

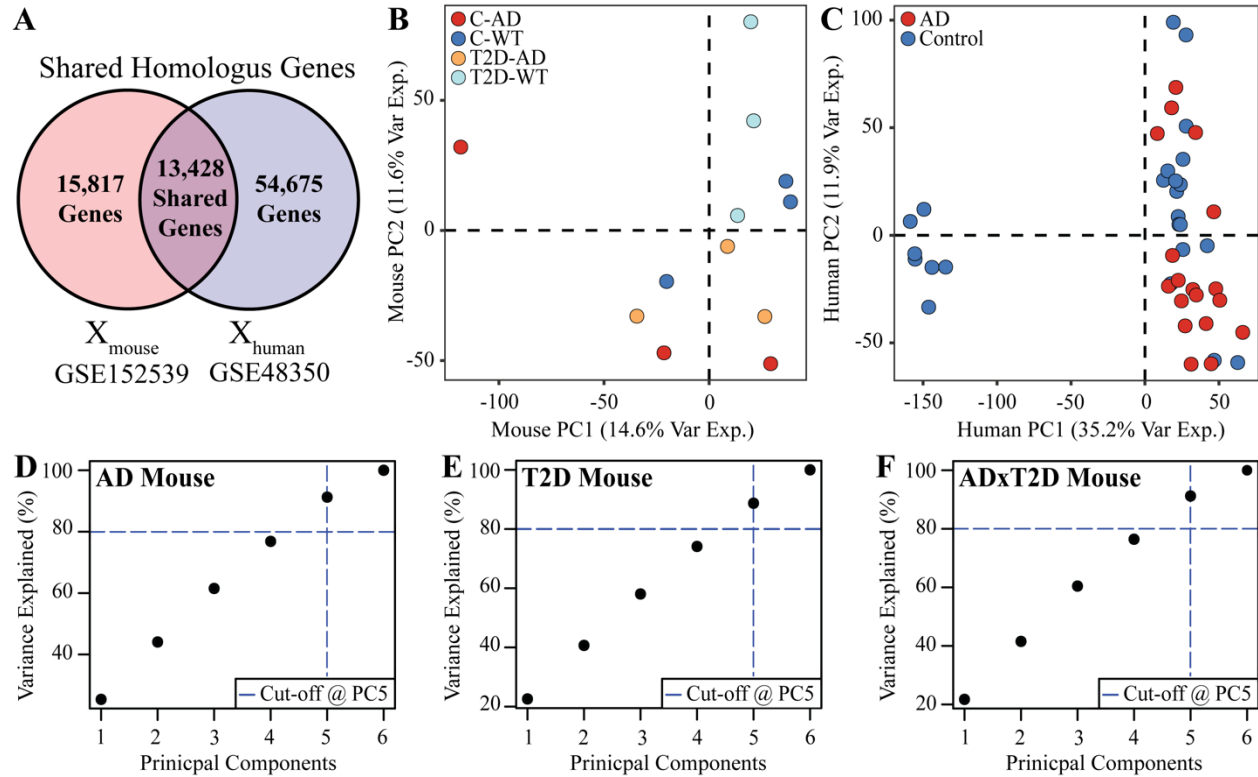
# **Cross-Species Modeling Identifies Gene Signatures in Type 2 Diabetes Mouse Models Predictive of Inflammatory and Estrogen Signaling Pathways Associated with Alzheimer's Disease Outcomes in Humans**

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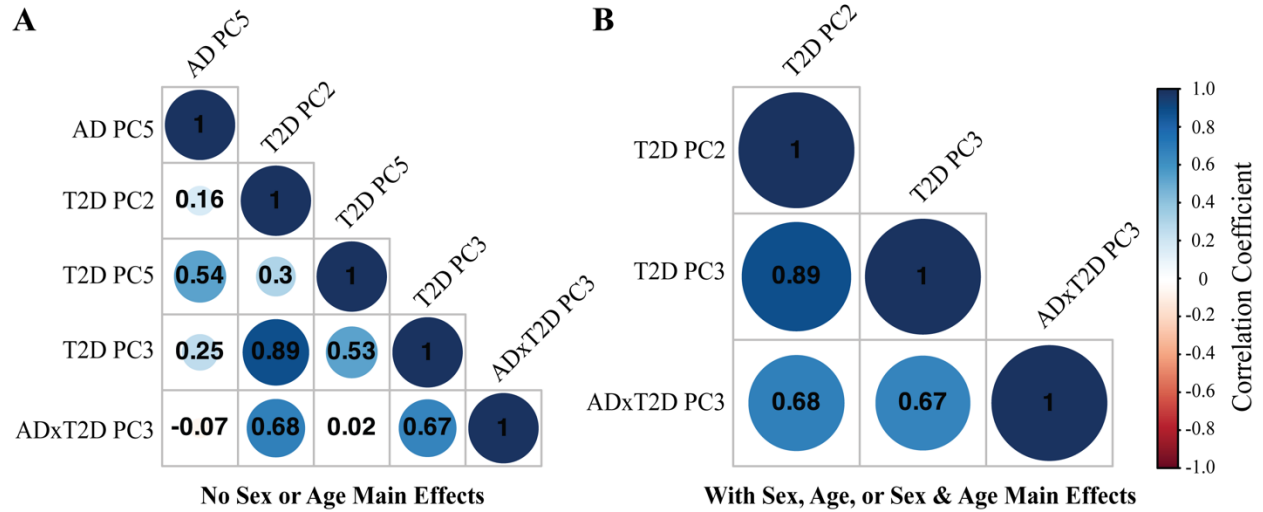
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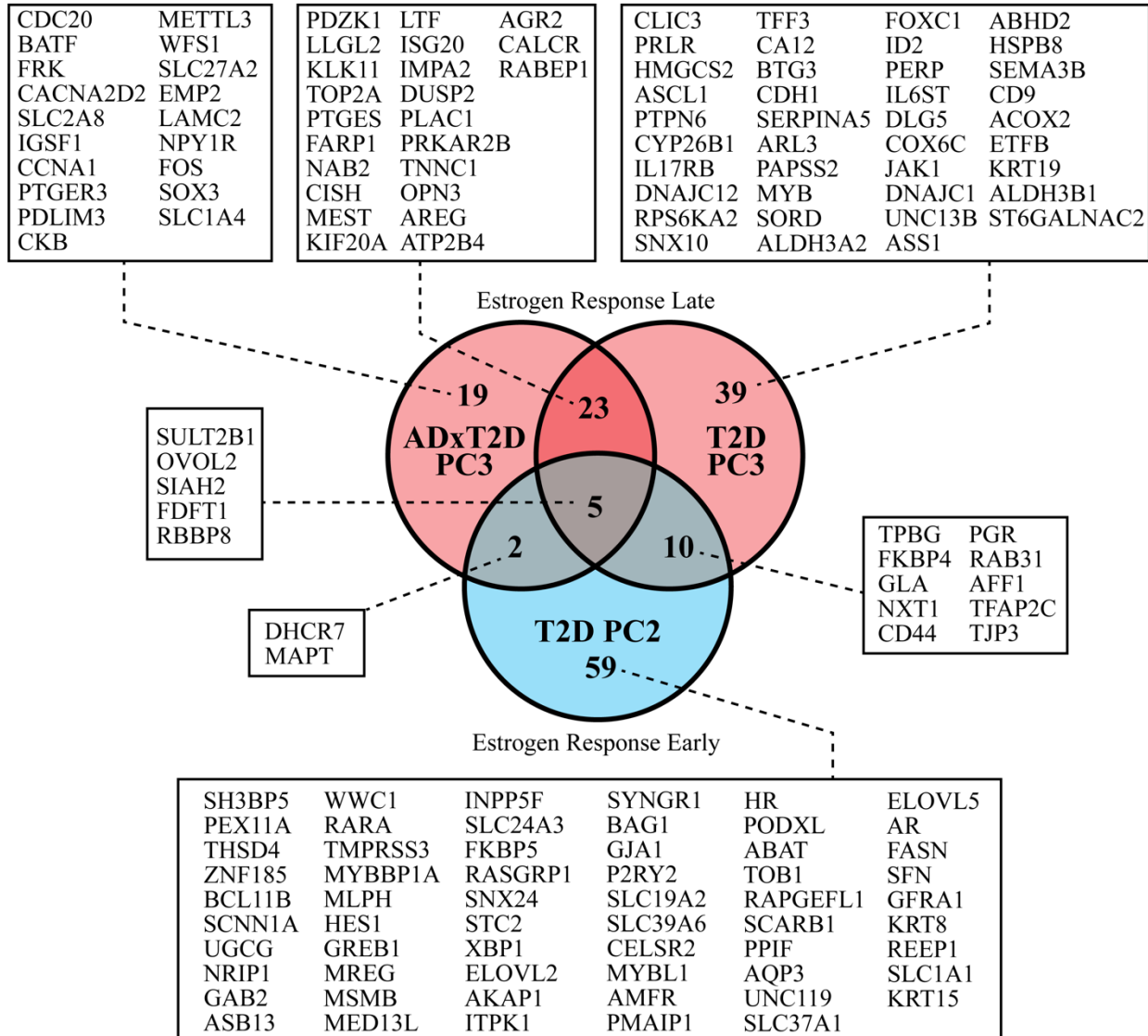
## Supplementary Information



**Supplementary Figure S1. Overview of the publicly available human and mouse data.** (A) The mouse and human dataset share 13,428 homologous gene pairs. (B) PCA of the four mouse conditions. (C) PCA of the human and control groups. (D-F) Cumulative variance explained plots for each of the respective mouse conditions, each with a PC cut-off of 5 PCs.



**Supplementary Figure S2. Spearman correlation plots of the selected PCs from LASSO. (A)** Correlation plot for the model without sex or age as included main effects. **(B)** Correlation plot for models with sex, age, or sex and age as included main effects in the LASSO model. Models with sex, age, or sex and age main effects all contained the same selected PCs from LASSO.



**Supplementary Figure S3. Number of shared genes enriched for estrogen pathways.** Mouse T2D PC3 and ADxT2D PC3 identified “Estrogen Response Late” to be enriched in AD (red), whereas mouse T2D PC2 was enriched for “Estrogen Response Early” in human control groups (blue). Overlapped genes represent gene signatures that were enriched in more than one mouse PC.