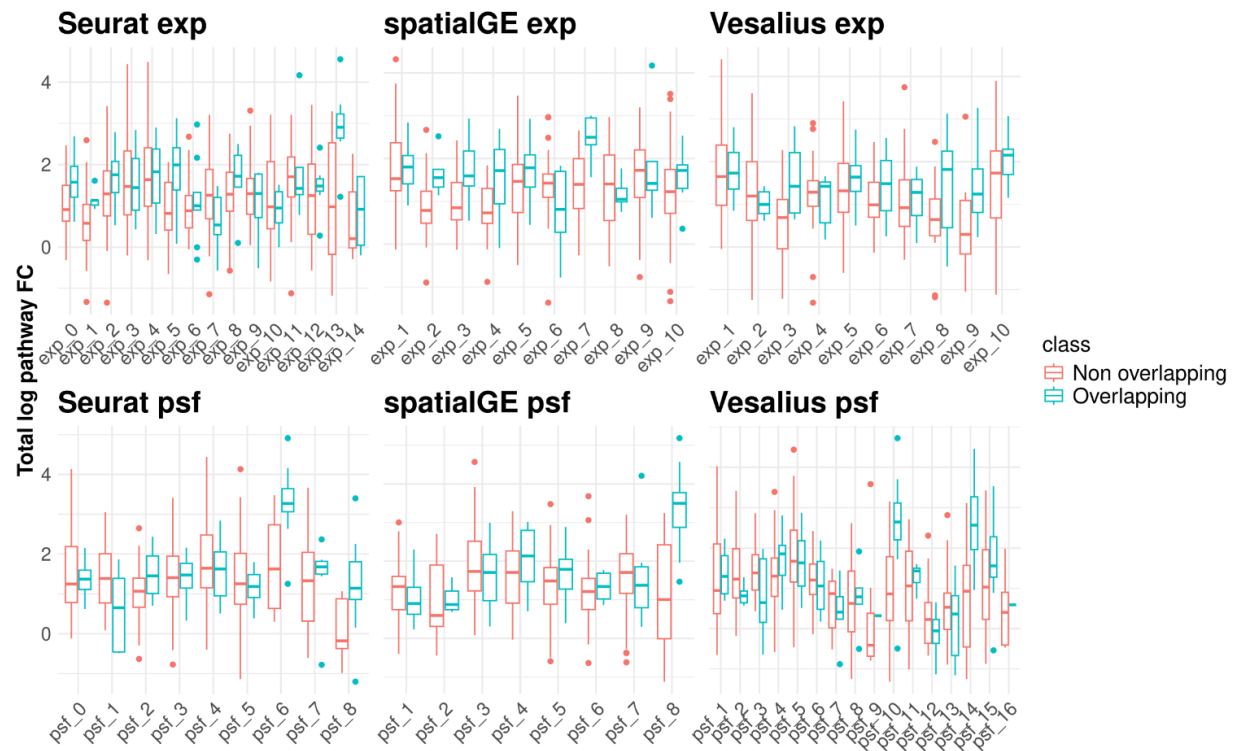
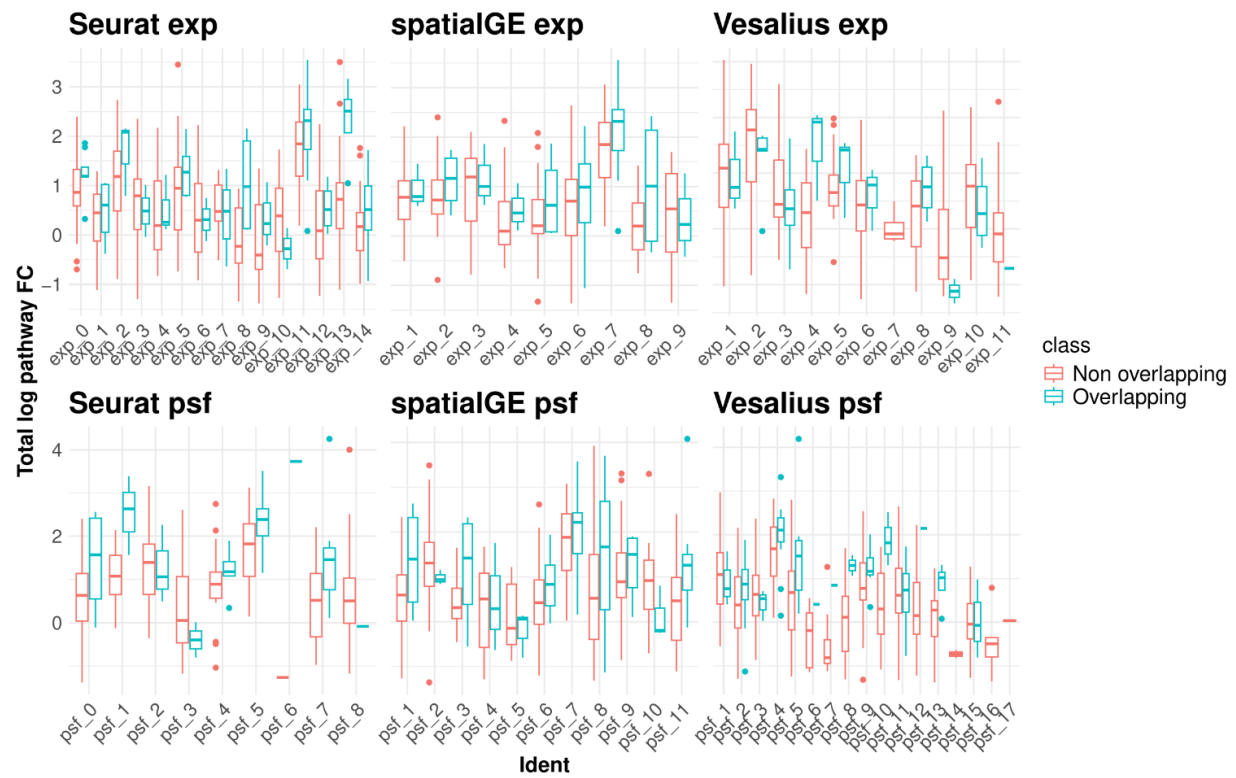
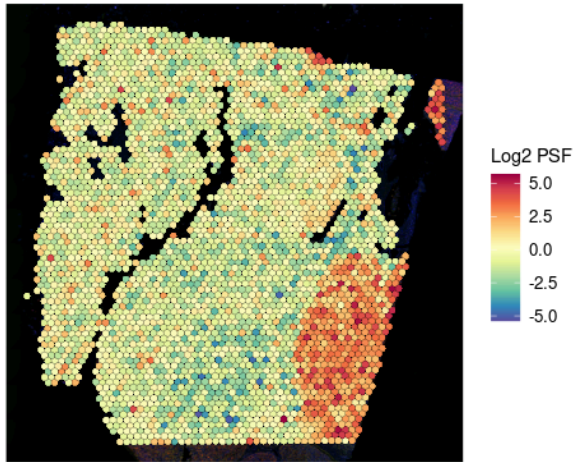


A**B**

Hippo_signaling_pathway
BIRC2 -> Anti-apoptotic genes; Pro-proliferation genes



ErbB_signaling_pathway
JUN -> DNA; Angiogenesis

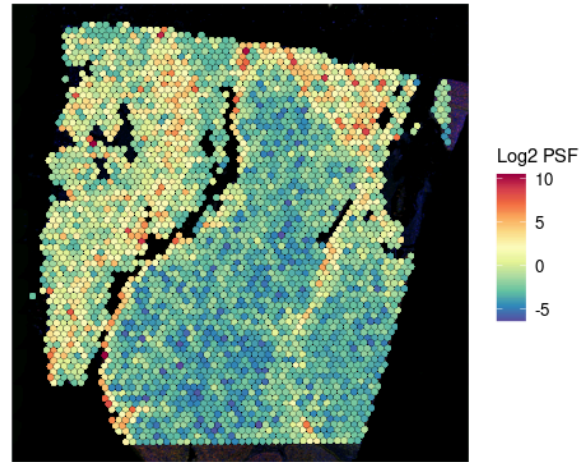


Figure S3. Visualization of PSF-derived activity values for two significantly deregulated pathways highlights the spatial distribution of pathway activity across the melanoma tissue slice. Each panel represents a single pathway branch, with the terminal (sink) node and its associated downstream biological processes indicated. Notably, activation of the BIRC2 branch of the Hippo signaling pathway linked to anti-apoptosis and proliferation is concentrated in the lower right region of the tissue, corresponding to the proliferative melanoma cell cluster identified by Schmidt et al. [ref]. Similarly, the JUN branch of the ErbB signaling pathway, associated with gene expression and angiogenesis, shows elevated activity in the upper right corner of the slice, aligning with the immune-active melanoma type 2 region described in the same study.

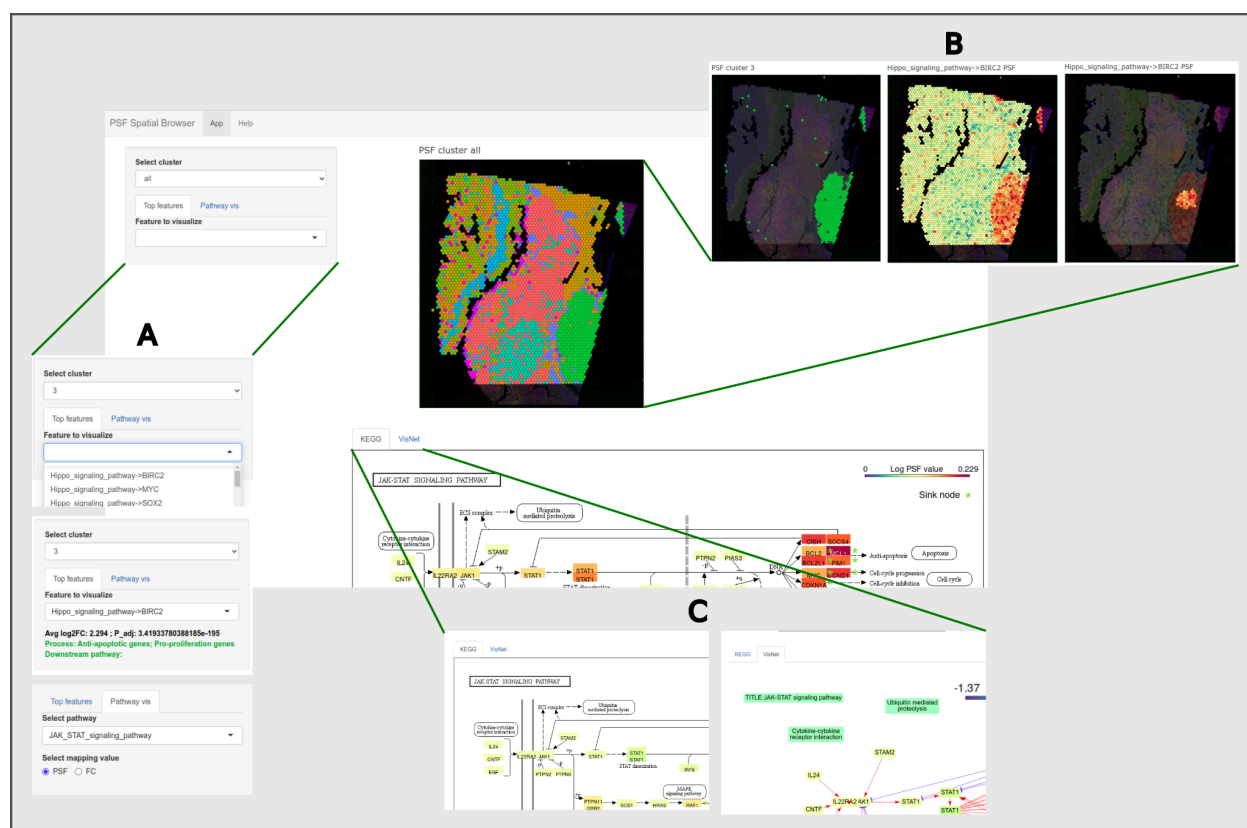


Figure S4. PSF Spatial Browser interface and visualization modules. **A.** The main control panel (top to bottom) includes: a dropdown menu to select a cluster of interest; an input panel to select top cluster-specific features; and a feature information box displaying fold change, adjusted p-value, and associated downstream biological processes for the selected pathway branch. The pathway visualization module allows users to select a specific pathway and data type (gene expression or pathway activity) to render on the pathway map. **B.** Visualization modes of the interactive spatial plot. From left to right: highlighting of a selected cluster, overlay of pathway activity or gene expression values on the spatial tissue map, and custom spot selection. **C.** Pathway visualization options. On the left, a KEGG pathway image-based view allows hovering over nodes to display gene names, expression fold changes, and PSF activity scores. On the right, an interactive network-based visualization provides an alternative view of the pathway topology. In both modes, selected genes can be mapped onto the spatial tissue plot to visualize their expression or activity values.