

Supplementary Materials

Lack of resolution of inflammation marks malignant pleural mesothelioma progression

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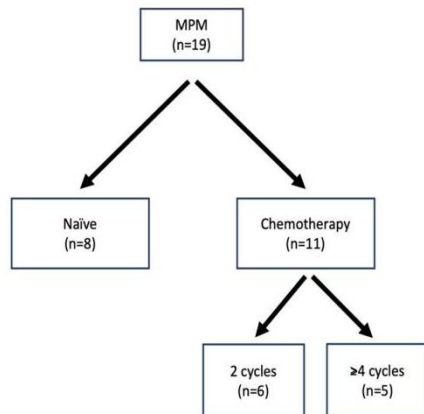
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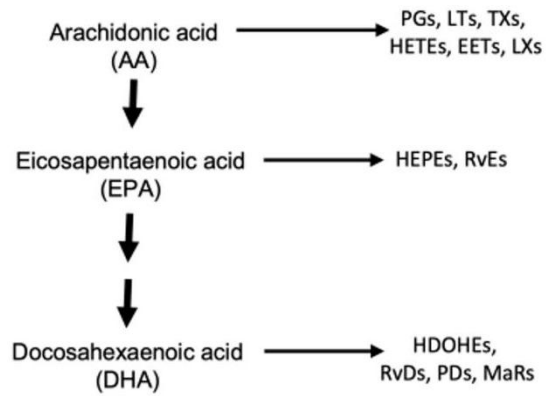
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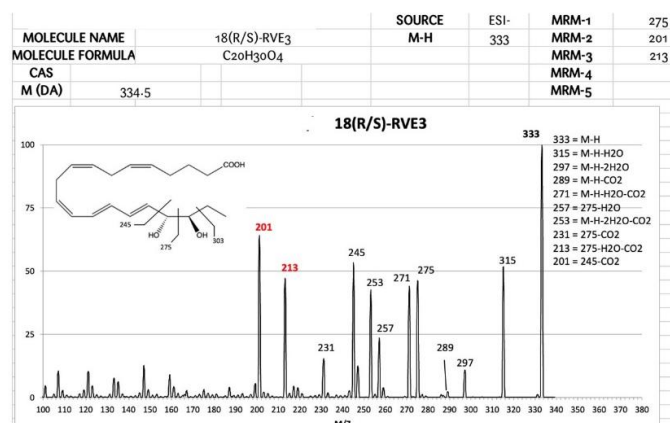


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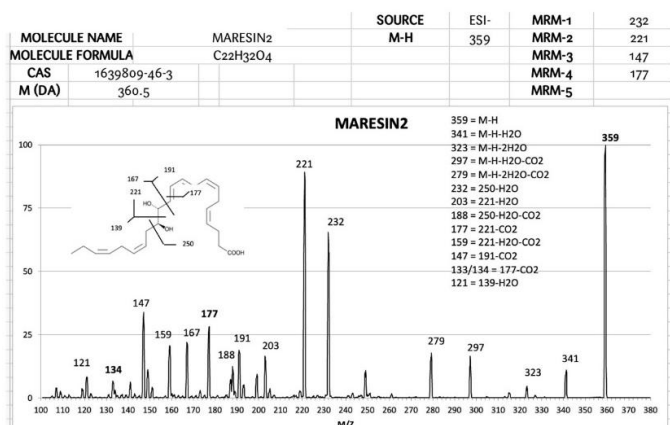


Supplementary Figure 1. Experimental scheme. (A) composition and workflow of experimental groups. MPM pleural exudates ($n = 19$) were obtained from patients treated ($n = 6$ with two cycles; $n = 5$ with four or more cycles) or not ($n = 8$) with chemotherapy. (B) Schematic representation of the classes of oxylipins and metabolites derived from AA, EPA, and DHA and analyzed in this study.

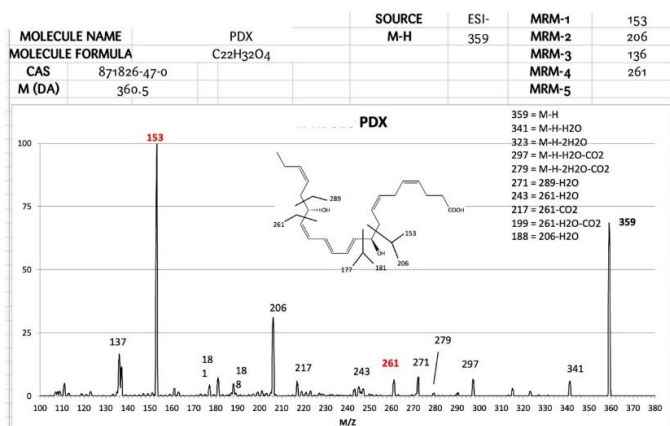
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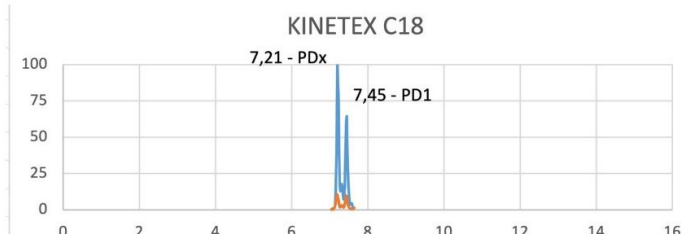
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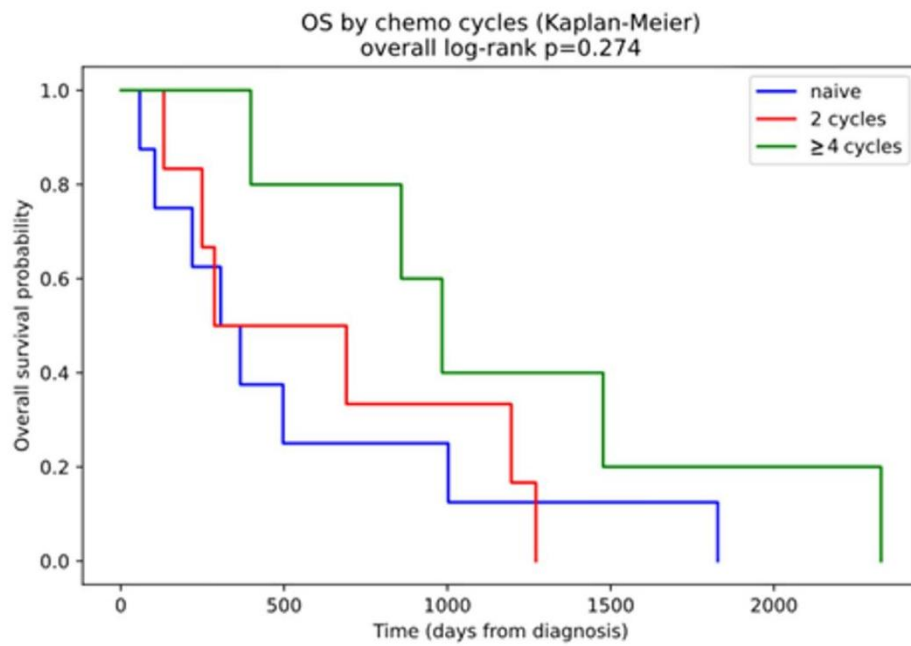
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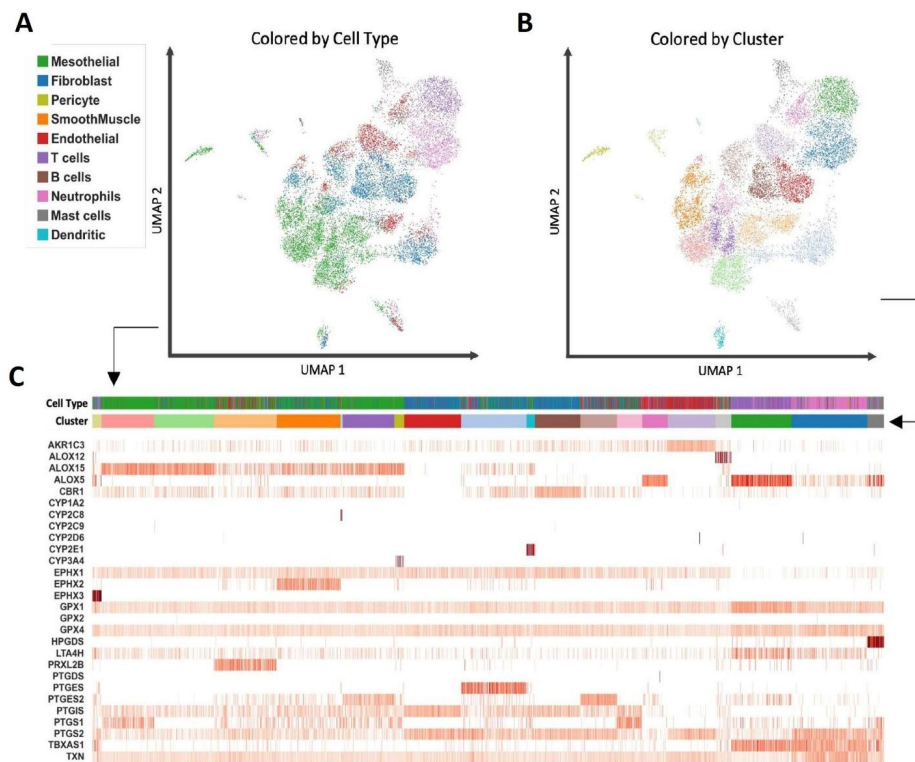
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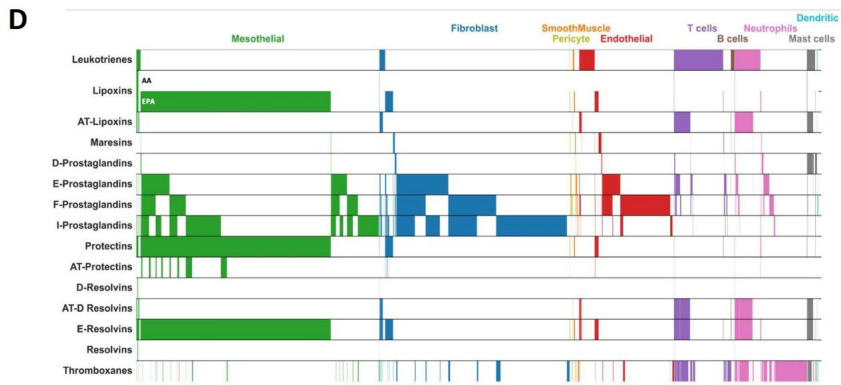


Supplementary Figure 2. Identification of SPMs. (A-C) Representative mass spectra of 18R/S-RvE3 (A), MaR2 (B), and PDX (C); (D) Distinction between PDX and PD1 isomers and their relative Multiple Reaction Monitoring (MRM).

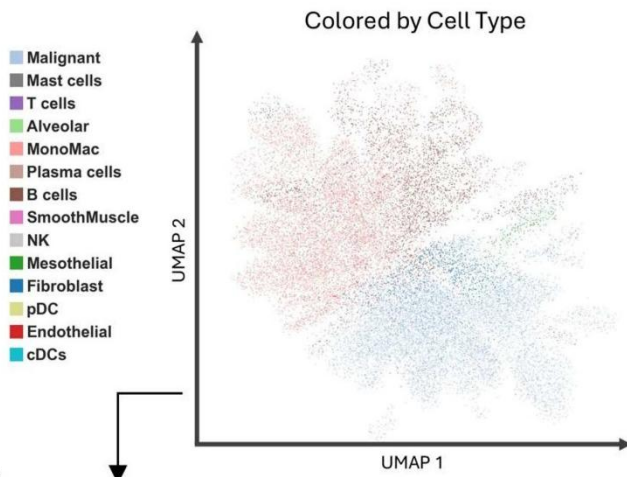
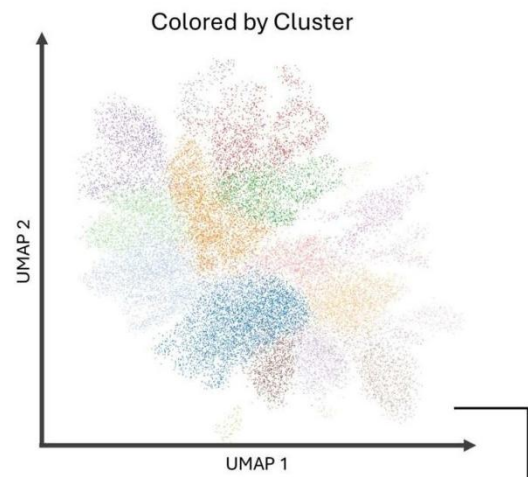
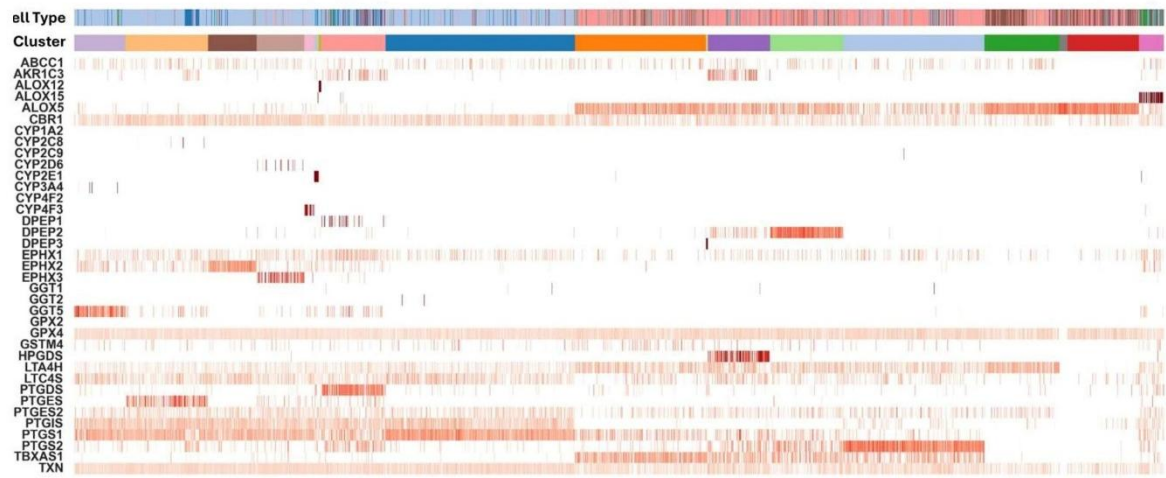


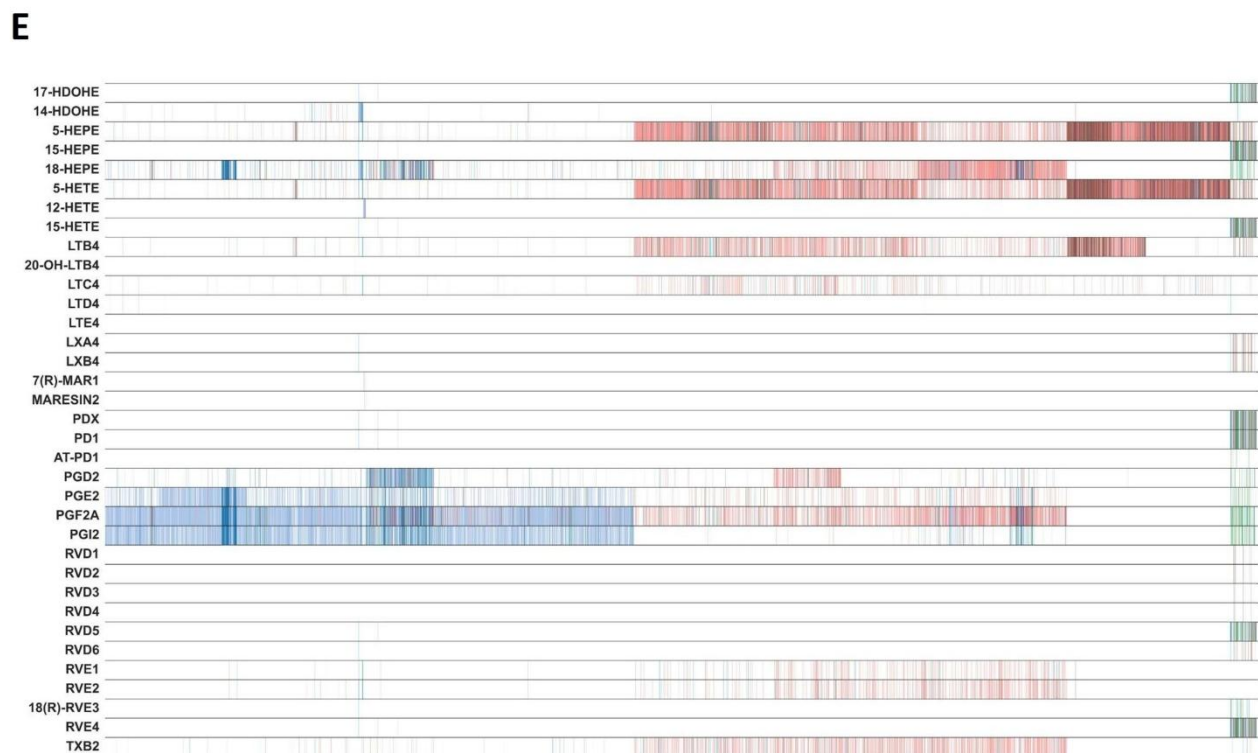
Supplementary Figure 3. Overall survival of patients enrolled in this study by treatment (number of cycles). No statistically significant differences were recorded between the three groups of MPM patients. Multiparametric log-rank test. Table: results (P values) of the log rank test with intergroup comparisons.



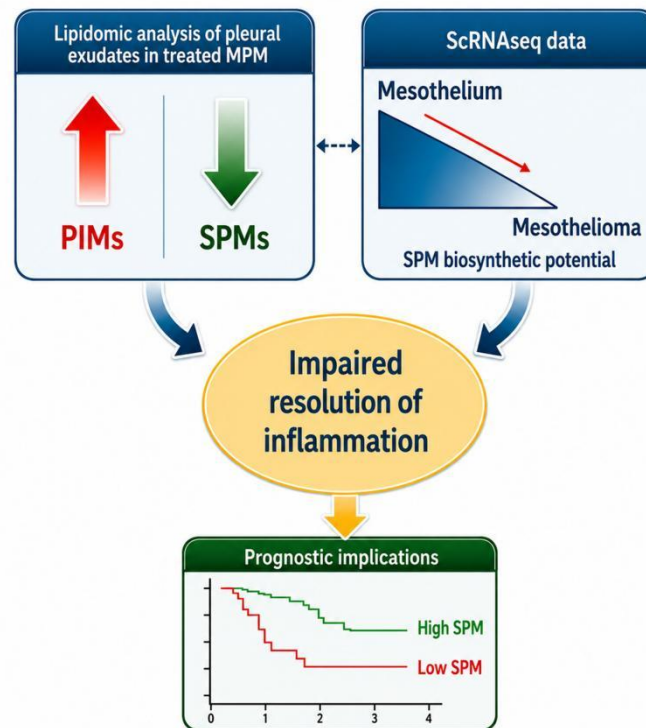


Supplementary Figure 4. Inflammation-resolution biosynthetic pathways of lipid mediators are differentially altered in MPM cell types. Predictive model. (A and B) UMAP plots are sorted by cell type and clusters in the normal pleura of control subjects; (C) Heatmaps highlighting SPM enzymes within the cell clusters of control subjects; (D and E) Heatmaps highlighting individual lipids in cells that express all required enzymes for their synthesis, as measured by targeted lipidomics in the human pleura of control subjects.

A**B****C**



Supplementary Figure 5. Inflammation-resolution biosynthetic pathways of lipid mediators are differentially altered in MPM cell types - predictive model. (A and B) UMAP plots are sorted by cell type and clusters in MPM patients; (C) Heatmaps highlighting SPM enzymes within the cell clusters of MPM patients; (D and E) Heatmaps highlighting individual lipids in cells that express all required enzymes for their synthesis, as measured by targeted lipidomics of MPM patients.



Graphical Abstract. Unresolved inflammation in malignant pleural mesothelioma. The graphical abstract illustrates the imbalance between pro-inflammatory lipid mediators and specialized pro-resolving mediators in malignant pleural mesothelioma. Pleural exudate analysis shows increased prostaglandins in the PIMs compartment and reduced SPMs, including maresins, resolvins, and protectins. Single-cell RNA sequencing data indicate reduced expression of SPM enzymes in mesothelioma cells compared with mesothelial cells. Chemotherapy further decreases SPMs and increases prostaglandin levels, promoting persistent, unresolved inflammation and impaired inflammatory resolution. Low SPM levels are associated with poorer survival outcomes. The AI tool ChatGPT (version 5.5, released 2026-07-08) was used solely for to cosmetically improve the graphical abstract.