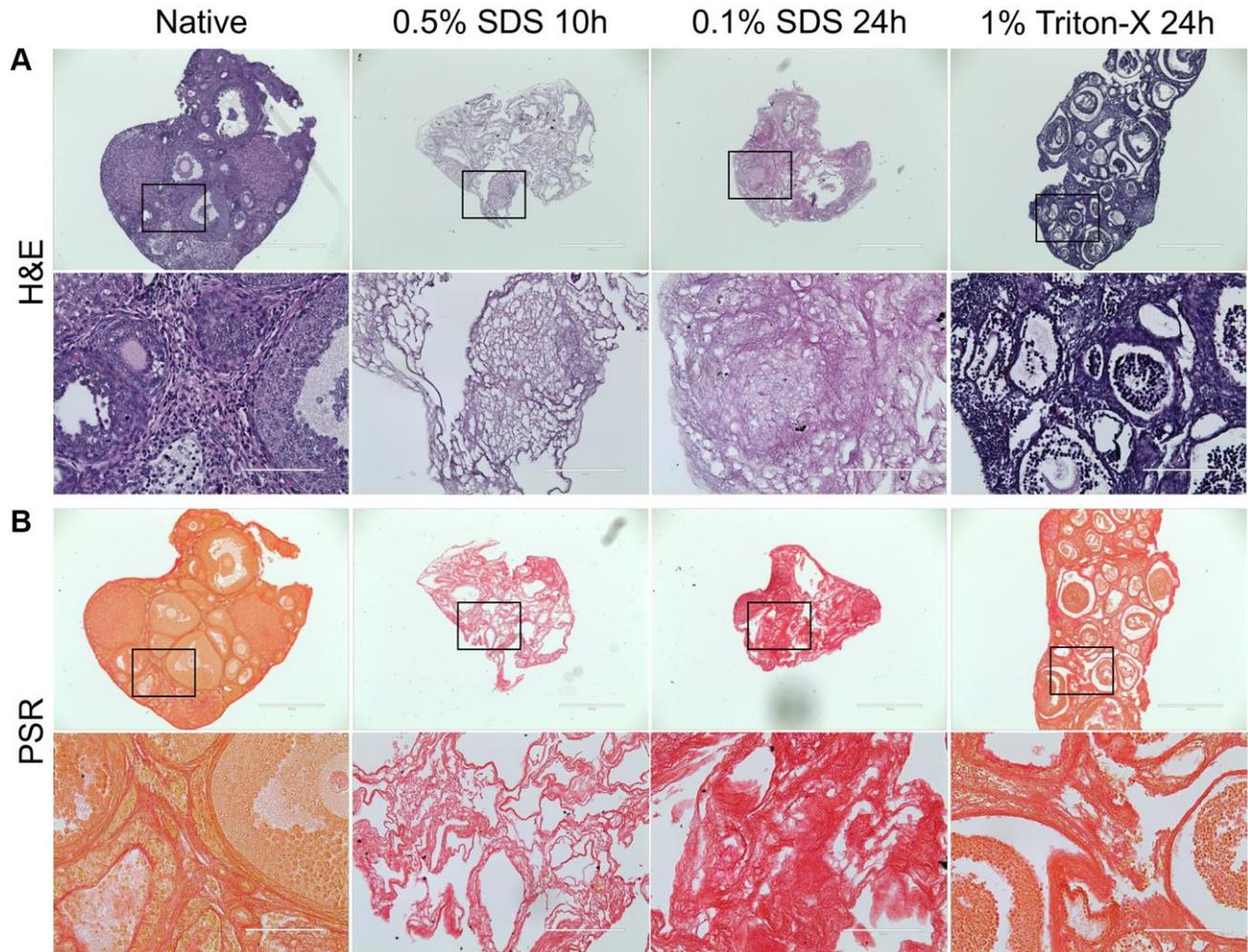
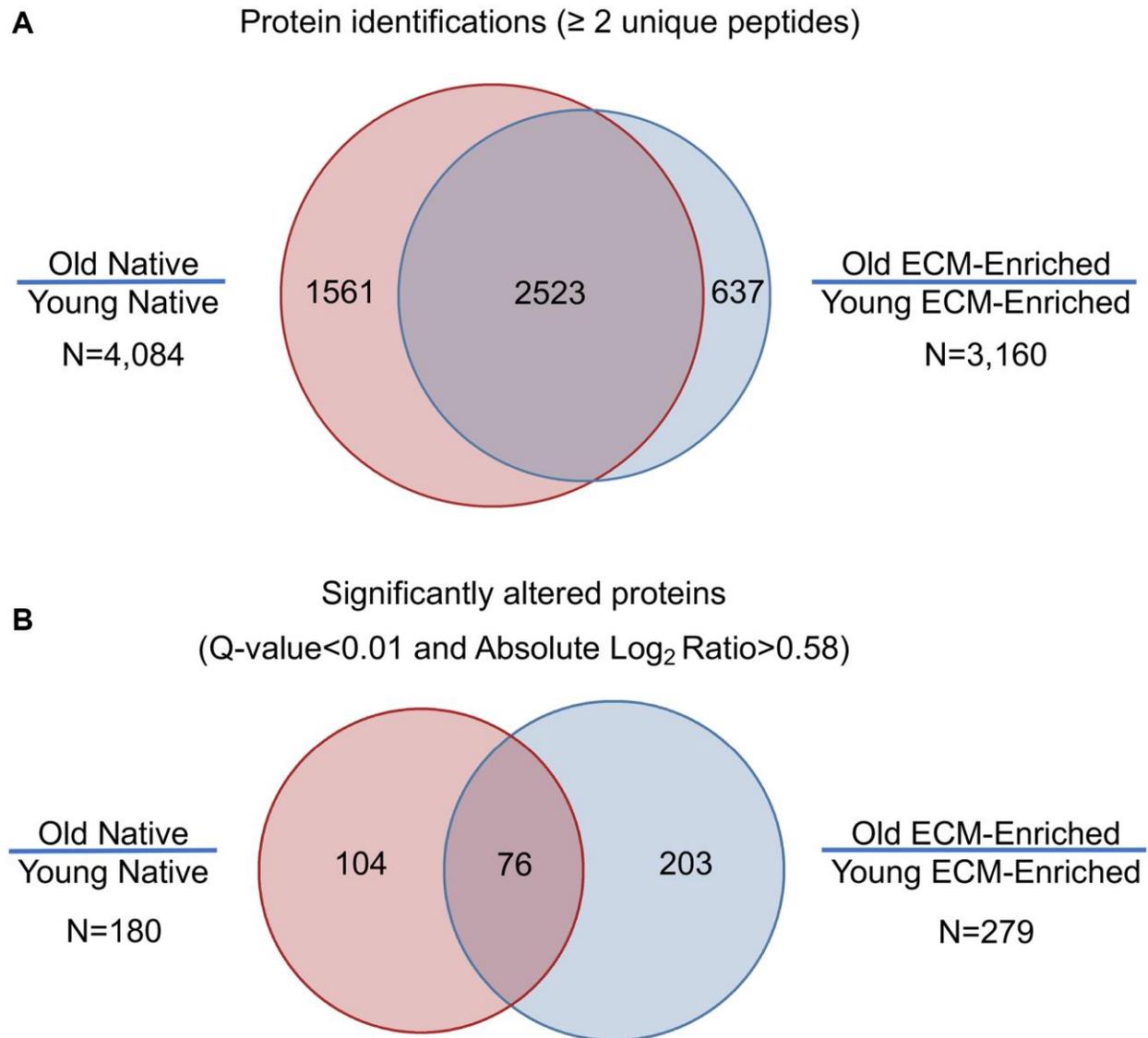


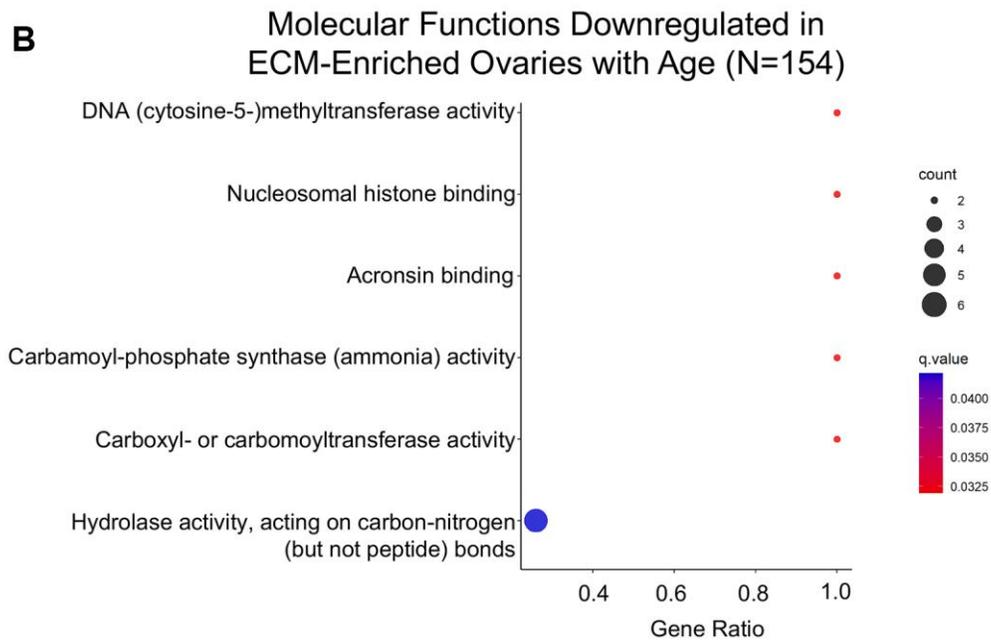
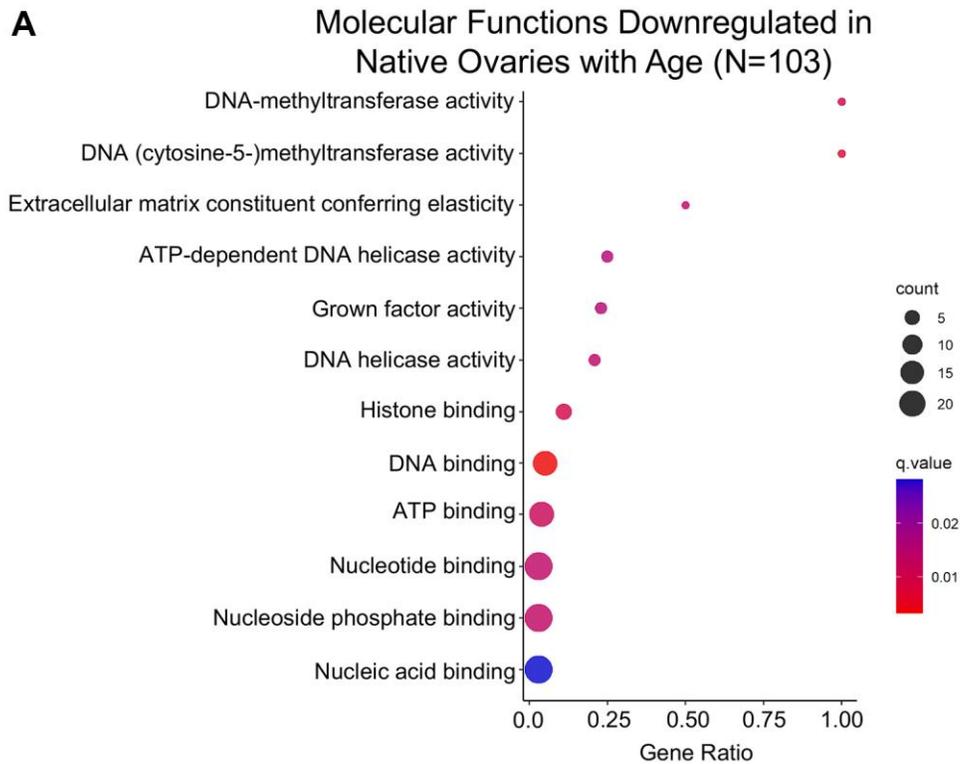
## SUPPLEMENTARY FIGURES



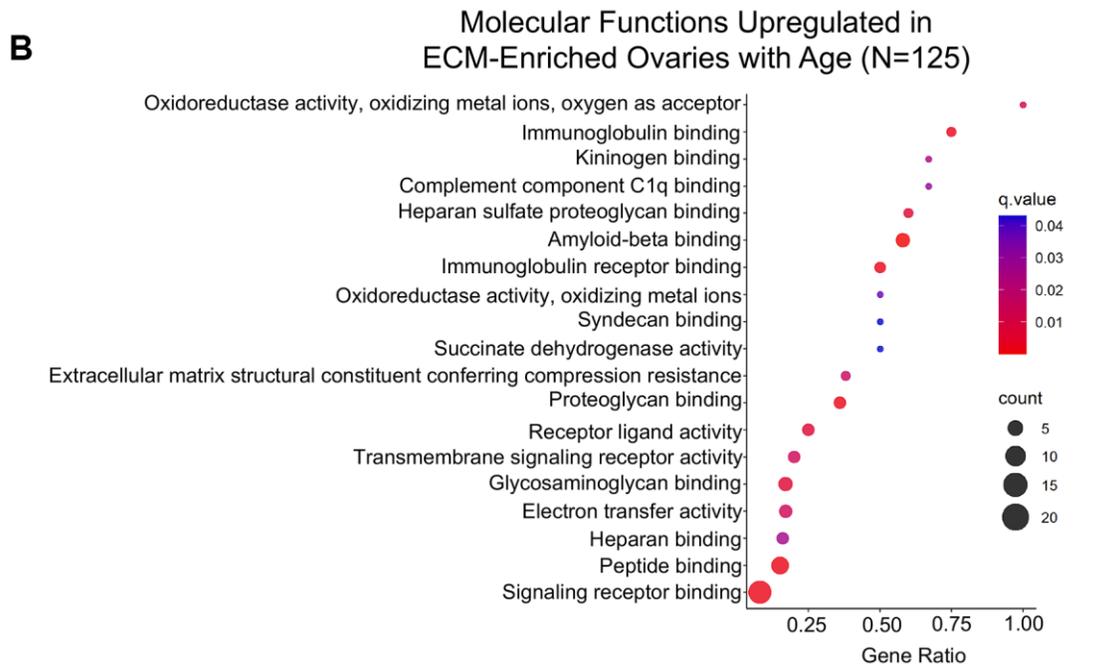
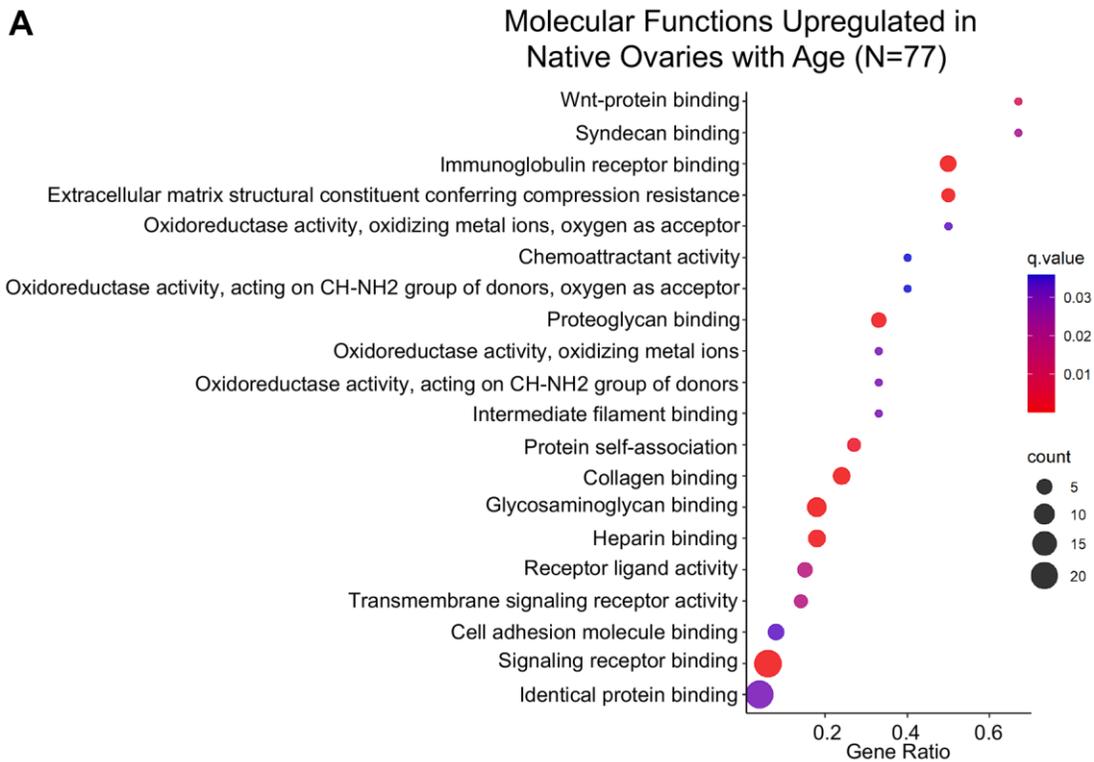
**Supplementary Figure 1. Detergents used for ECM-enrichment.** Representative images of H&E (A) and PSR (B) stained native ovarian tissue sections or ovarian tissue sections following treatment with 0.5% SDS for 10 h, 0.1% SDS for 24 h, or 1% Triton-X for 24 h. Bottom row of each panel is optical zoom of boxed region from top row. Scale bar for top row for each panel = 400  $\mu$ m. Scale bar for bottom row for each panel = 100  $\mu$ m. *N* = 1 ovary per group.



**Supplementary Figure 2. The ovarian proteome is significantly altered during reproductive aging.** (A) Comparison of protein identifications of native ( $N = 4,084$ ) and ECM-enriched ( $N = 3,160$ ) ovaries from reproductively young and old mice. Quantifiable proteins had 2 or more unique peptides per unique protein identification. (B) Comparison of proteins significantly altered with age in native ( $N = 180$ ) and ECM-enriched ( $N = 279$ ) ovaries. Criteria for significantly altered proteins are as follows:  $q$ -value < 0.01 and  $|\log_2(\text{Old/Young})| > 0.58$ .



**Supplementary Figure 3. Molecular functions associated with DNA replication, epigenetic modification, and DNA packaging are downregulated in the ovary with age.** GO analysis of proteins significantly downregulated with age from (A) native and (B) ECM-enriched ovaries was performed using consensus pathway database (CPDB) at level 3,  $q$ -value < 0.05. The level of enrichment (corrected gene ratio) is depicted from 0–1, corresponding to 0–100% enrichment of the listed pathway.



**Supplementary Figure 4. Molecular functions associated with oxidative stress and ECM protein binding are upregulated in the ovary with age.** GO analysis of proteins significantly upregulated with age from (A) native and (B) ECM-enriched ovaries was performed using consensus pathway database (CPDB) at level 3,  $q$ -value < 0.05. The level of enrichment (corrected gene ratio) is depicted from 0–1, corresponding to 0–100% enrichment of the listed pathway.