



Supplemental Figure 1. Gene expression changes in the sphingolipid pathway in HMexposed lung tissues following MnCl<sub>2</sub> exposure. A. Volcano plot displaying differential gene expression between MnCl<sub>2</sub>-exposed and unexposed (control) lung tissues. B,D. Heatmap (B) and table (D) highlighting significantly altered genes with MnCl<sub>2</sub> exposure. C. Cell deconvolution analysis correlating gene expression of sphingolipid pathway with scaled abundance of specific cell populations in the lung tissue following MnCl<sub>2</sub> exposure.





Gene	Fold Change	P value
ARSJ	2.22	0.05
ACER3	2.36	0.04
GLB1L	2.36	0.01
CERS3	2.43	0.01
ARSH	1.86	0.04
STS	1.69	0.03
PLPP2	2.09	0.02
CERS4	1.99	0.05

Supplemental Figure 2. Gene expression changes in the sphingolipid pathway in HMexposed lung tissues following CdCl<sub>2</sub> exposure. **A**. Volcano plot displaying differential gene expression between CdCl<sub>2</sub>-exposed and unexposed (control) lung tissues. **B**,**D**. Heatmap (**B**) and table (**D**) highlighting significantly altered genes with CdCl<sub>2</sub> exposure. **C**. Cell deconvolution analysis correlating gene expression of sphingolipid pathway with scaled abundance of specific cell populations in the lung tissue following CdCl<sub>2</sub> exposure.













**Supplemental Figure 3. Cell abundance changes following heavy metal exposure. A.** Cell abundance plot showing differential cell abundance between NaAsO<sub>2</sub>-exposed and unexposed (control) lung tissues. **B.** Cell abundance plot showing differential cell abundance between MnCl<sub>2</sub>- exposed and unexposed (control) lung tissues. **C.** Cell abundance plot showing differential cell abundance plot showing differ



Supplemental Figure 4. Gene expression changes in the complement pathway in HMexposed lung tissues following MnCl<sub>2</sub> exposure. A. Volcano plot displaying differential gene expression between MnCl<sub>2</sub>-exposed and unexposed (control) lung tissues. B,D. Heatmap (B) and table (D) highlighting significantly altered genes with MnCl<sub>2</sub> exposure. C. Cell deconvolution analysis correlating gene expression of complement pathway with scaled abundance of specific cell populations in the lung tissue following MnCl<sub>2</sub> exposure.



Supplemental Figure 5. Gene expression changes in the complement pathway in HMexposed lung tissues following CdCl<sub>2</sub> exposure. **A**. Volcano plot displaying differential gene expression between CdCl<sub>2</sub>-exposed and unexposed (control) lung tissues. **B**,**D**. Heatmap (**B**) and table (**D**) highlighting significantly altered genes with CdCl<sub>2</sub> exposure. **C**. Cell deconvolution analysis correlating gene expression of complement pathway with scaled abundance of specific cell populations in the lung tissue following CdCl<sub>2</sub> exposure.



Supplemental Figure 6. Gene expression changes in the mitophagy pathway in HMexposed lung tissues following CdCl<sub>2</sub> exposure. **A**. Volcano plot displaying differential gene expression between CdCl<sub>2</sub>-exposed and unexposed (control) lung tissues. **B**,**D**. Heatmap (**B**) and table (**D**) highlighting significantly altered genes with CdCl<sub>2</sub> exposure. **C**. Cell deconvolution analysis correlating gene expression of mitophagy pathway with scaled abundance of specific cell populations in the lung tissue following CdCl<sub>2</sub> exposure.



Supplemental Figure 7. Gene expression changes in the mitophagy pathway in HMexposed lung tissues following MnCl<sub>2</sub> exposure. A. Volcano plot displaying differential gene expression between MnCl<sub>2</sub>-exposed and unexposed (control) lung tissues. B. Heatmap highlighting significantly altered genes with MnCl<sub>2</sub> exposure. C. Cell deconvolution analysis correlating gene expression of mitophagy pathway with scaled abundance of specific cell populations in the lung tissue following MnCl<sub>2</sub> exposure.



Supplemental Figure 8. Gene expression changes in the STING pathway in HM-exposed lung tissues following CdCl<sub>2</sub> exposure. A. Volcano plot displaying differential gene expression between CdCl<sub>2</sub>-exposed and unexposed (control) lung tissues. B. Heatmap highlighting significantly altered genes with CdCl<sub>2</sub> exposure. C. Cell deconvolution analysis correlating gene expression of STING pathway with scaled abundance of specific cell populations in the lung tissue following CdCl<sub>2</sub> exposure.



Supplemental Figure 9. Gene expression changes in the STING pathway in HM-exposed lung tissues following MnCl<sub>2</sub> exposure. **A**. Volcano plot displaying differential gene expression between MnCl<sub>2</sub>-exposed and unexposed (control) lung tissues. **B**,**D**. Heatmap (**B**) and table (**D**) highlighting significantly altered genes with MnCl<sub>2</sub> exposure. **C**. Cell deconvolution analysis correlating gene expression of STING pathway with scaled abundance of specific cell populations in the lung tissue following MnCl<sub>2</sub> exposure.



CdCl2 v <u>Control In</u>flammasome heatmap

Cell Type

Supplemental Figure 10. Gene expression changes in the inflammasome pathway in HMexposed lung tissues following CdCl<sub>2</sub> exposure. **A**. Volcano plot displaying differential gene expression between CdCl<sub>2</sub>-exposed and unexposed (control) lung tissues. **B**,**D**. Heatmap (**B**) and table (**D**) highlighting significantly altered genes with CdCl<sub>2</sub> exposure. **C**. Cell deconvolution analysis correlating gene expression of inflammasome pathway with scaled abundance of specific cell populations in the lung tissue following CdCl<sub>2</sub> exposure.



Pvalue

Supplemental Figure 11. Gene expression changes in the inflammasome pathway in HMexposed lung tissues following MnCl<sub>2</sub> exposure. **A**. Volcano plot displaying differential gene expression between MnCl<sub>2</sub>-exposed and unexposed (control) lung tissues. **B**. Heatmap highlighting significantly altered genes with MnCl<sub>2</sub> exposure. **C**. Cell deconvolution analysis correlating gene expression of inflammasome pathway with scaled abundance of specific cell populations in the lung tissue following MnCl<sub>2</sub> exposure.



Supplemental Figure 12. Gene expression changes in the airway remodeling pathway in HM-exposed lung tissues following CdCl<sub>2</sub> exposure. A. Volcano plot displaying differential gene expression between CdCl<sub>2</sub>-exposed and unexposed (control) lung tissues. B. Heatmap highlighting significantly altered genes with CdCl<sub>2</sub> exposure. C. Cell deconvolution analysis correlating gene expression of airway remodeling pathway with scaled abundance of specific cell populations in the lung tissue following CdCl<sub>2</sub> exposure.



Supplemental Figure 13. Gene expression changes in the airway remodeling pathway in HM-exposed lung tissues following MnCl<sub>2</sub> exposure. **A**. Volcano plot displaying differential gene expression between MnCl<sub>2</sub>-exposed and unexposed (control) lung tissues. **B**. Heatmap highlighting significantly altered genes with MnCl<sub>2</sub> exposure. **C**. Cell deconvolution analysis correlating gene expression of airway remodeling pathway with scaled abundance of specific cell populations in the lung tissue following MnCl<sub>2</sub> exposure



Supplemental Figure 14. Correlation of gene expression between complement and sphingolipid pathways following NaAsO<sub>2</sub> exposure. Dot plot correlating expression of sphingolipid metabolism genes (y-axis) with expression of complement genes (x-axis) following NaAsO<sub>2</sub> exposure.



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Sphingolipid

and



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Supplemental Figure 15. Correlation of gene expression between sphingolipid, inflammasome, STING, and mitophagy pathways following NaAsO<sub>2</sub> exposure **A**. Dot plot correlating expression of sphingolipid genes (y-axis) with expression of inflammasome genes (xaxis) following NaAsO<sub>2</sub> exposure. **B**. Dot plot correlating expression of sphingolipid genes (y-axis) with expression of mitophagy genes (x-axis) following NaAsO<sub>2</sub> exposure. **C**. Dot plot correlating expression of sphingolipid genes (y-axis) with expression of STING genes (x-axis) following NaAsO<sub>2</sub> exposure. **D**. Dot plot correlating expression of inflammasome genes (y-axis) with expression of STING genes (x-axis) following NaAsO<sub>2</sub> exposure. **E**. Dot plot correlating expression of mitophagy genes (y-axis) with expression of STING genes (x-axis) following of mitophagy genes (y-axis) with expression of STING genes (x-axis) following naAsO<sub>2</sub> exposure.



**Supplemental Figure 16. Correlation of gene expression between complement, mitophagy, inflammasome, and STING pathways following NaAsO**<sup>2</sup> **exposure A.** Dot plot correlating expression of mitophagy genes (y-axis) with expression of complement genes (x-axis) following NaAsO<sub>2</sub> exposure. **B.** Dot plot correlating expression of inflammasome genes (y-axis) with expression of complement genes (x-axis) following NaAsO<sub>2</sub> exposure. **C.** Dot plot correlating expression of STING genes (y-axis) with expression of complement genes (x-axis) following NaAsO<sub>2</sub> exposure. **D.** Dot plot correlating expression of inflammasome genes (y-axis) with expression of mitophagy genes (x-axis) following NaAsO<sub>2</sub> exposure. **C.** Dot plot correlating expression of mitophagy genes (x-axis) following NaAsO<sub>2</sub> exposure.



Supplemental Figure 17. Correlation of gene expression between airway remodeling pathway and sphingolipid, complement, mitophagy, STING, or inflammasome pathways following NaAsO<sub>2</sub> exposure A. Dot plot correlating expression of sphingolipid genes (y-axis) with expression of airway remodeling genes (x-axis) following NaAsO<sub>2</sub> exposure. B. Dot plot correlating expression of complement genes (y-axis) with expression of airway remodeling genes (x-axis) following NaAsO<sub>2</sub> exposure. G. Dot plot correlating expression of mitophagy genes (y-axis) with expression of airway remodeling genes (x-axis) following NaAsO<sub>2</sub> exposure. C. Dot plot correlating expression of mitophagy genes (y-axis) with expression of airway remodeling genes (x-axis) following NaAsO<sub>2</sub> exposure. D. Dot plot correlating expression of STING genes (y-axis) with expression of airway remodeling genes (x-axis) following NaAsO<sub>2</sub> exposure. E. Dot plot correlating expression of inflammasome genes (y-axis) with expression of airway remodeling genes (x-axis) following NaAsO<sub>2</sub> exposure. Use the plot correlating expression of airway remodeling genes (y-axis) with expression of airway remodeling genes (y-axis) with expression of airway remodeling genes (y-axis) with expression of airway remodeling genes (y-axis) following NaAsO<sub>2</sub> exposure. E. Dot plot correlating expression of inflammasome genes (y-axis) with expression of airway remodeling genes (x-axis) following NaAsO<sub>2</sub> exposure.