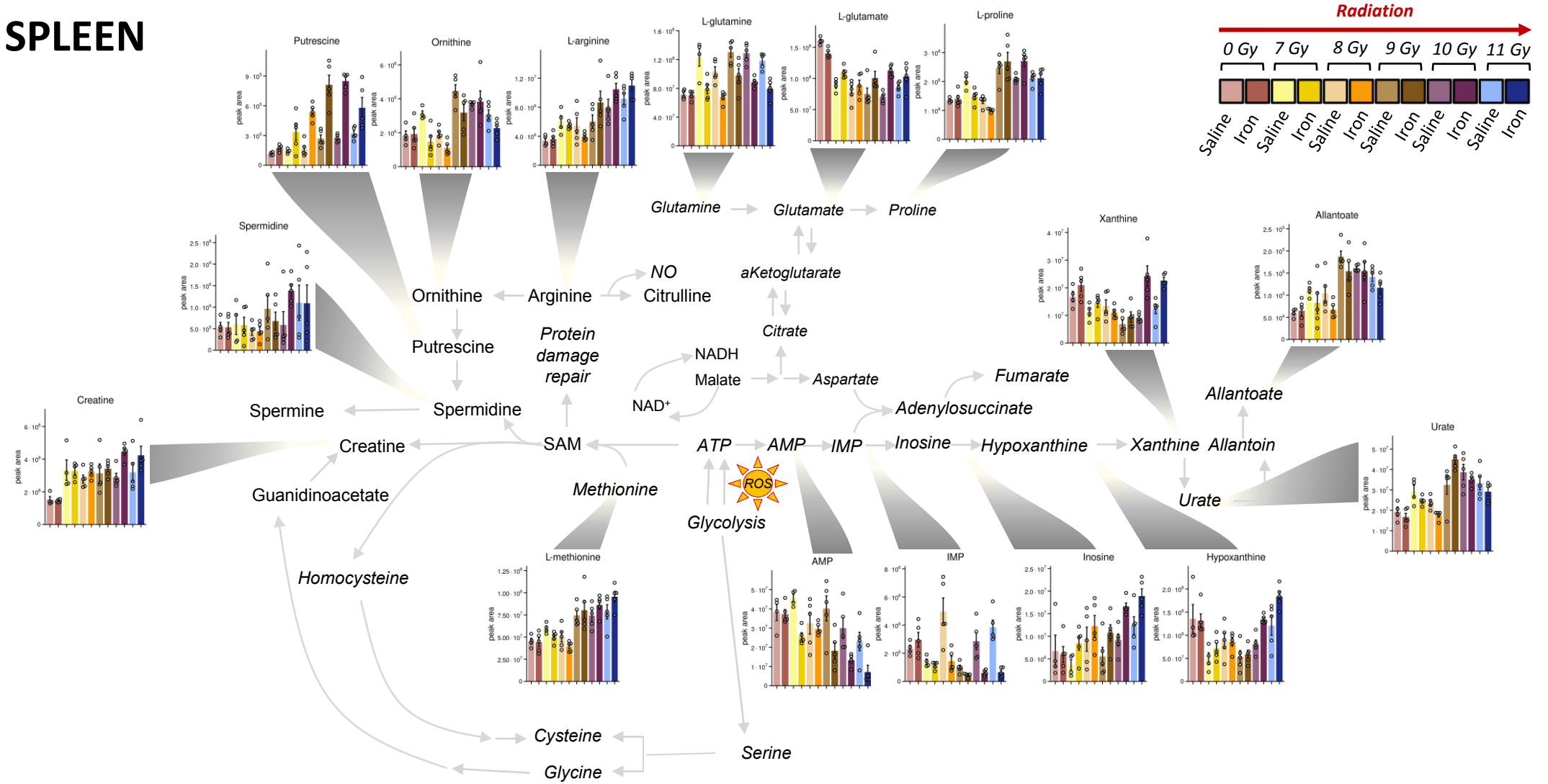


SPLEEN



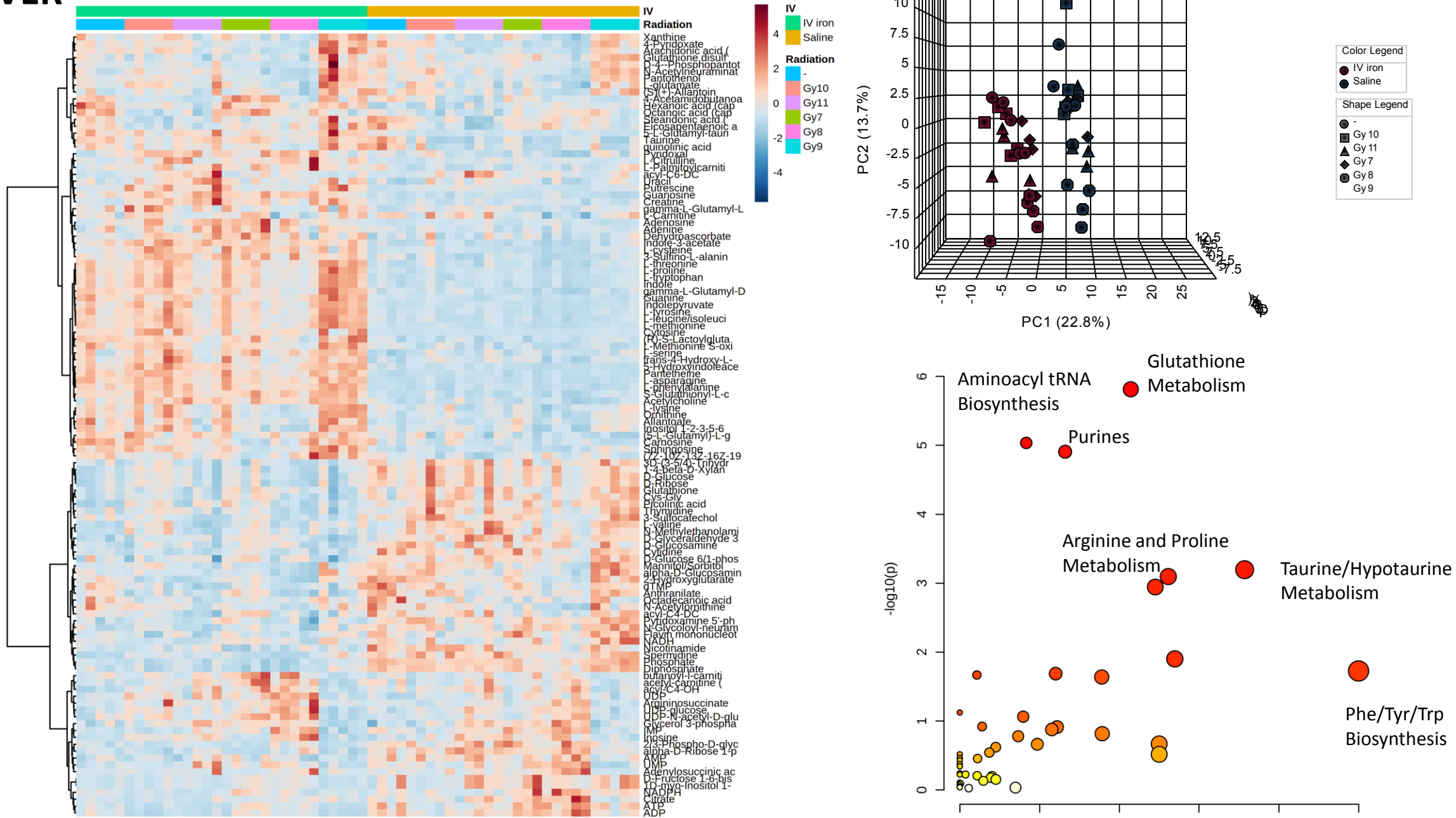
Supp Fig 2.H– Bar plots on the impact of radiation with and without iron infusion in the spleen TCA cycle and glycolysis pathway.

SPLEEN



Supp Fig 2.1 – Bar plots on the impact of radiation with and without iron infusion in the spleen protein damage and repair pathways.

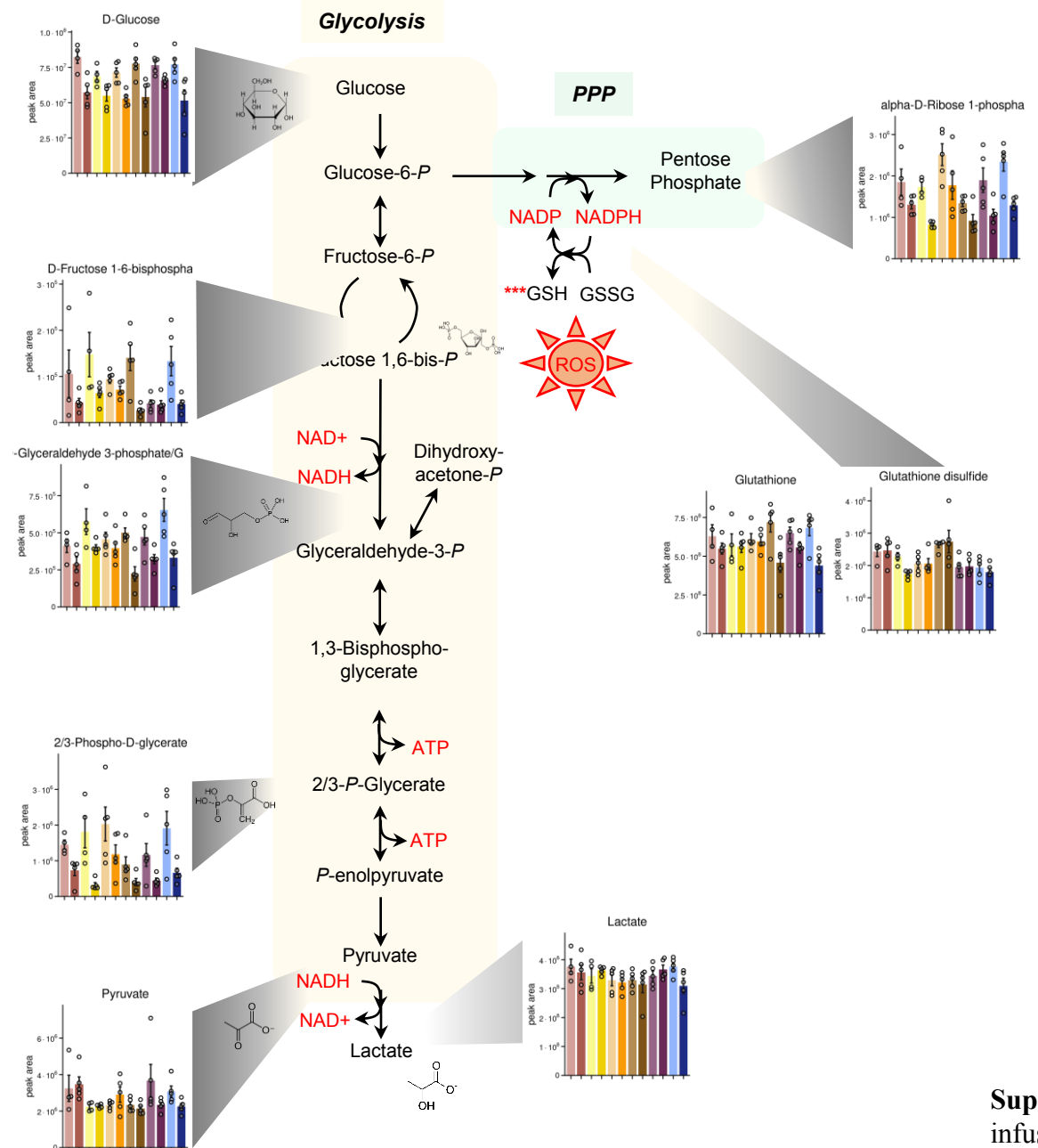
LIVER



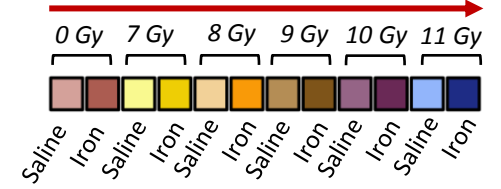
Supp Fig 2.J – Heat map (features significant by ANOVA), Principal Component Analysis, and Pathway Analysis of top metabolic effects for liver metabolites in response to radiation with and without iron infusion.

LIVER

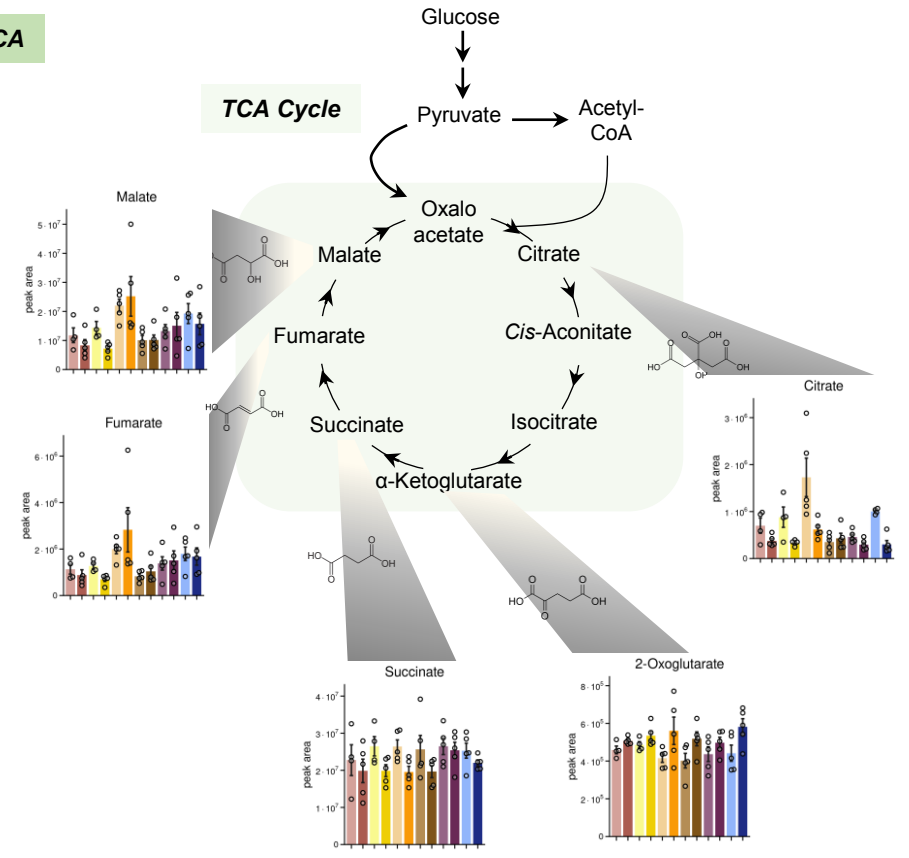
Glycolysis



Radiation



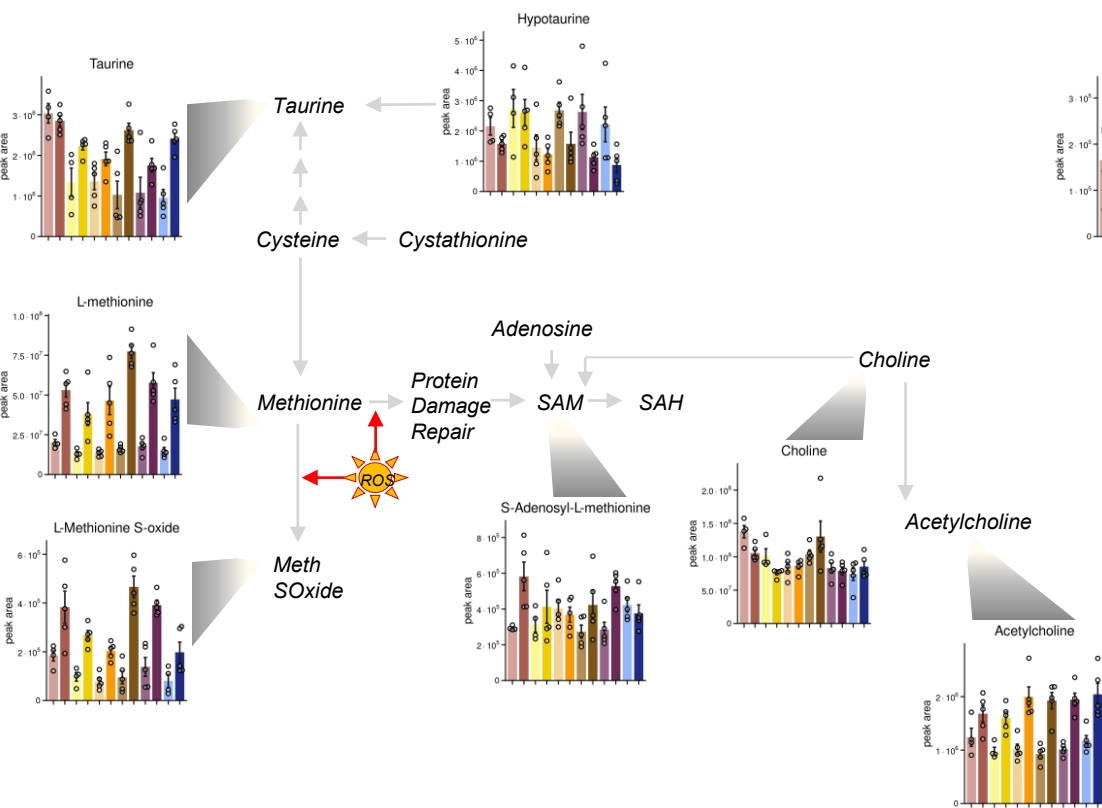
TCA



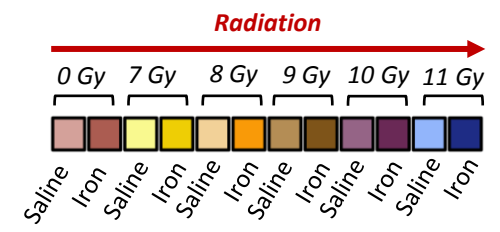
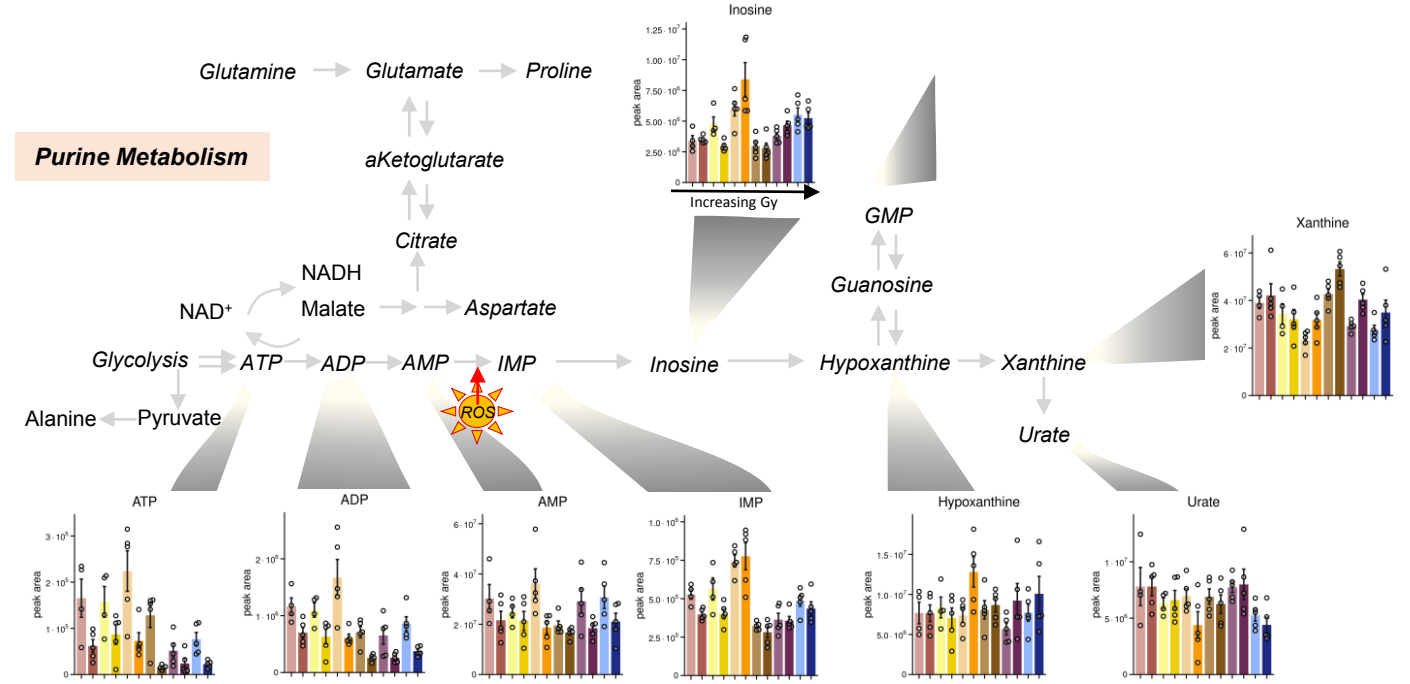
Supp Fig 2.K– Bar plots on the impact of radiation with and without iron infusion in the liver TCA cycle and glycolysis pathway.

LIVER

Methionine Metabolism

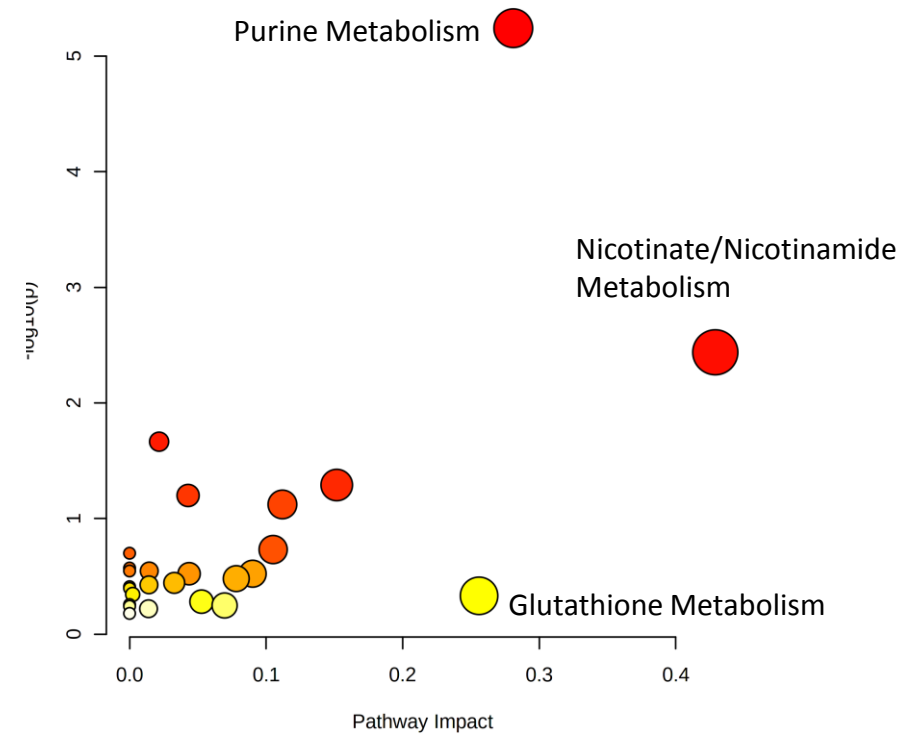
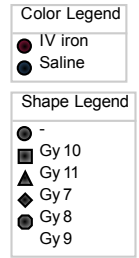
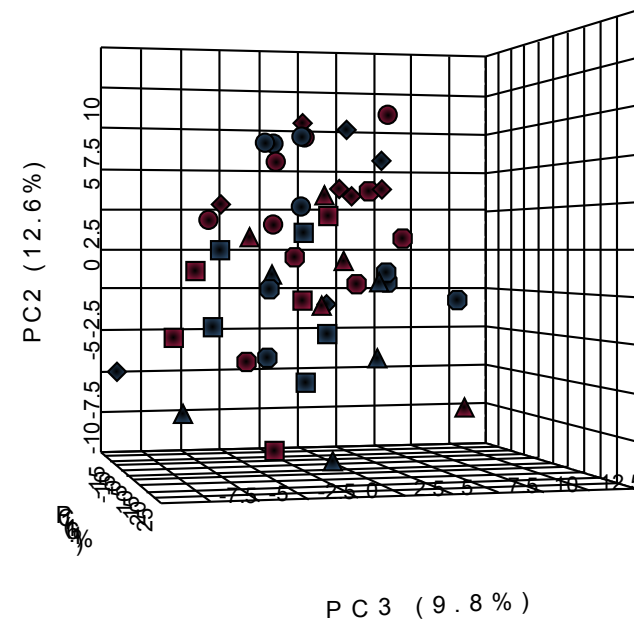
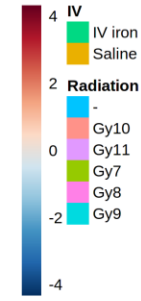
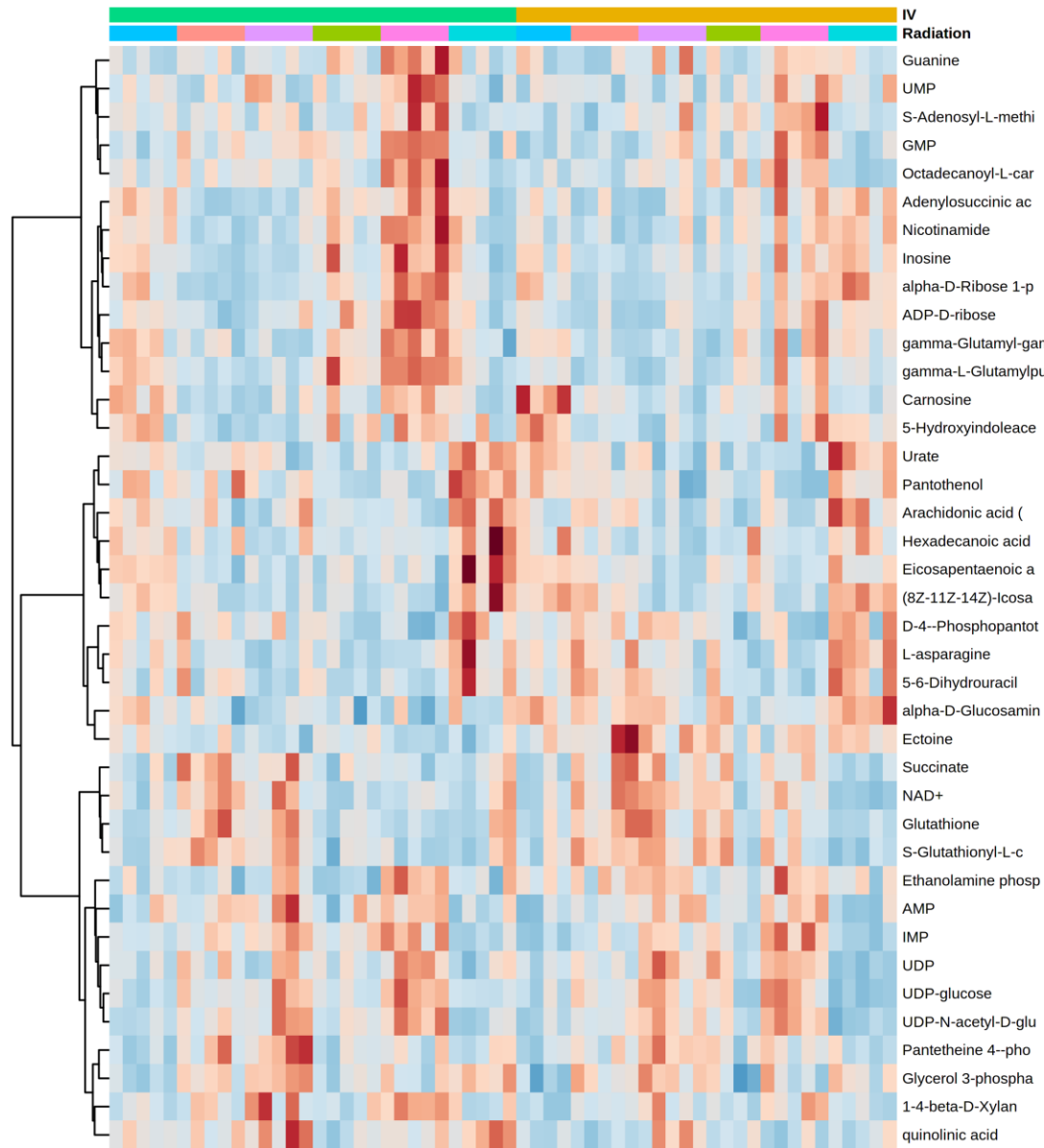


Purine Metabolism



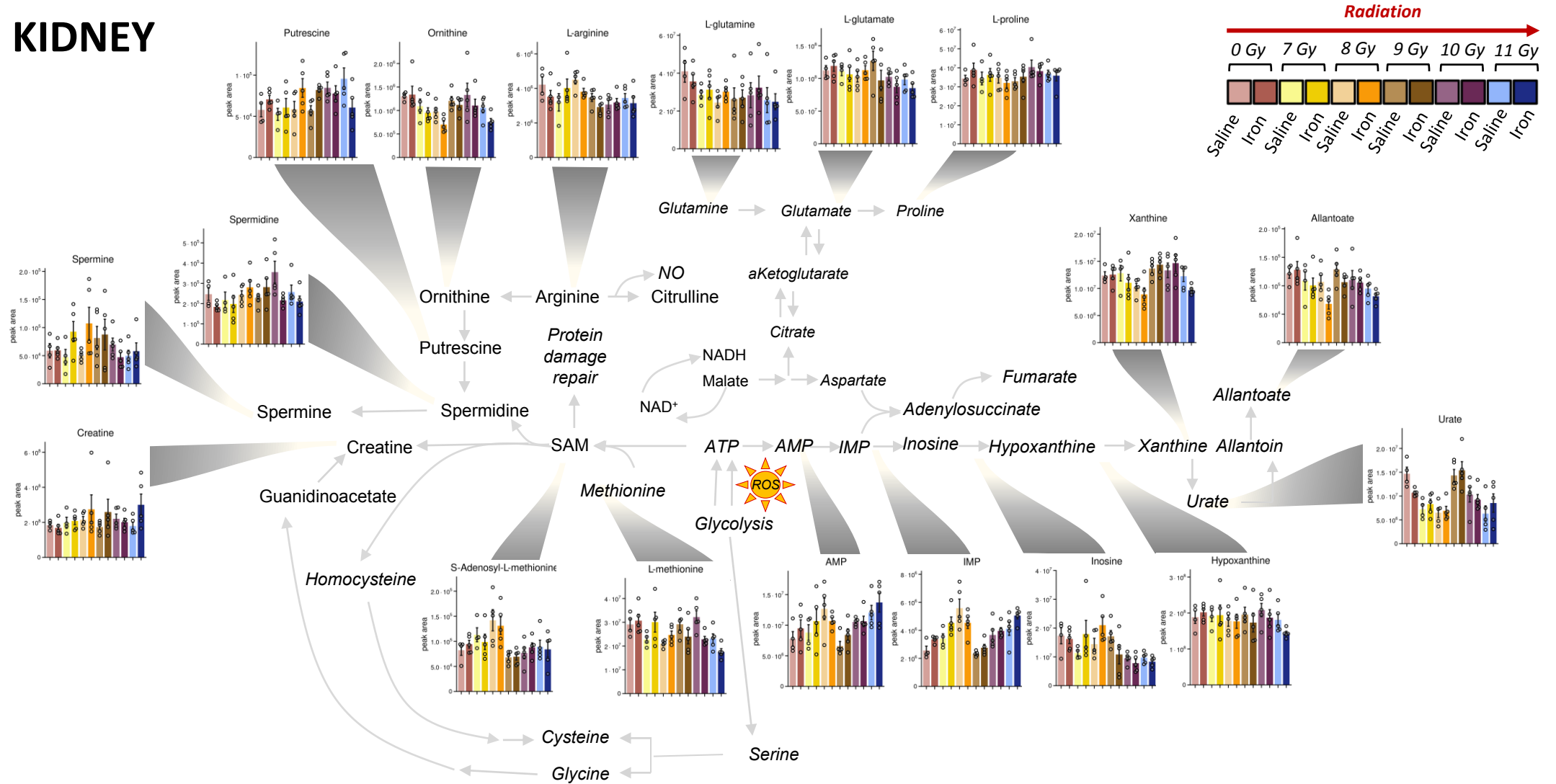
Supp Fig 2.L– Bar plots on the impact of radiation with and without iron infusion in liver purine and methionine metabolism.

KIDNEY



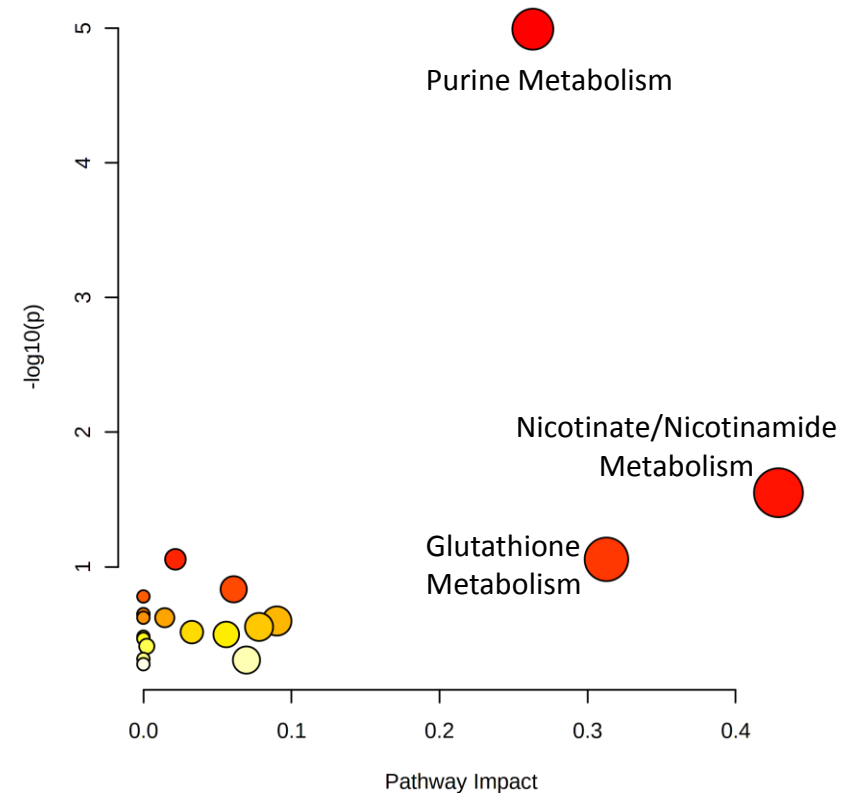
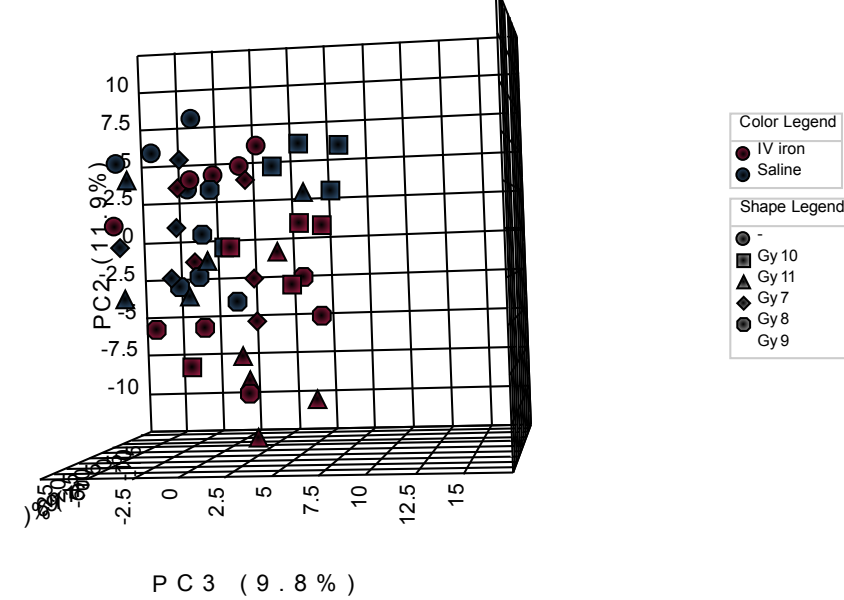
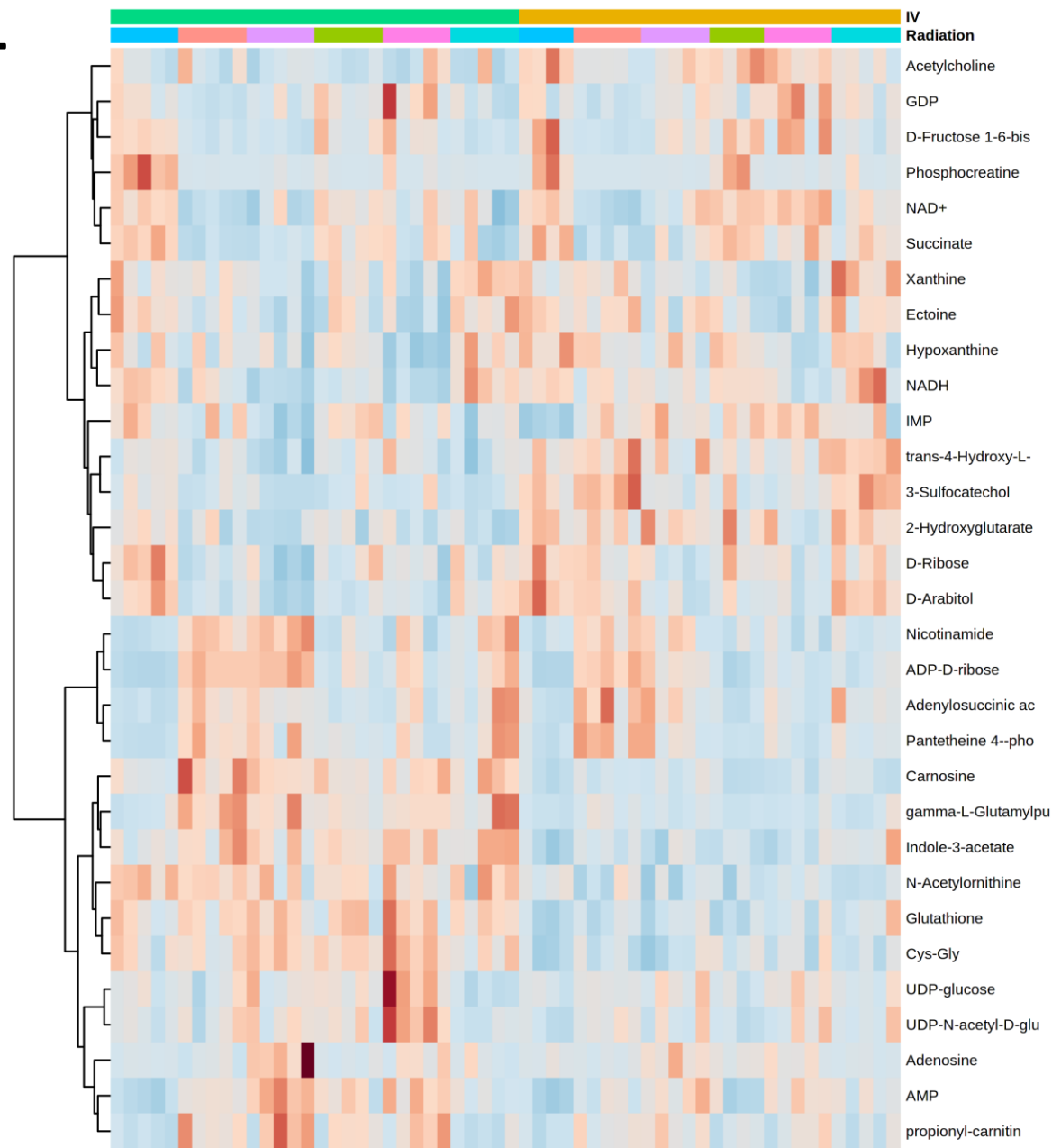
Supp Fig 2.M – Heat map (features significant by ANOVA), Principal Component Analysis, and Pathway Analysis of top metabolic effects for kidney metabolites in response to radiation with and without iron infusion.

KIDNEY



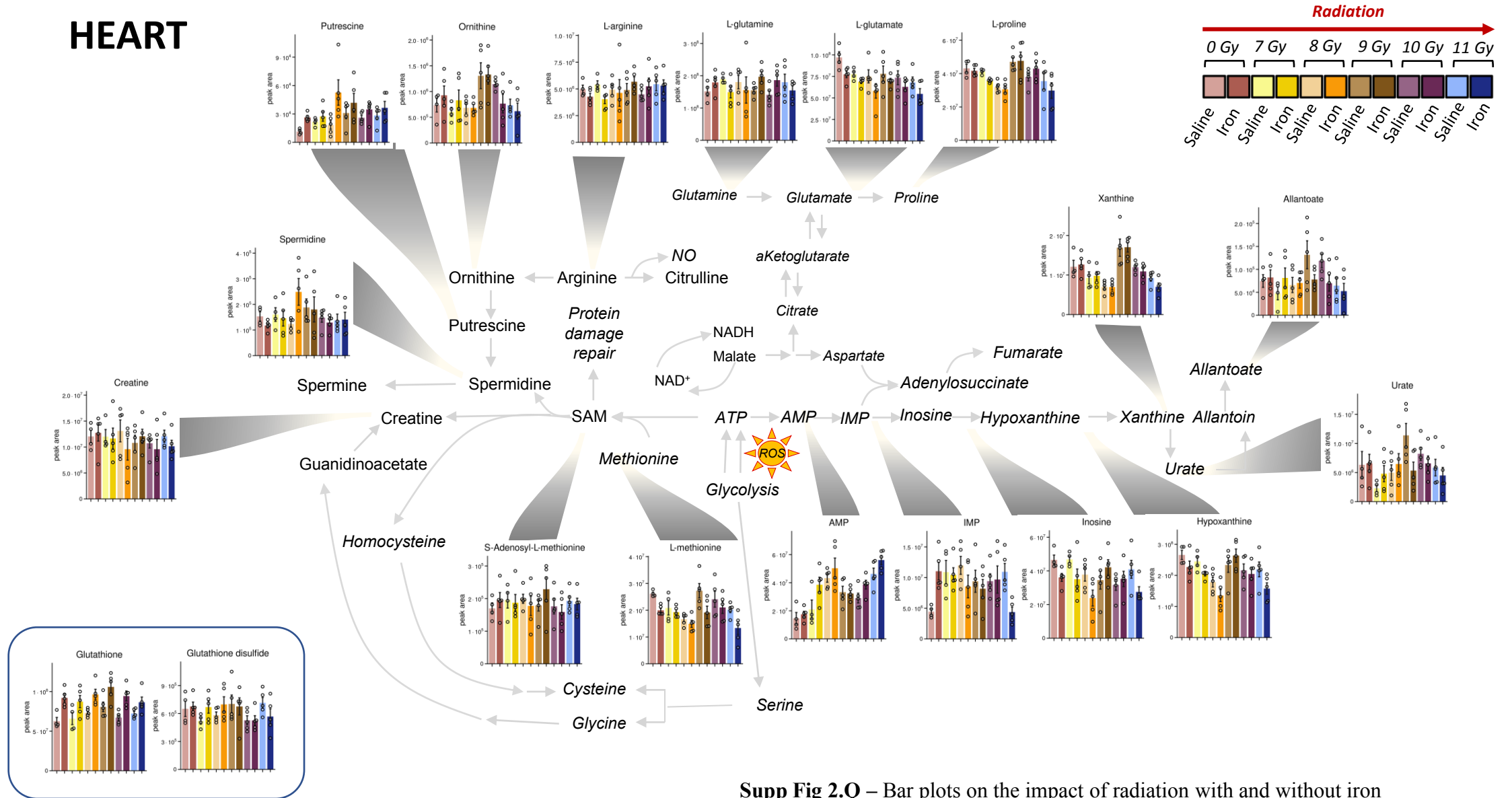
Supp Fig 2.0 – Bar plots on the impact of radiation with and without iron infusion in the kidney protein damage and repair pathways.

HEART



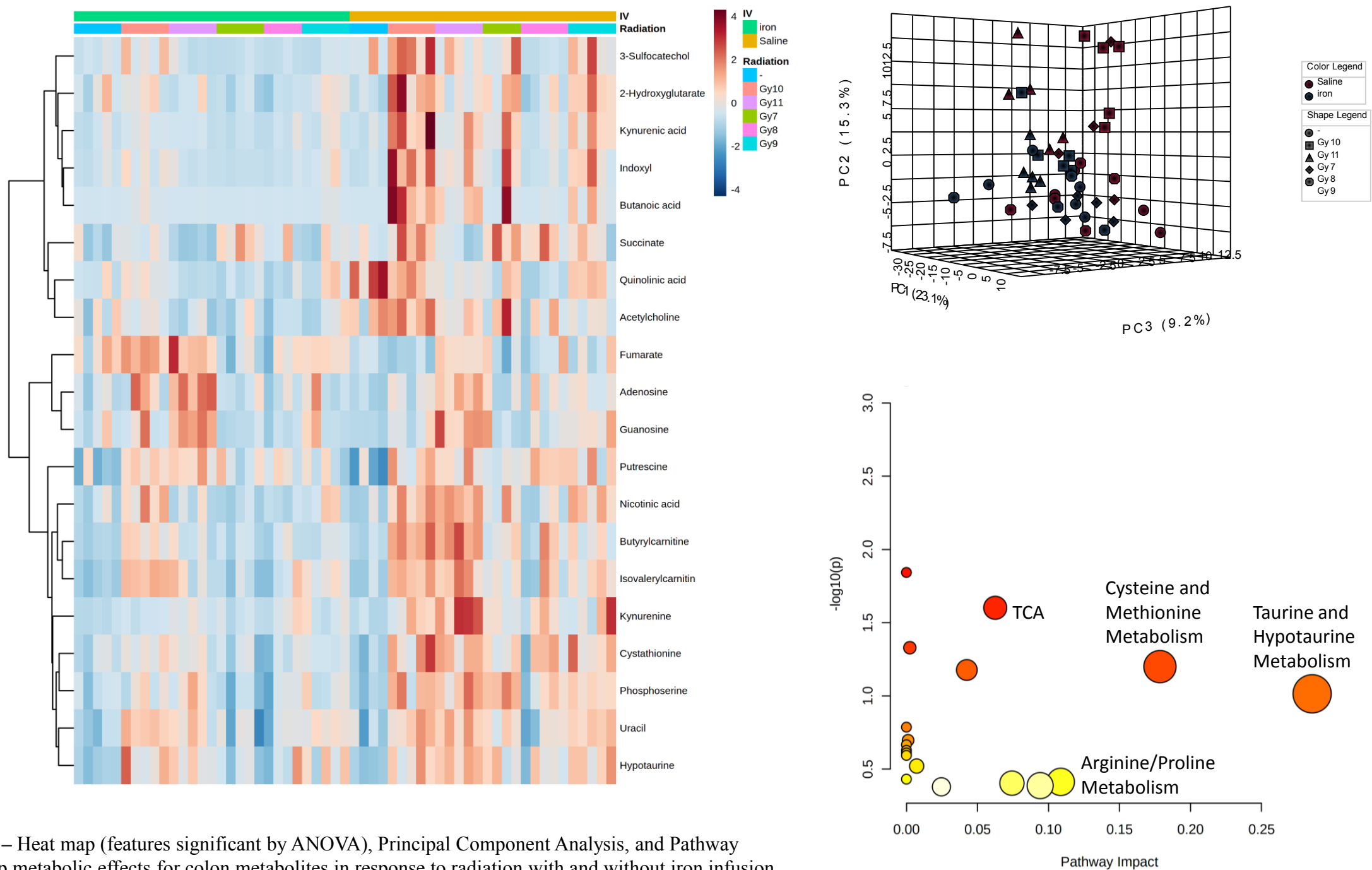
Supp Fig 2.P – Heat map (features significant by ANOVA), Principal Component Analysis, and Pathway Analysis of top metabolic effects for heart metabolites in response to radiation with and without iron infusion.

HEART

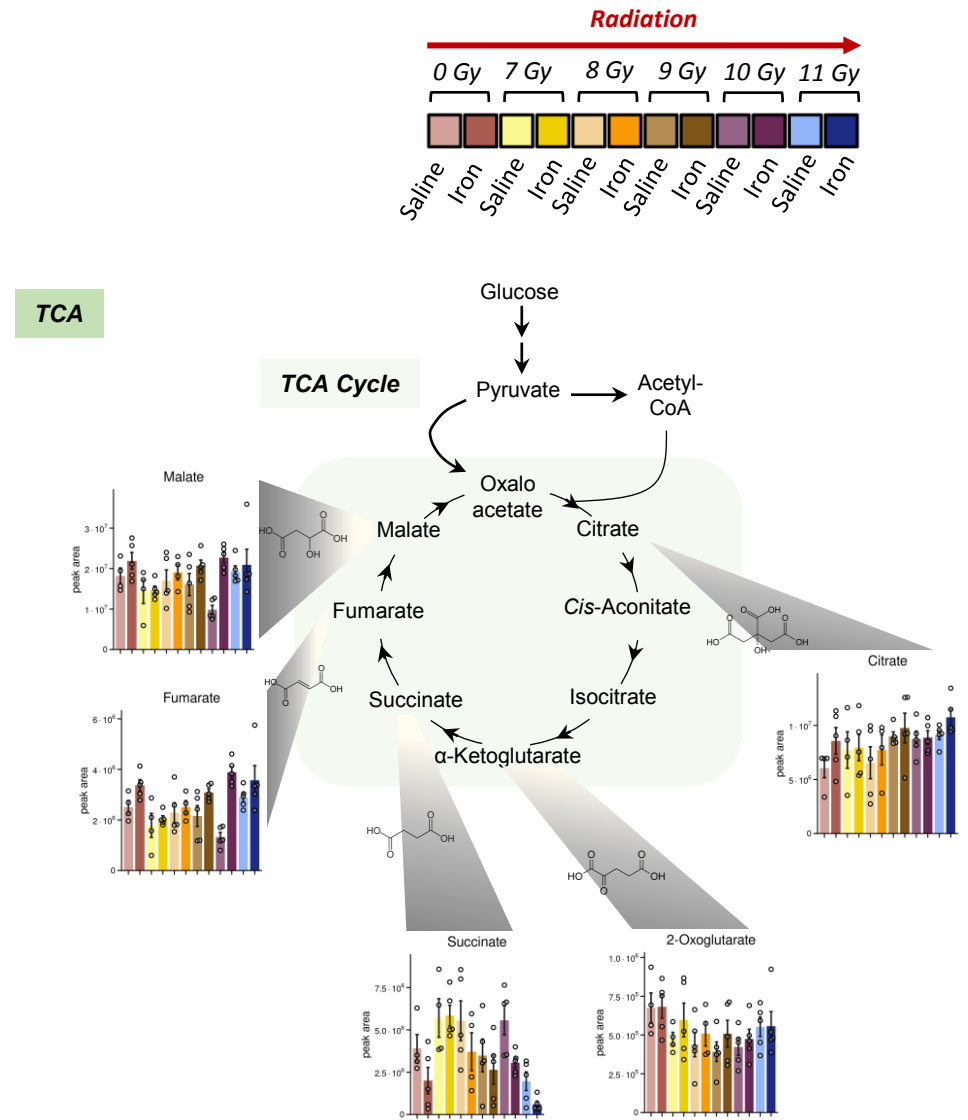
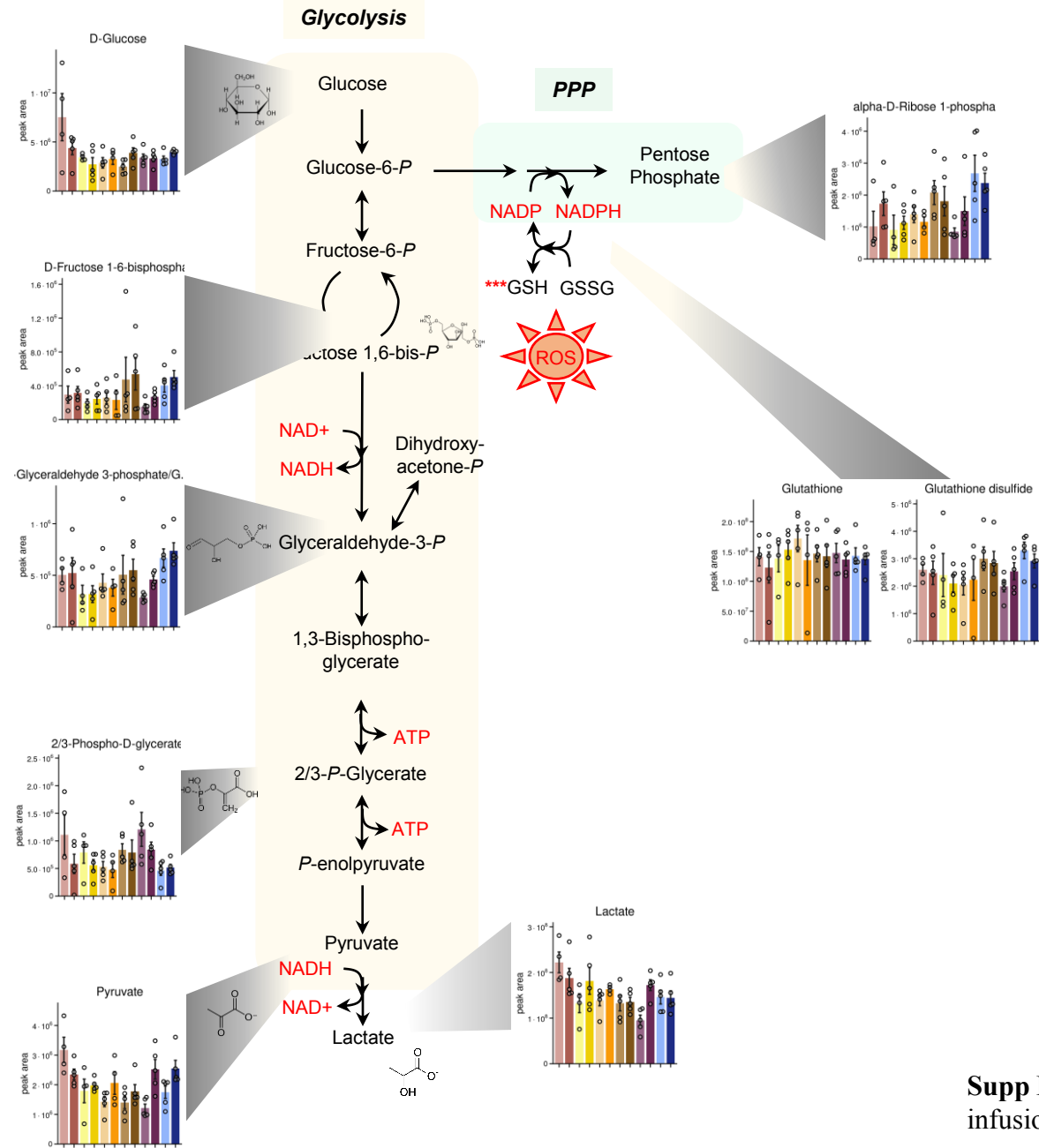


Supp Fig 2.Q – Bar plots on the impact of radiation with and without iron infusion in the heart protein damage and repair pathways.

COLON

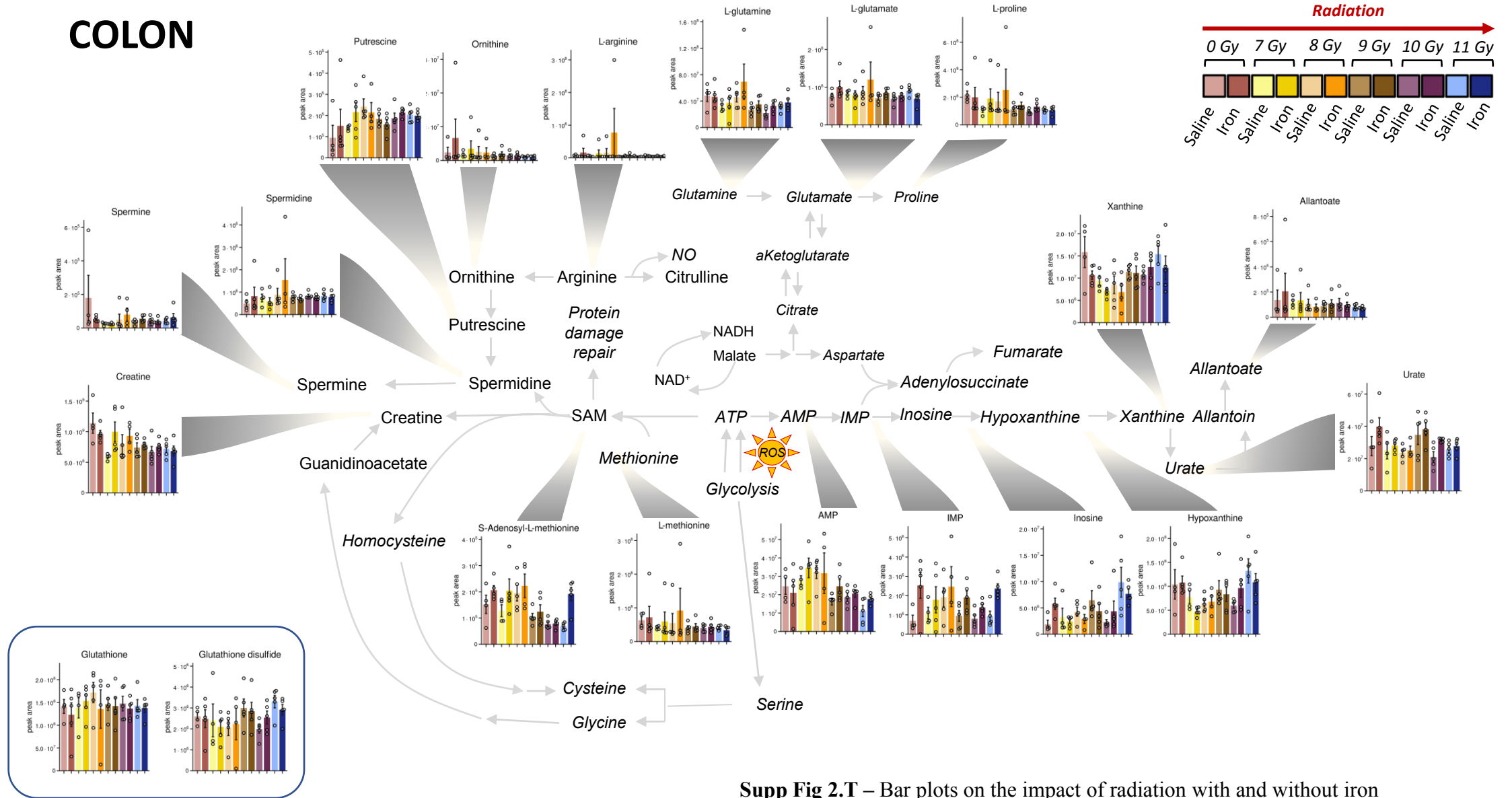


Supp Fig 2.R – Heat map (features significant by ANOVA), Principal Component Analysis, and Pathway Analysis of top metabolic effects for colon metabolites in response to radiation with and without iron infusion.



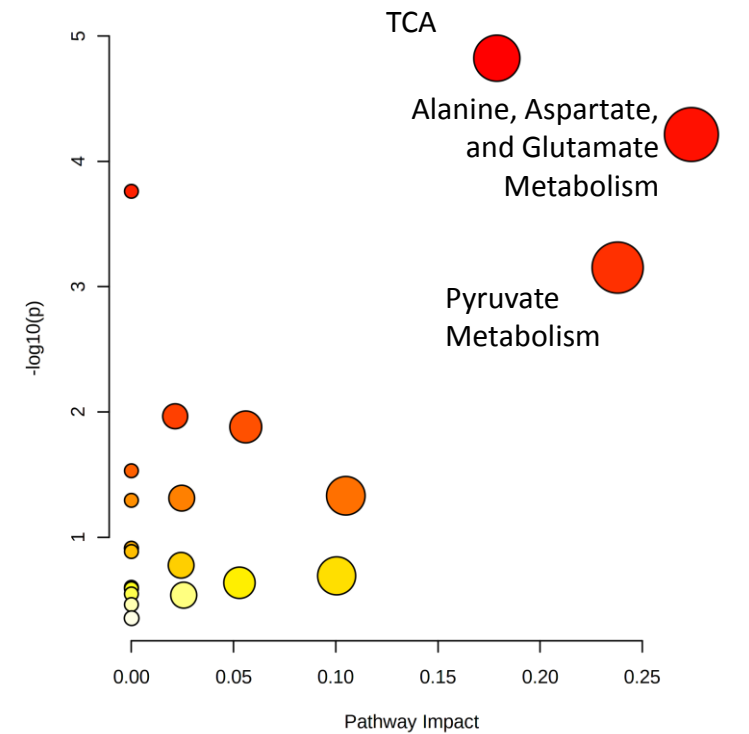
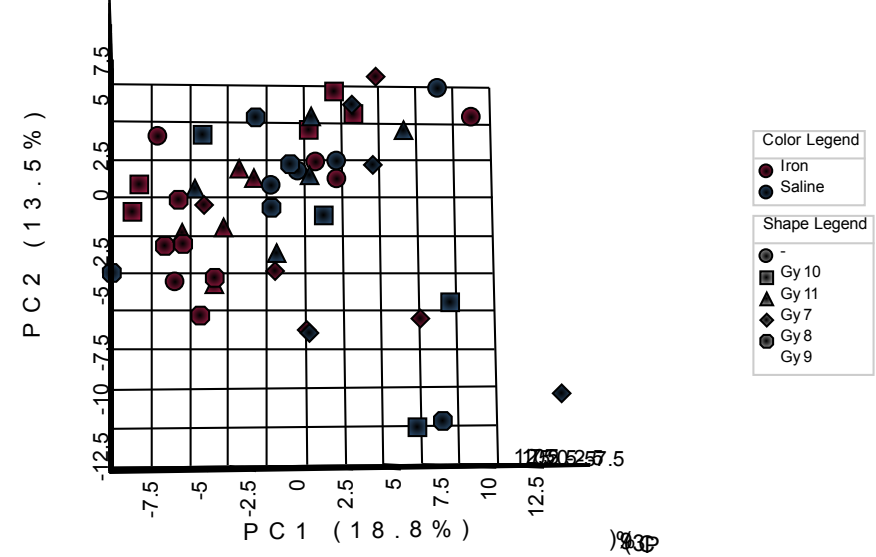
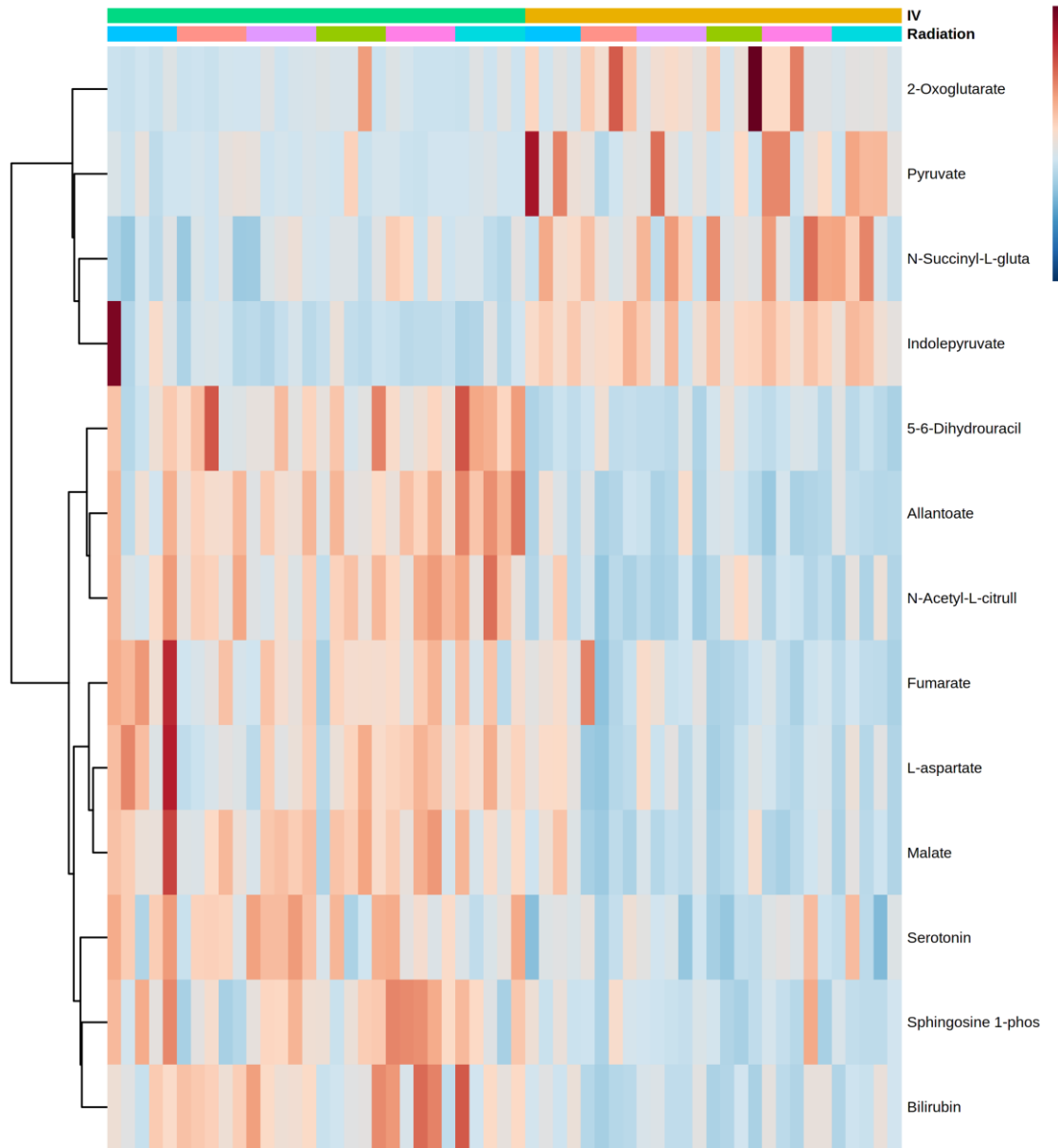
Supp Fig 2.S– Bar plots on the impact of radiation with and without iron infusion in the colon TCA cycle and glycolysis pathway.

COLON

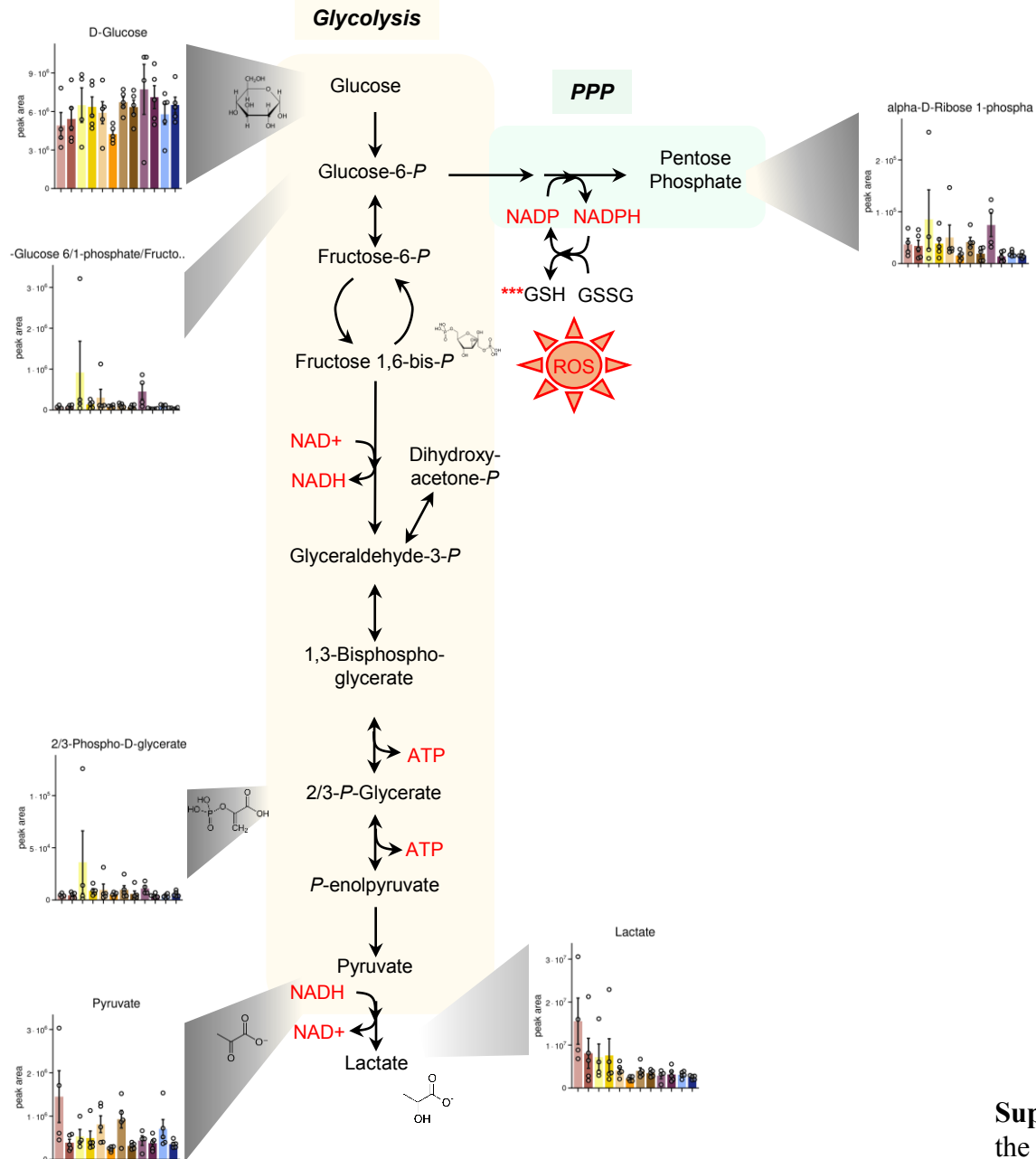


Supp Fig 2.T – Bar plots on the impact of radiation with and without iron infusion in the colon protein damage and repair pathways.

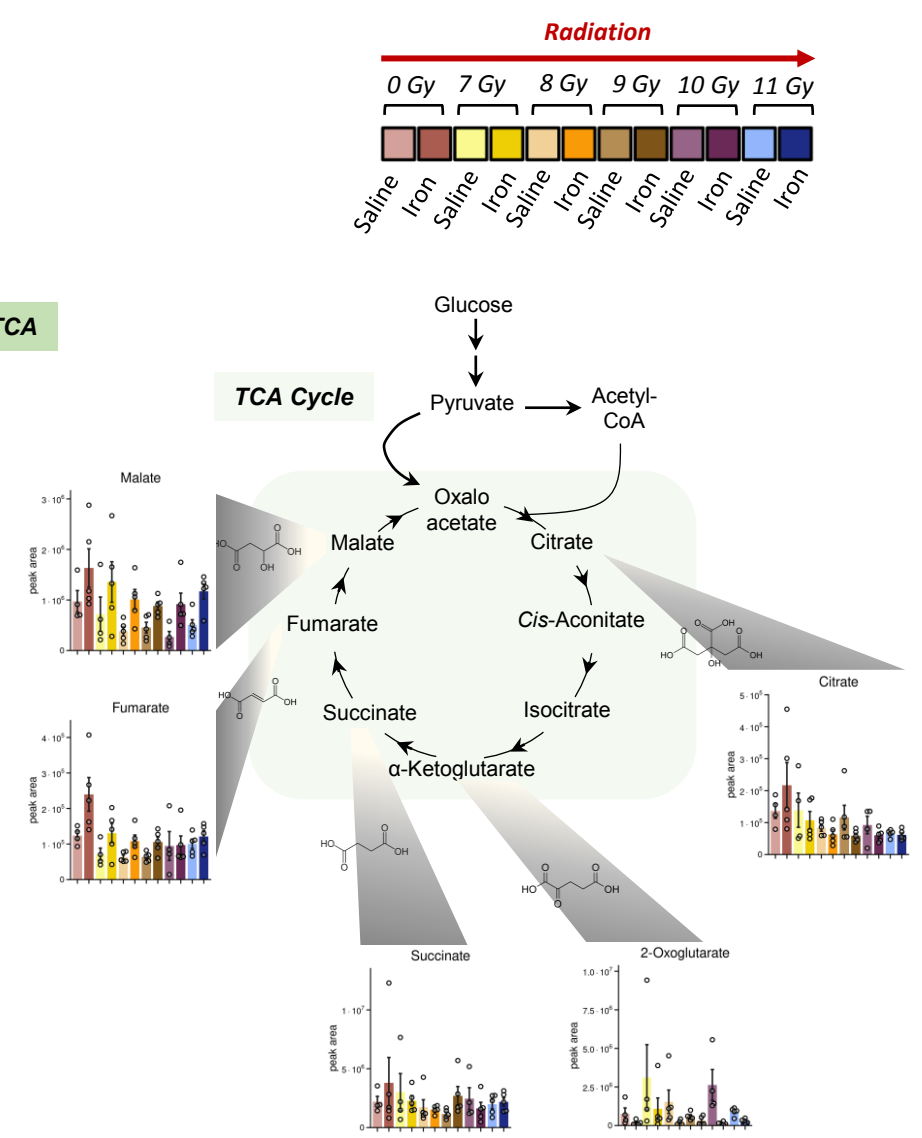
PRE STOOL



Supp Fig 2.U – Heat map (features significant by ANOVA), Principal Component Analysis, and Pathway Analysis of top metabolic effects for stool metabolites prior to radiation with and without iron infusion.

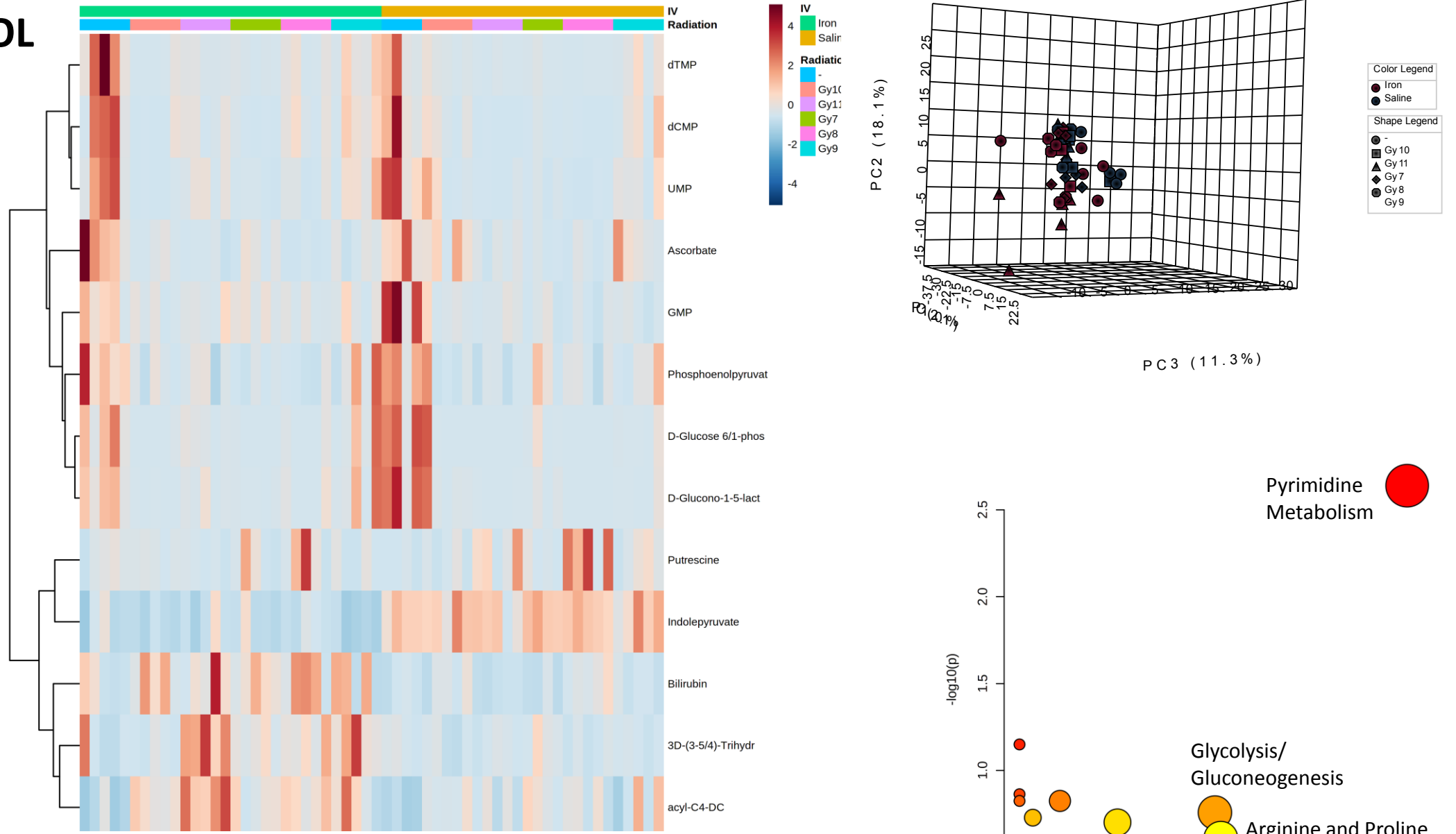


TCA



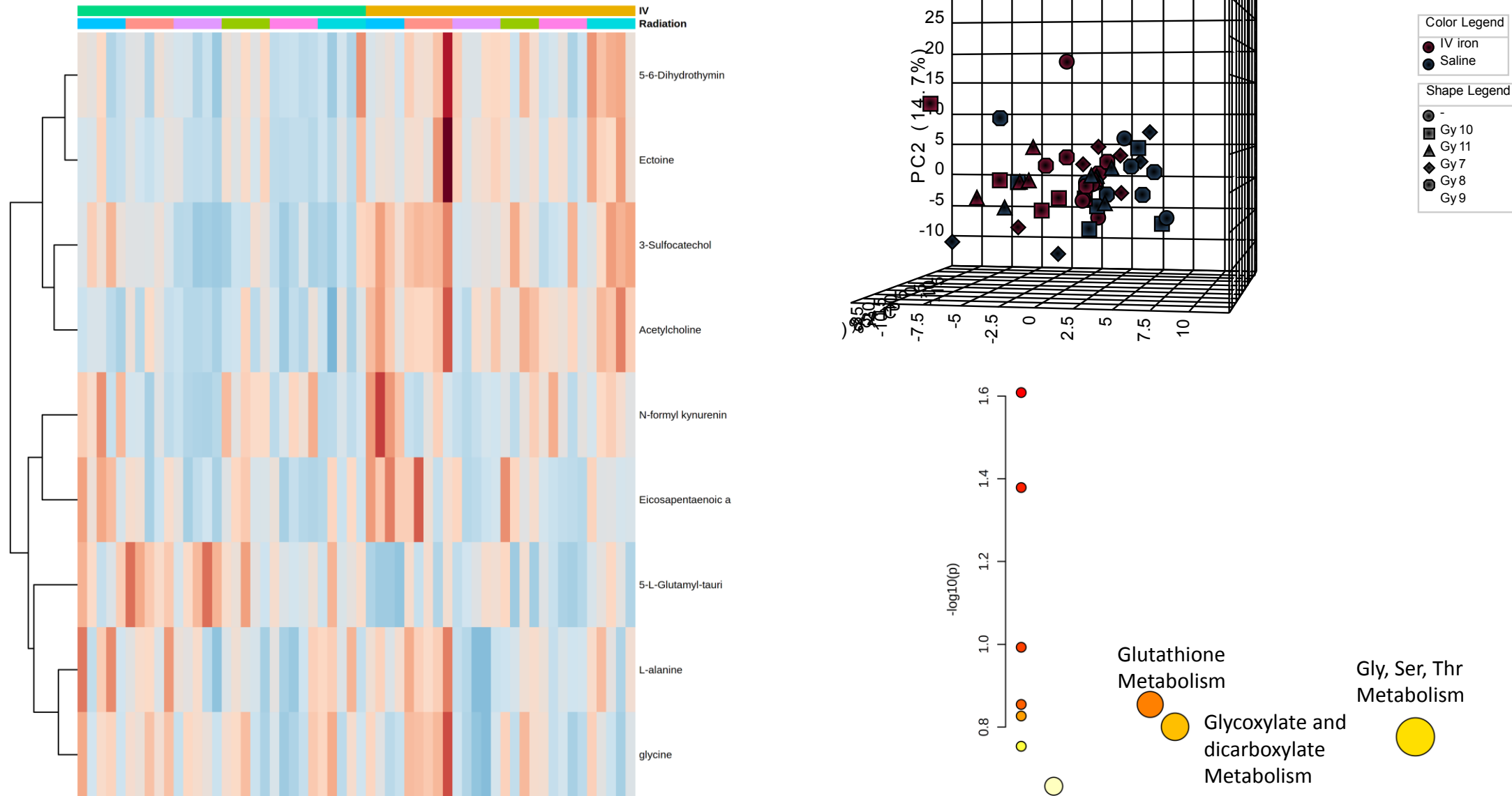
Supp Fig 2.V– Bar plots on the impact of iron infusion (prior to radiation) in the stool TCA cycle and glycolysis pathway.

POST STOOL



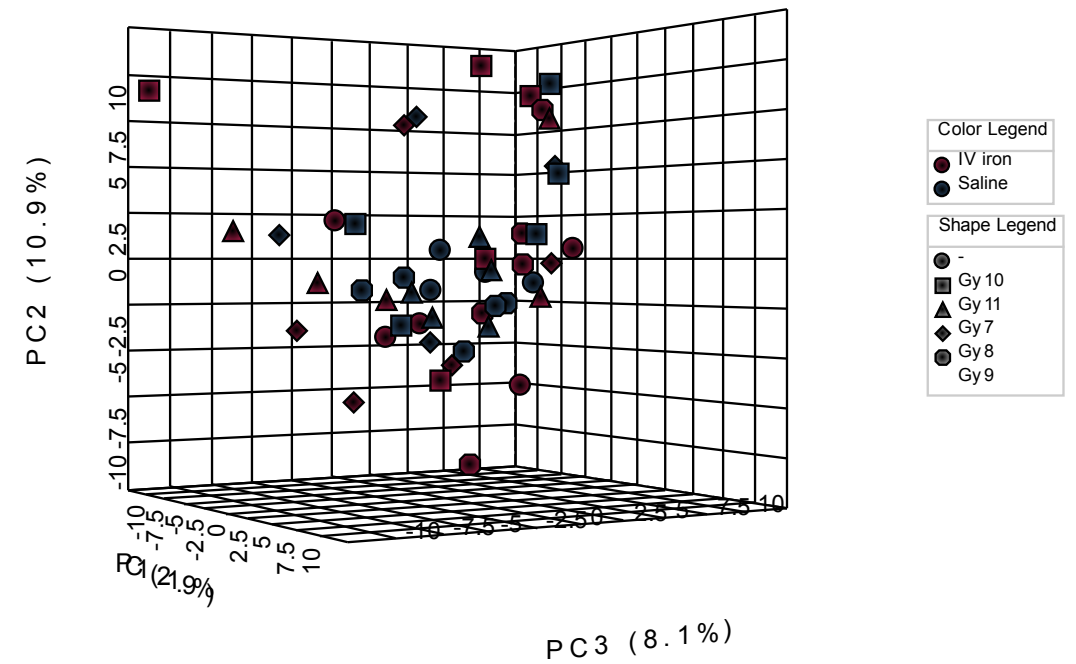
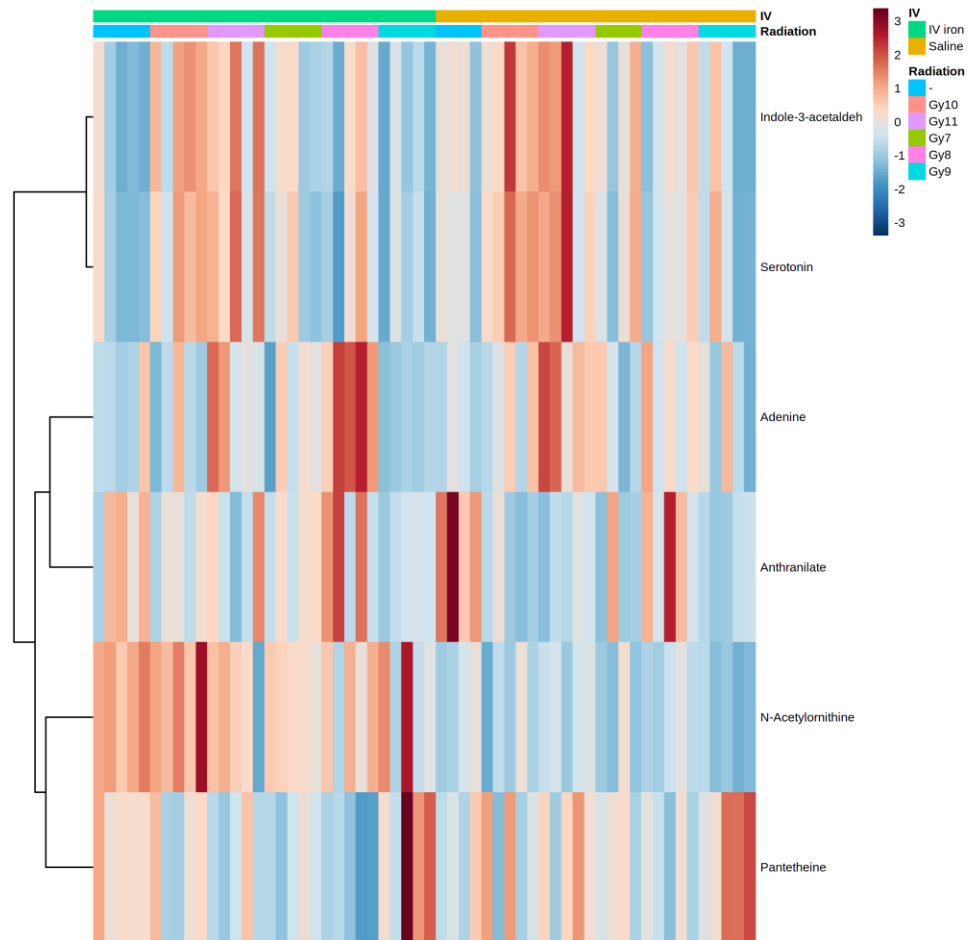
Supp Fig 2.W – Heat map (features significant by ANOVA), Principal Component Analysis, and Pathway Analysis of top metabolic effects for stool metabolites in response to radiation with and without iron infusion.

DUODENUM



Supp Fig 2.X – Heat map (features significant by ANOVA), Principal Component Analysis, and Pathway Analysis of top metabolic effects for duodenum metabolites prior to radiation with and without iron infusion.

BRAIN



Supp Fig 2.Y – Heat map (features significant by ANOVA) and Principal Component Analysis for brain metabolites prior to radiation with and without iron infusion.