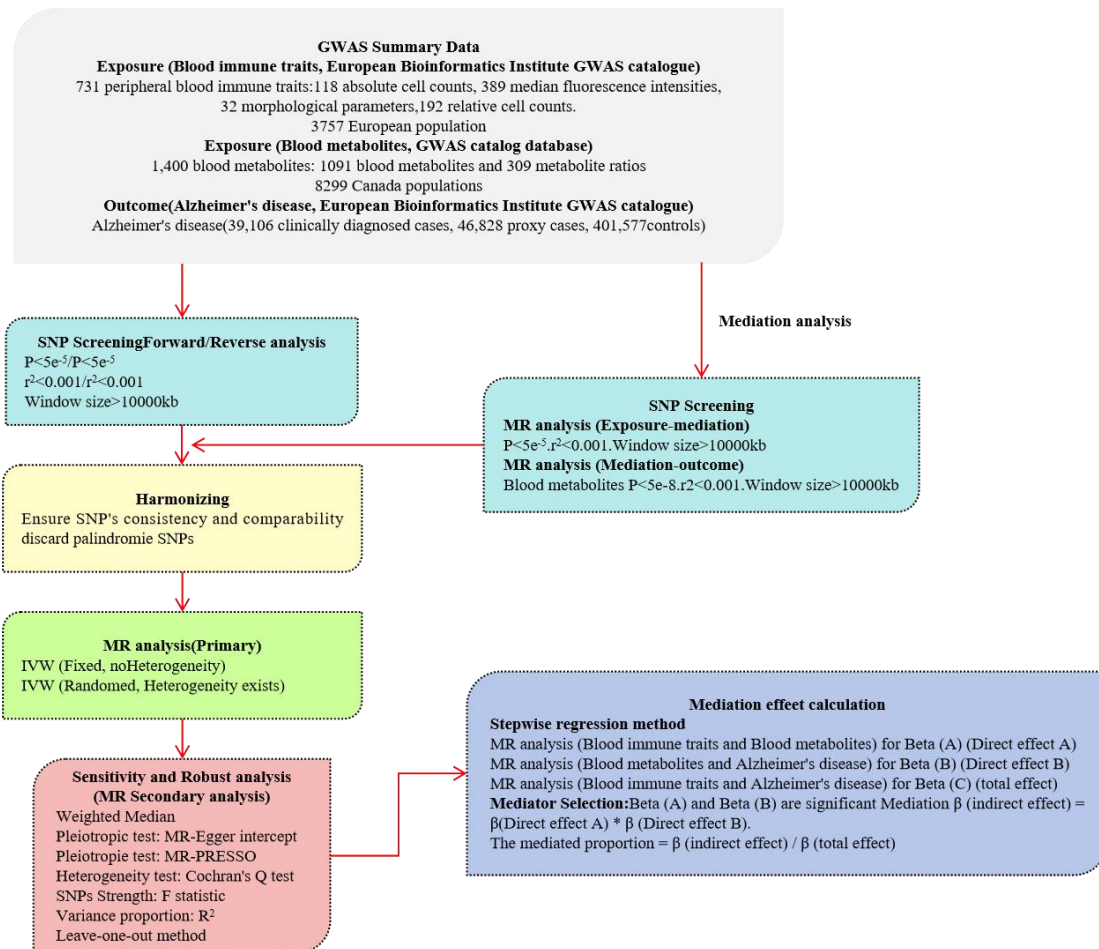
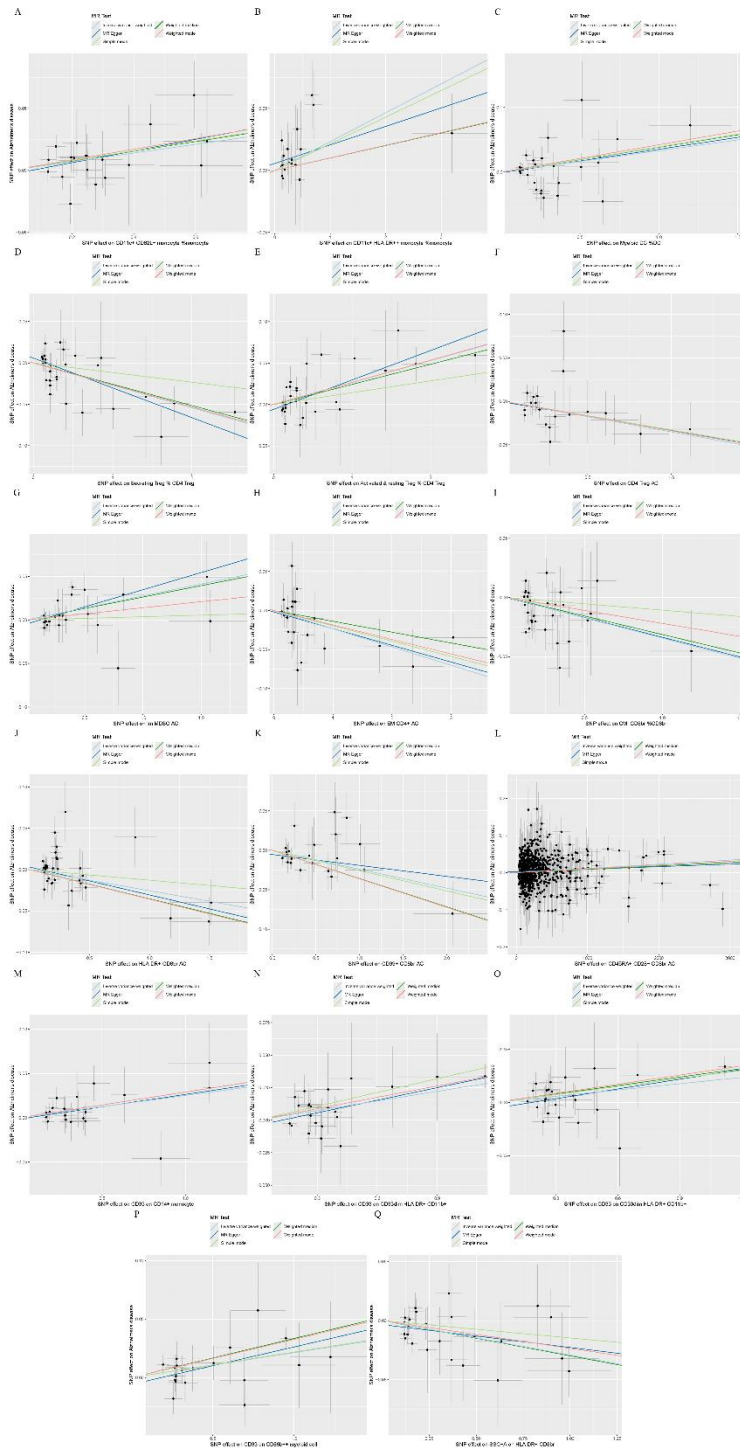
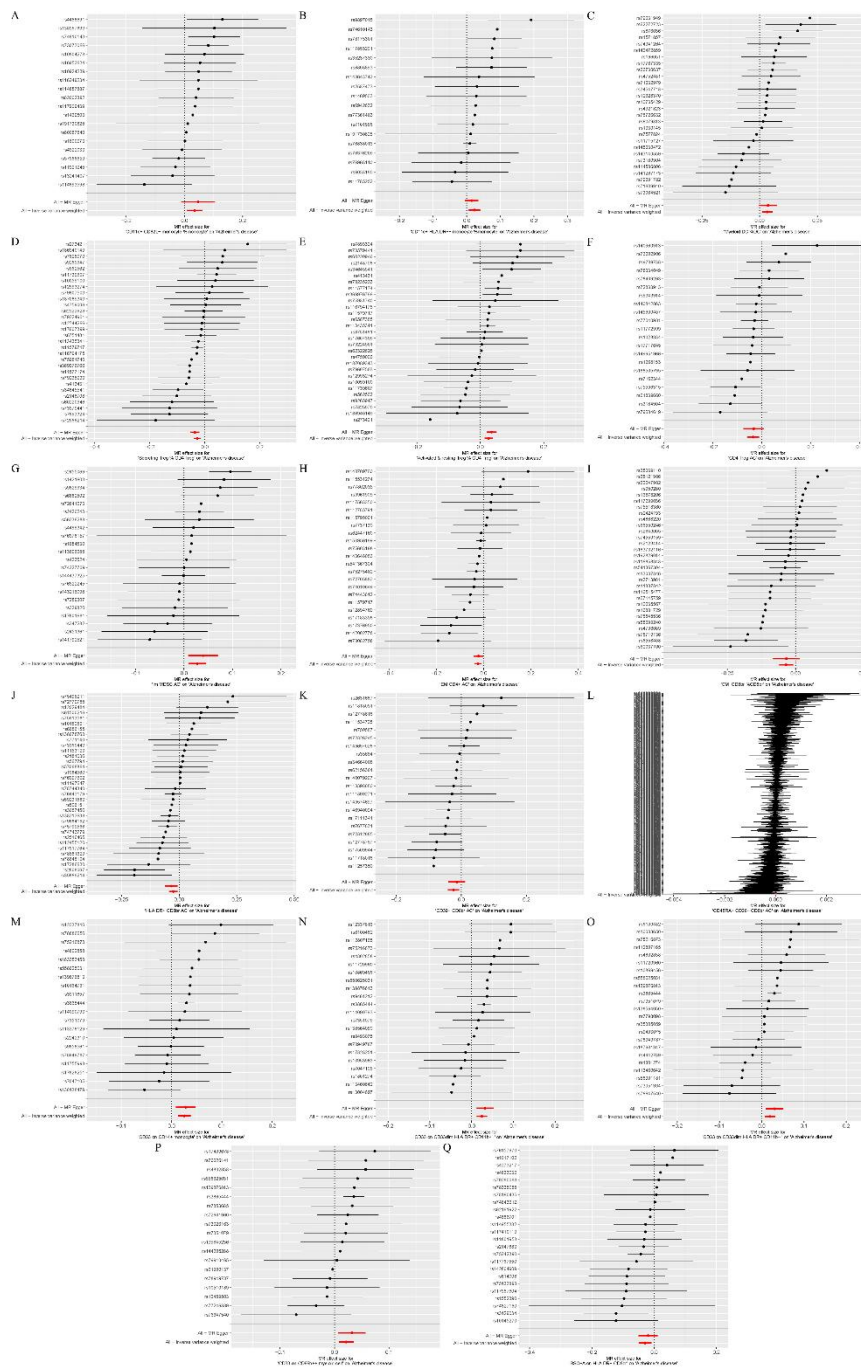




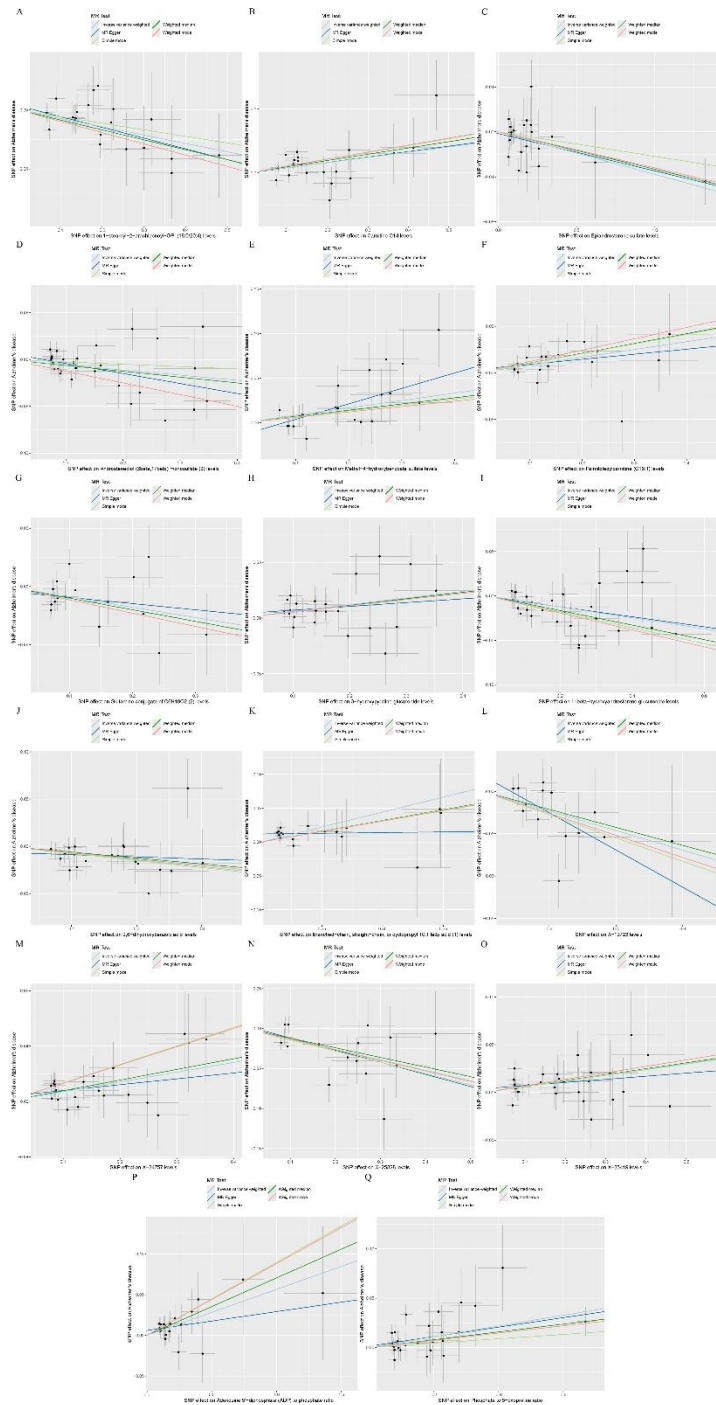
Supplement Figure 1. Describe measurement, quality control and selection of genetic variants



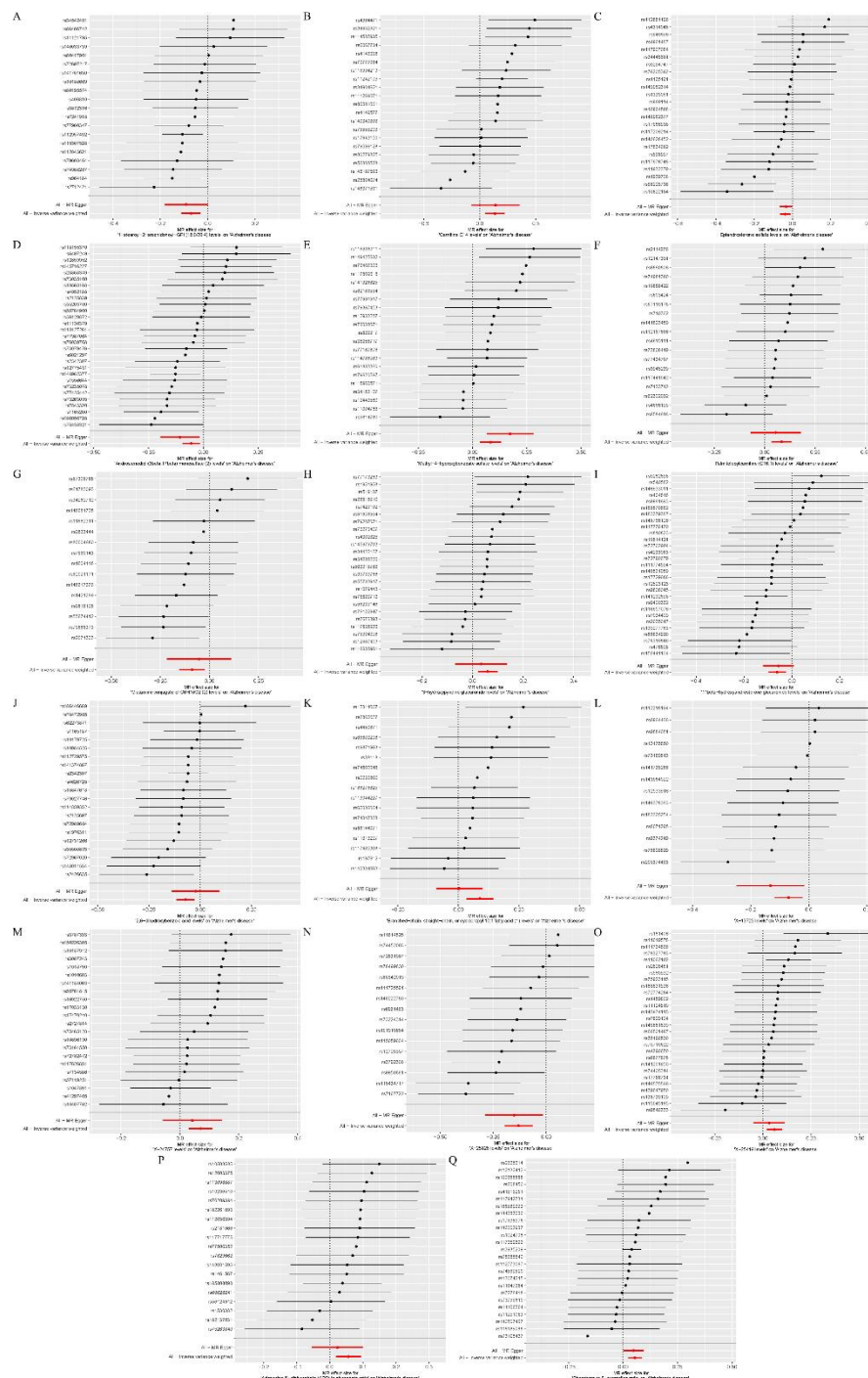
Supplement Figure 2. MR Scatter Plot: Causal Effect of Immune Cell Traits on AD Risk.(A) CD11c+ CD62L- monocyte of monocyte;(B)CD11c+ HLA DR++ monocyte of monocyte;(C) Myeloid DC of DC;(D) Secreting Treg of CD4 Treg;(E)Activated & resting Treg of CD4 Treg;(F) CD4 Treg AC;(G) Im MDSC AC;(H) EM CD4+ AC;(I) CM CD8br of CD8br;(J) HLA DR+ CD8br AC;(K) CD39+ CD8br AC;(L)CD45RA+ CD28- CD8br AC;(M)CD33 on CD14+ monocyte;(N) CD33 on CD33dim HLA DR+ CD11b+;(O) CD33 on CD33dim HLA DR+ CD11b-;(P) CD33 on CD66b++ myeloid cell;(Q) SSC-A on HLA DR+ CD8br.



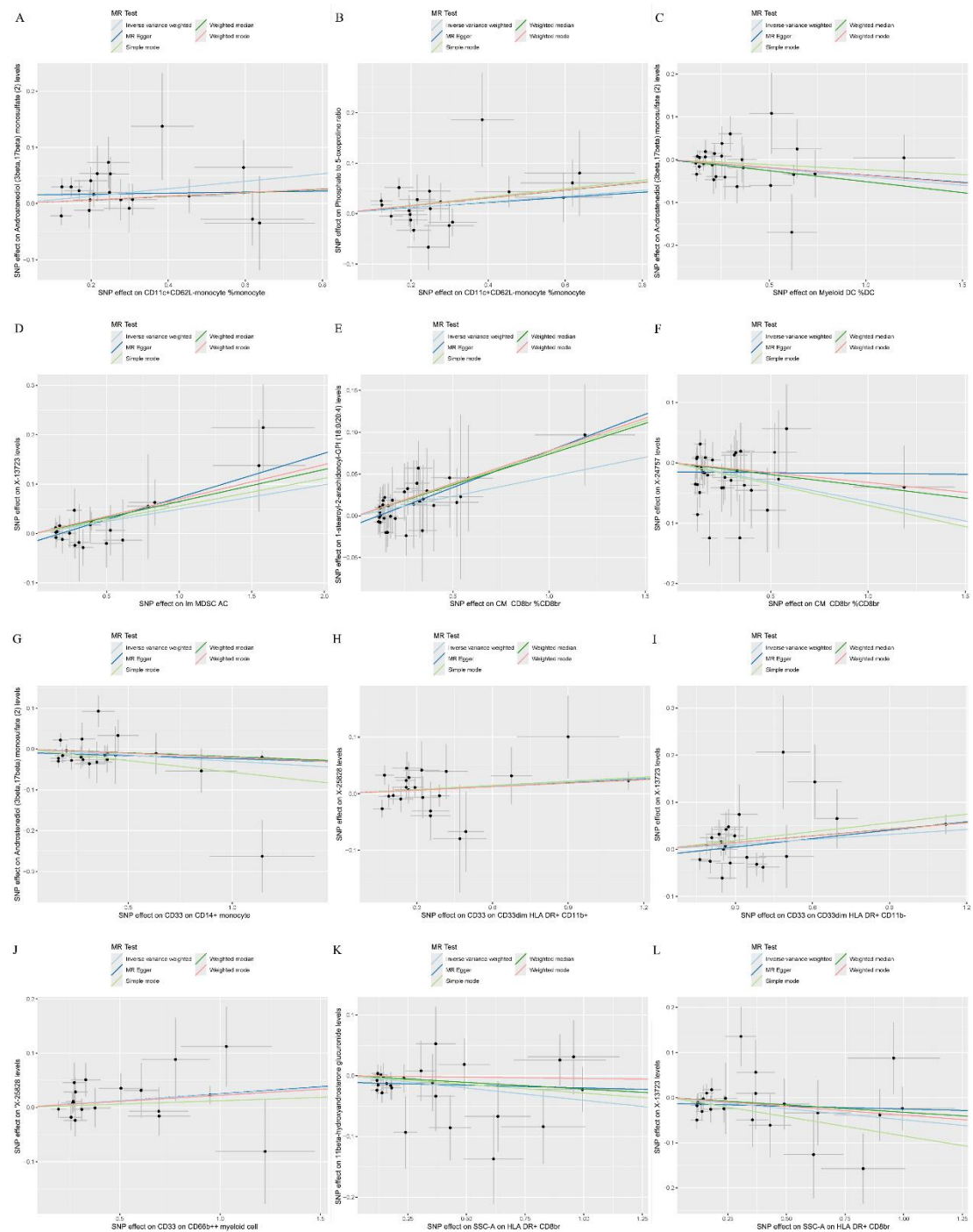
Supplement Figure 3. MR Forest Plot: Causal Effect of Immune Cell Traits on AD Risk. The error line represents a 95% confidence interval. (A) CD11c+ CD62L- monocyte of monocyte; (B) CD11c+ HLA DR++ monocyte of monocyte; (C) Myeloid DC of DC; (D) Secreting Treg of CD4 Treg; (E) Activated & resting Treg of CD4 Treg; (F) CD4 Treg AC; (G) Im MDSC AC; (H) EM CD4+ AC; (I) CM CD8br of CD8br; (J) HLA DR+ CD8br AC; (K) CD39+ CD8br AC; (L) CD45RA+ CD28- CD8br AC; (M) CD33 on CD14+ monocyte; (N) CD33 on CD33dim HLA DR+ CD11b+; (O) CD33 on CD33dim HLA DR+ CD11b-; (P) CD33 on CD66b++ myeloid cell; (Q) SSC-A on HLA DR+ CD8br.



Supplement Figure 4. MR Scatter Plot: Causal Effect of Metabolites on AD Risk. The error line represents a 95% confidence interval.(A) 1-stearoyl-2-arachidonoyl-GPI (18:0/20:4) levels;(B) Carnitine C14 levels;(C) Epiandrosterone sulfate levels;(D) Androstenediol (3beta,17beta) monosulfate (2) levels;(E) Methyl-4-hydroxybenzoate sulfate levels;(F) Palmitoleoylcarnitine (C16:1) levels;(G) Glutamine conjugate of C₆H₁₀O₂ (2) levels;(H) 3-hydroxypyridine glucuronide levels;(I) 11beta-hydroxyandrosterone glucuronide levels;(J) 2,6-dihydroxybenzoic acid levels;(K) Branched-chain, straight-chain, or cyclopropyl 10:1 fatty acid (1) levels;(L) X-13723 levels;(M) X-24757 levels;(N) X-25828 levels;(O) X-25419 levels;(P) Adenosine 5'-diphosphate (ADP) to phosphate ratio;(Q) Phosphate to 5-oxoproline ratio.



Supplement Figure 5. MR Forest Plot: Causal Effect of Metabolites on AD Risk.(A) 1-stearoyl-2-arachidonoyl-GPI (18:0/20:4) levels;(B) Carnitine C14 levels;(C) Epiandrosterone sulfate levels;(D) Androstenediol (3beta,17beta) monosulfate (2) levels;(E) Methyl-4-hydroxybenzoate sulfate levels;(F) Palmitoleoylcarnitine (C16:1) levels;(G) Glutamine conjugate of C₆H₁₀O₂ (2) levels;(H) 3-hydroxypyridine glucuronide levels;(I) 11beta-hydroxyandosterone glucuronide levels;(J) 2,6-dihydroxybenzoic acid levels;(K) Branched-chain, straight-chain, or cyclopropyl 10:1 fatty acid (1) levels;(L) X-13723 levels;(M) X-24757 levels;(N) X-25828 levels;(O)X-25419 levels;(P)Adenosine 5'-diphosphate (ADP) to phosphate ratio;(Q)Phosphate to 5-oxoproline ratio.



Supplement Figure 6. Causal Effect of Metabolites on Immune Cell Traits.(A) CD11c+ CD62L-monocyte of monocyte on Androstenediol (3beta,17beta) monosulfate (2) levels;(B) CD11c+ CD62L-monocyte of monocyte on Phosphate to 5-oxoproline ratio;(C) Myeloid DC of DC on Androstenediol (3beta,17beta) monosulfate (2) levels;(D) Im MDSC AC on X-13723 levels;(E) CM CD8br of CD8br on 1-stearoyl-2-arachidonoyl-GPI (18:0/20:4) levels;(F) CM CD8br of CD8br on X-24757 levels;(G) CD33 on CD14+ monocyte on Androstenediol (3beta,17beta) monosulfate (2) levels;(H) CD33 on CD33dim HLA DR+ CD11b+ on X-25828 levels;(I) CD33 on CD33dim HLA DR+ CD11b- on X-13723 levels;(J) CD33 on CD66b++ myeloid cell on X-25828 levels;(K) SSC-A on HLA DR+ CD8br on 11beta-hydroxyandrosterone glucuronide levels;(L) SSC-A on HLA DR+ CD8br on X-13723 levels,

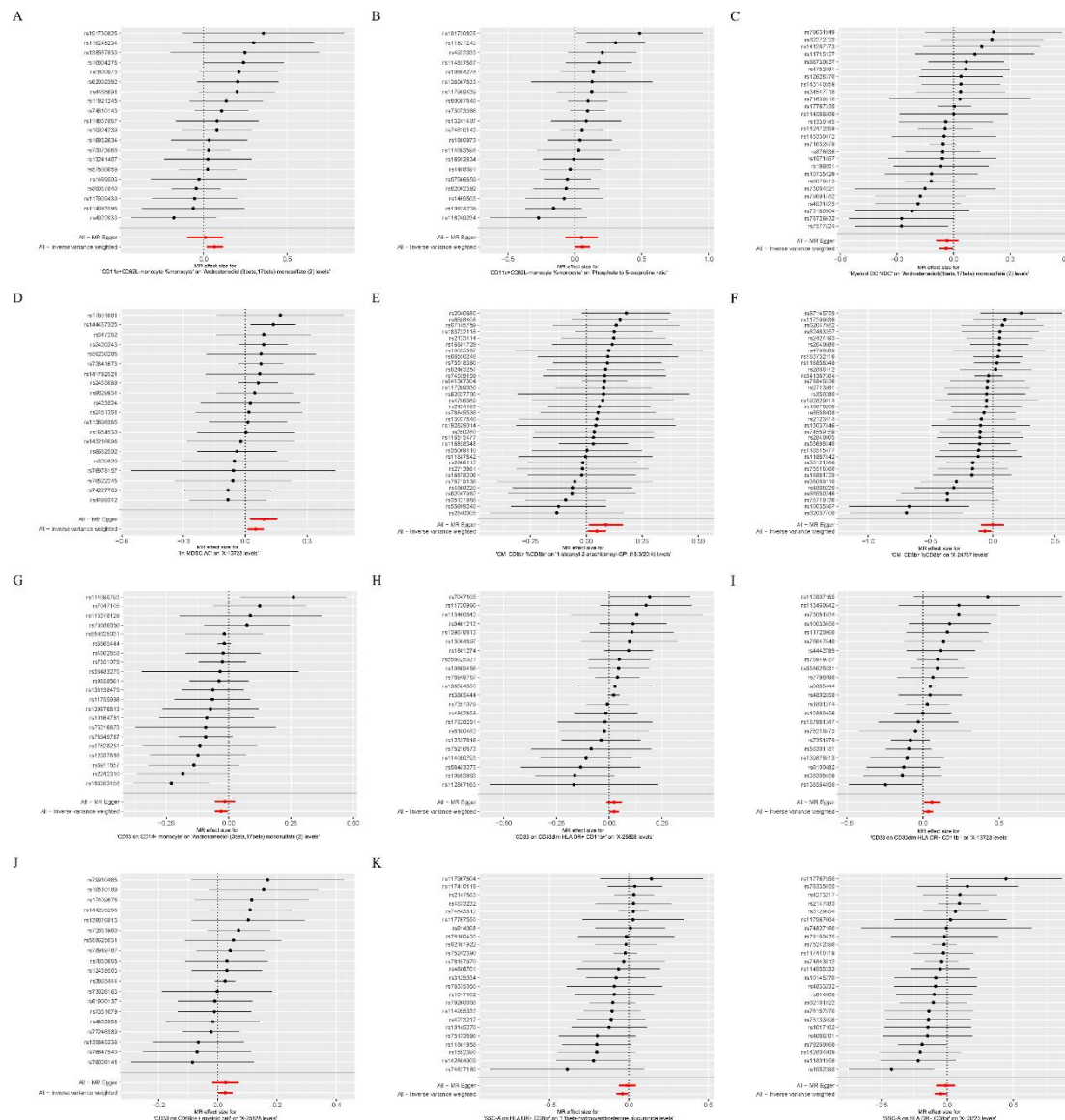


Fig 7. MR Forest Plot: Causal Effect of Metabolites on Immune Cell Traits. The error line represents a 95% confidence interval.(A)CD11c+ CD62L- monocyte of monocyte on Androstenediol (3beta,17beta) monosulfate (2) levels;(B)CD11c+ CD62L- monocyte of monocyte on Phosphate to 5-oxoproline ratio;(C)Myeloid DC of DC on Androstenediol (3beta,17beta) monosulfate (2) levels;(D)Im MDSC AC on X-13723 levels;(E)CM CD8br of CD8br on 1-stearoyl-2-arachidonoyl-GPI (18:0/20:4) levels;(F)CM CD8br of CD8br on X-24757 levels;(G)CD33 on CD14+ monocyte on Androstenediol (3beta,17beta) monosulfate (2) levels;(H)CD33 on CD33dim HLA DR+ CD11b+ on X-25828 levels;(I)CD33 on CD33dim HLA DR+ CD11b- on X-13723 levels;(J)CD33 on CD66b++ myeloid cell on X-25828 levels;(K)SSC-A on HLA DR+ CD8br on 11beta-hydroxyandrosterone glucuronide levels;(L)SSC-A on HLA DR+ CD8br on X-13723 levels.