

1 **Single-cell and spatial transcriptomics reveal P4HA2-mediated**
2 **radiotherapy resistance mechanisms in breast cancer**

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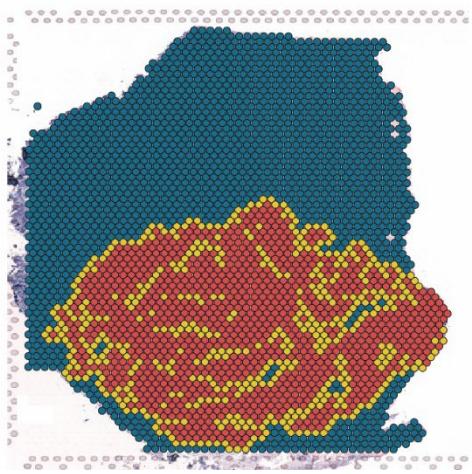
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19 **Supplementary Materials Legends**

Tissue_group
● Malignant ● Mixed ● Normal

A

GSM6760695



B

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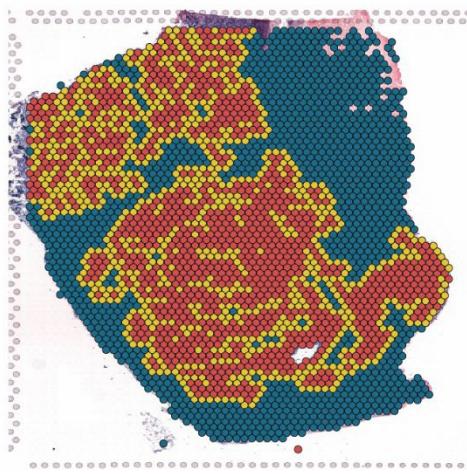
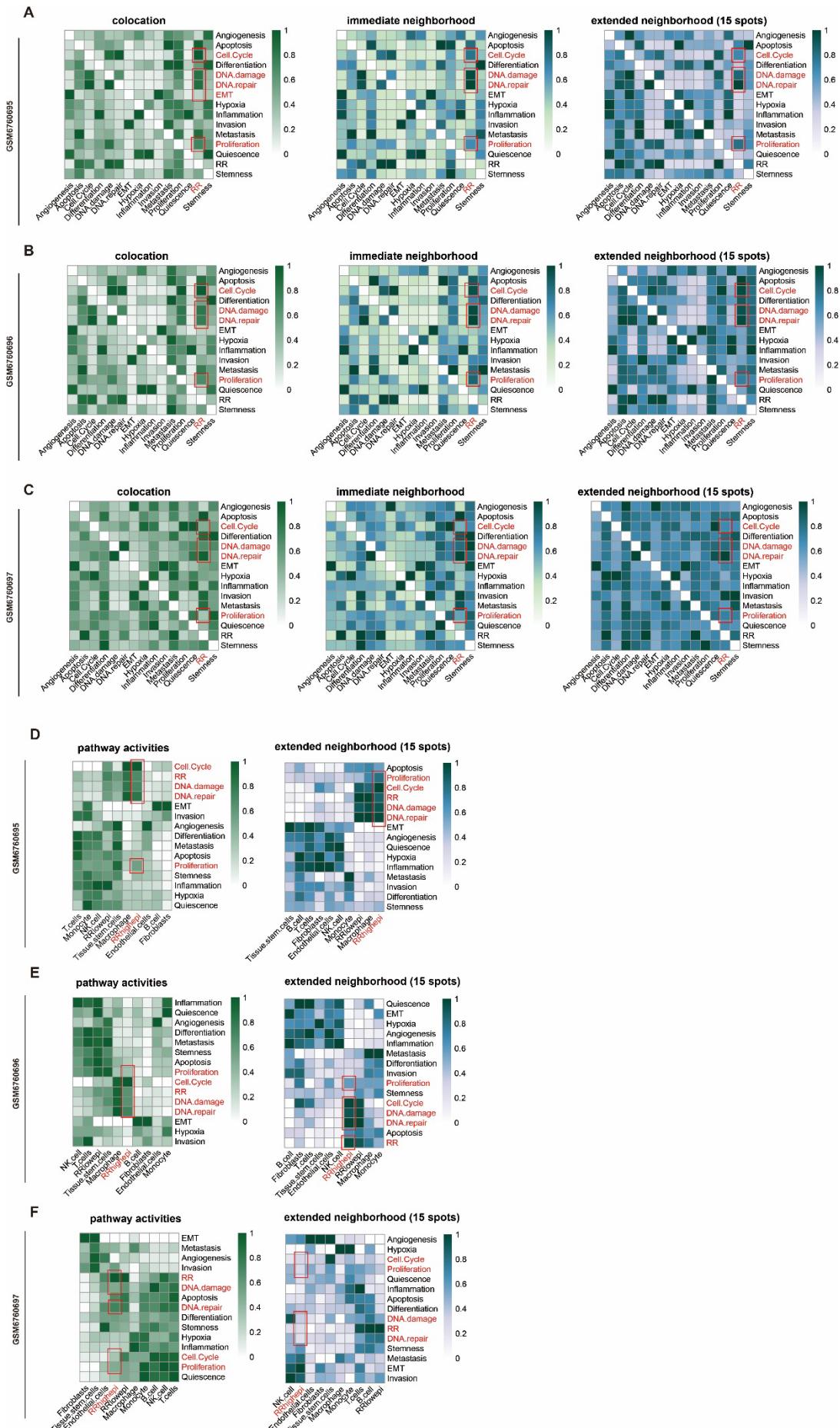
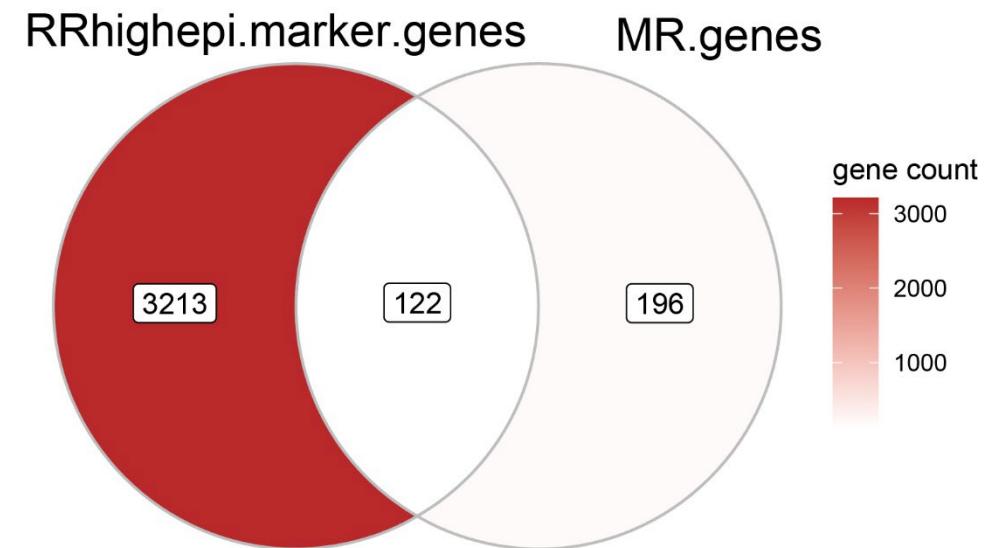


Figure S1. Identification and characterization of benign and malignant regions in spatial transcriptomics based on R package Cottrazm. (A-B) Delineation of benign and malignant regions in spatial transcriptomics.



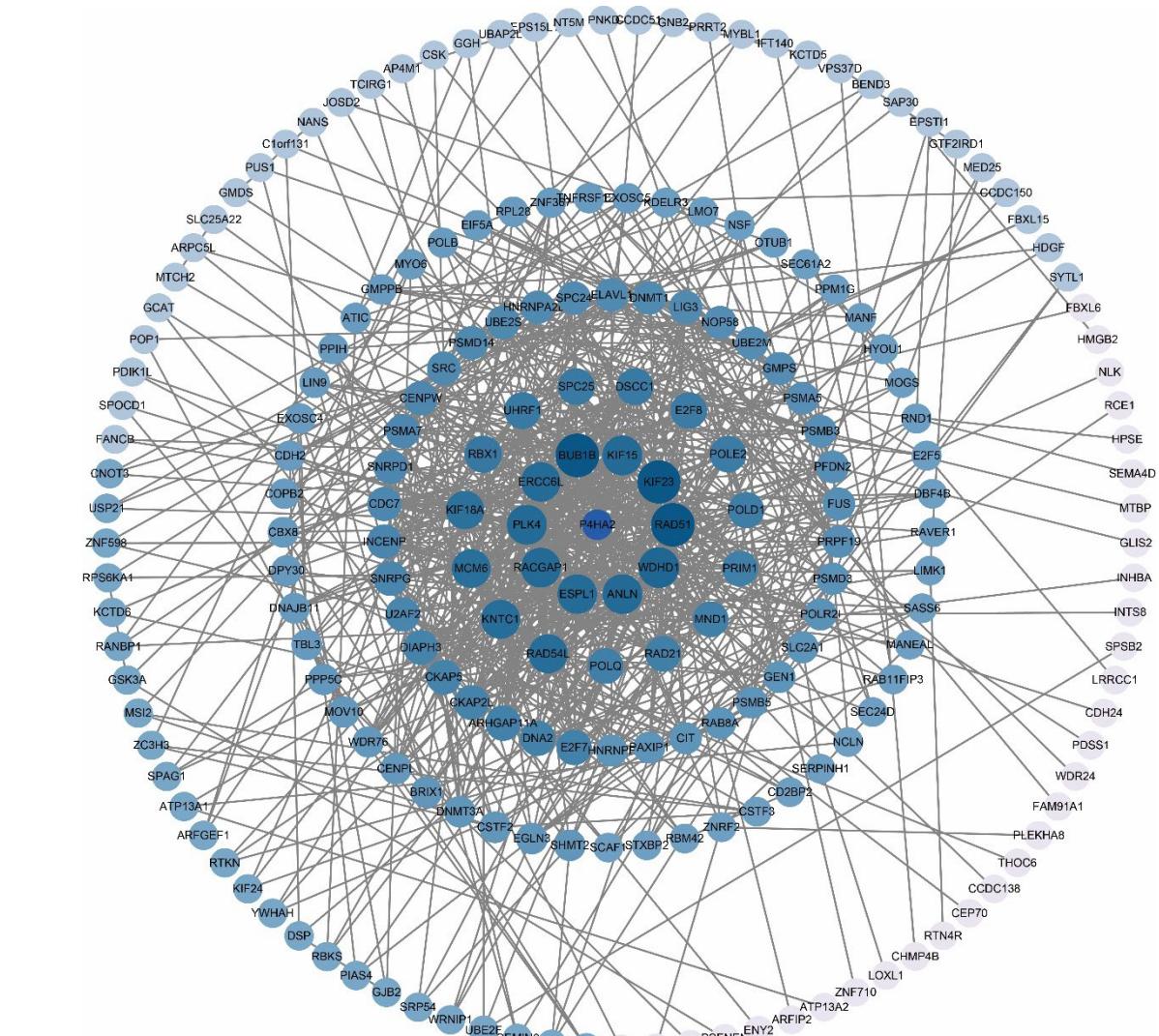
25 **Figure S2. Cell and pathway dependency analysis in spatial transcriptomics.** (A-
26 C) Heatmap showing pathway-pathway dependency analysis in spatial transcriptomics
27 colocation, immediate neighborhood, and extended neighborhood (15 spots) regions.
28 (D-F) Heatmap showing cell-pathway dependency analysis in spatial transcriptomics
29 intra and para regions.

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31 **Figure S3. Intersection of RRhighhepi genes and genes filtered by Mendelian**

32 randomization to obtain genes for establishing prognostic model (ML.genes).



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34 **Figure S4. Interaction between P4HA2 and the radiation resistance gene panel.**

35 Supplementary Tables:

Table S1. Differentially Expressed Genes in TCGA and GSE120798 and Antibody Information.

38 **Table S2. The gene panel derived from Radiotherapy resistance.**

39 **Table S3. Mendelian randomization analysis of genes and their corresponding**
40 **GWAS queue information related to the causal relationship between**
41 **Radiotherapy resistance genomic panel and breast cancer.**

42 **Table S4. The marker gene of RRhighepi.**

43 **Table S5. Intersection of RRhighhei and Genes Filtered by Mendelian**
44 **Randomization for Prognostic Model Construction (ML.genes).**

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