

**Supplementary Table S1:** TruSight™ Hereditary Cancer Panel

| Gen           | Chromosome |
|---------------|------------|
| <i>AIP</i>    | 11         |
| <i>ALK</i>    | 2          |
| <i>APC</i>    | 5          |
| <i>ATM</i>    | 11         |
| <i>BAP1</i>   | 3          |
| <i>BARD1</i>  | 2          |
| <i>BLM</i>    | 15         |
| <i>BMPR1A</i> | 10         |
| <i>BRCA1</i>  | 17         |
| <i>BRCA2</i>  | 13         |
| <i>BRIP1</i>  | 17         |
| <i>BUB1B</i>  | 15         |
| <i>CASR</i>   | 3          |
| <i>CDC73</i>  | 1          |
| <i>CDH1</i>   | 16         |
| <i>CDK4</i>   | 12         |
| <i>CDKN1B</i> | 12         |
| <i>CDKN1C</i> | 11         |
| <i>CDKN2A</i> | 9          |
| <i>CEBPA</i>  | 19         |
| <i>CEP57</i>  | 11         |
| <i>CHEK2</i>  | 22         |
| <i>CYLD</i>   | 16         |
| <i>DDB2</i>   | 11         |
| <i>DICER1</i> | 14         |
| <i>DIS3L2</i> | 2          |
| <i>EGFR</i>   | 7          |
| <i>EPCAM</i>  | 2          |
| <i>ERCC2</i>  | 19         |
| <i>ERCC3</i>  | 2          |
| <i>ERCC4</i>  | 16         |
| <i>ERCC5</i>  | 13         |
| <i>EXT1</i>   | 8          |

| Gen           | Chromosome |
|---------------|------------|
| <i>FANCB</i>  | X          |
| <i>FANCC</i>  | 9          |
| <i>FANCD2</i> | 3          |
| <i>FANCE</i>  | 6          |
| <i>FANCF</i>  | 11         |
| <i>FANCG</i>  | 9          |
| <i>FANCI</i>  | 15         |
| <i>FANCL</i>  | 2          |
| <i>FANCM</i>  | 14         |
| <i>FH</i>     | 1          |
| <i>FLCN</i>   | 17         |
| <i>GATA2</i>  | 3          |
| <i>GNAS</i>   | 20         |
| <i>GPC3</i>   | X          |
| <i>HNFI1A</i> | 12         |
| <i>HRAS</i>   | 11         |
| <i>KIT</i>    | 4          |
| <i>MAX</i>    | 14         |
| <i>MEN1</i>   | 11         |
| <i>MET</i>    | 7          |
| <i>MLH1</i>   | 3          |
| <i>MRE11A</i> | 11         |
| <i>MSH2</i>   | 2          |
| <i>MSH6</i>   | 2          |
| <i>MUTYH</i>  | 1          |
| <i>NBN</i>    | 8          |
| <i>NF1</i>    | 17         |
| <i>NF2</i>    | 22         |
| <i>NSD1</i>   | 5          |
| <i>PALB2</i>  | 16         |
| <i>PDE4D</i>  | 5          |
| <i>PHOX2B</i> | 4          |
| <i>PMS1</i>   | 2          |

| Gen            | Chromosome |
|----------------|------------|
| <i>PPM1D</i>   | 17         |
| <i>PRF1</i>    | 10         |
| <i>PRKARIA</i> | 17         |
| <i>PTCH1</i>   | 9          |
| <i>PTEN</i>    | 10         |
| <i>RAD50</i>   | 5          |
| <i>RAD51C</i>  | 17         |
| <i>RAD51D</i>  | 17         |
| <i>RBI</i>     | 13         |
| <i>RECQL4</i>  | 8          |
| <i>RET</i>     | 10         |
| <i>RHBDF2</i>  | 17         |
| <i>RUNX1</i>   | 21         |
| <i>SBDS</i>    | 7          |
| <i>SDHA</i>    | 5          |
| <i>SDHAF2</i>  | 11         |
| <i>SDHB</i>    | 1          |
| <i>SDHC</i>    | 1          |
| <i>SDHD</i>    | 11         |
| <i>SLX4</i>    | 16         |
| <i>SMAD4</i>   | 18         |
| <i>SMARCB1</i> | 22         |
| <i>STK11</i>   | 19         |
| <i>SUFU</i>    | 10         |
| <i>TMEM127</i> | 2          |
| <i>TP53</i>    | 17         |
| <i>TSC1</i>    | 9          |
| <i>TSC2</i>    | 16         |
| <i>VHL</i>     | 3          |
| <i>WRN</i>     | 8          |
| <i>WT1</i>     | 11         |
| <i>XPA</i>     | 9          |
| <i>XPC</i>     | 3          |

|              |    |              |    |
|--------------|----|--------------|----|
| <i>EXT2</i>  | 11 | <i>PMS2</i>  | 7  |
| <i>EZH2</i>  | 7  | <i>POLD1</i> | 19 |
| <i>FANCA</i> | 16 | <i>POLE</i>  | 12 |

**Supplementary Figure S1: Quality Control of RNA-Seq Data**

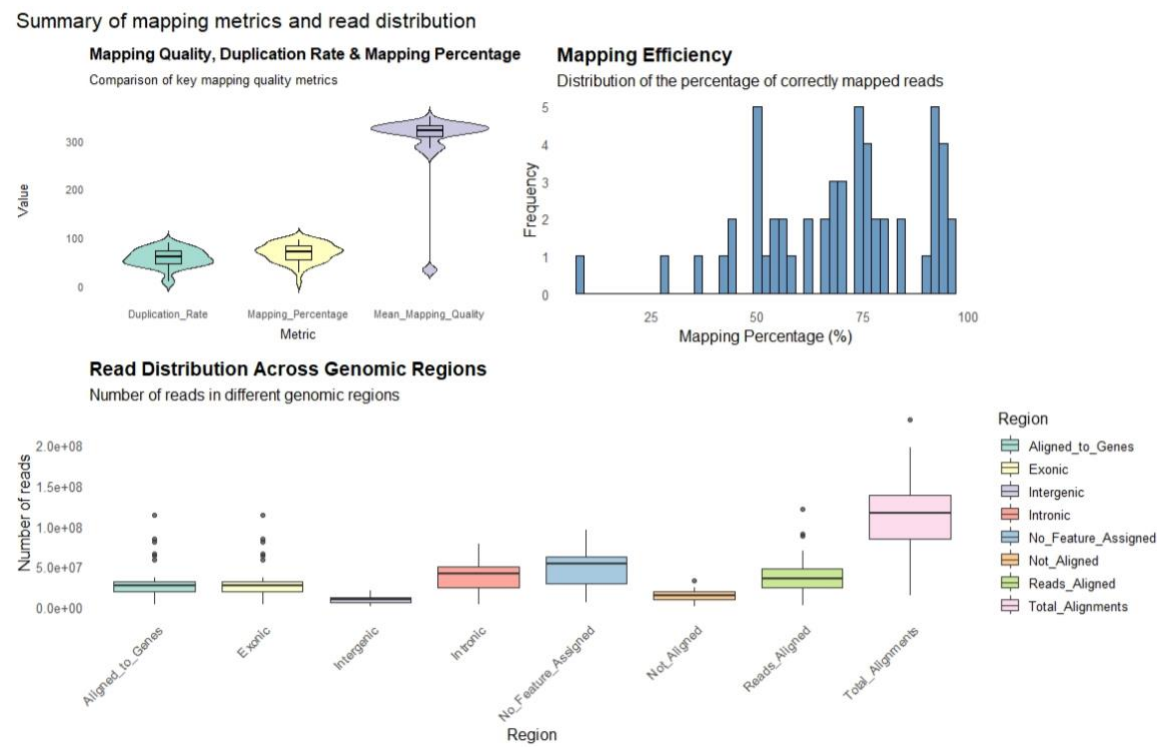


Figure S1: Summary of RNA-Seq mapping quality metrics and read distribution across genomic regions in the Colombian TNBC cohort. (A) Violin plots showing the distribution of mapping quality, duplication rate, and overall mapping percentage across samples. (B) Histogram representing the frequency distribution of correctly mapped reads (mapping efficiency). (C) Boxplots illustrating the number of reads assigned to different genomic regions, including exonic, intronic, and intergenic fractions. Quality metrics were obtained from Qualimap RNA-Seq reports and summarized in R.

**Supplementary Figure S2:** Distribution of pathogenic and likely pathogenic (P/LP) variants in 20 patients with hereditary TNBC.

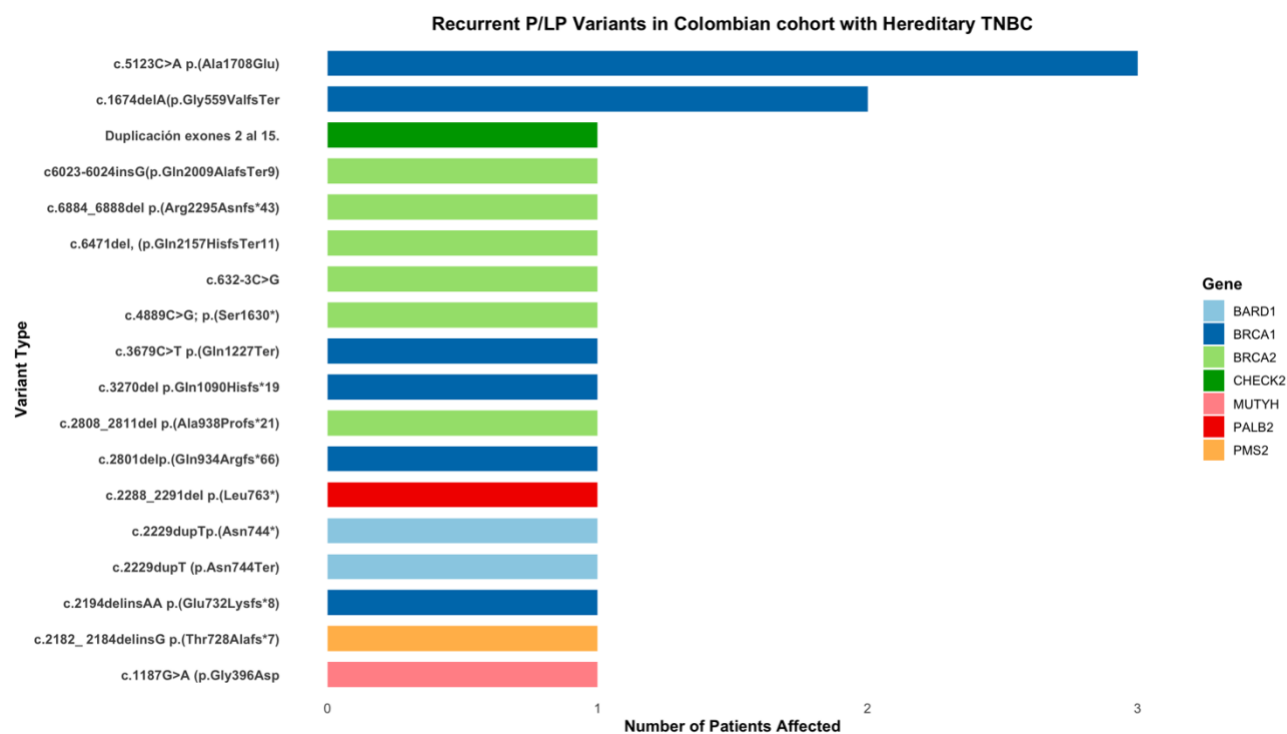
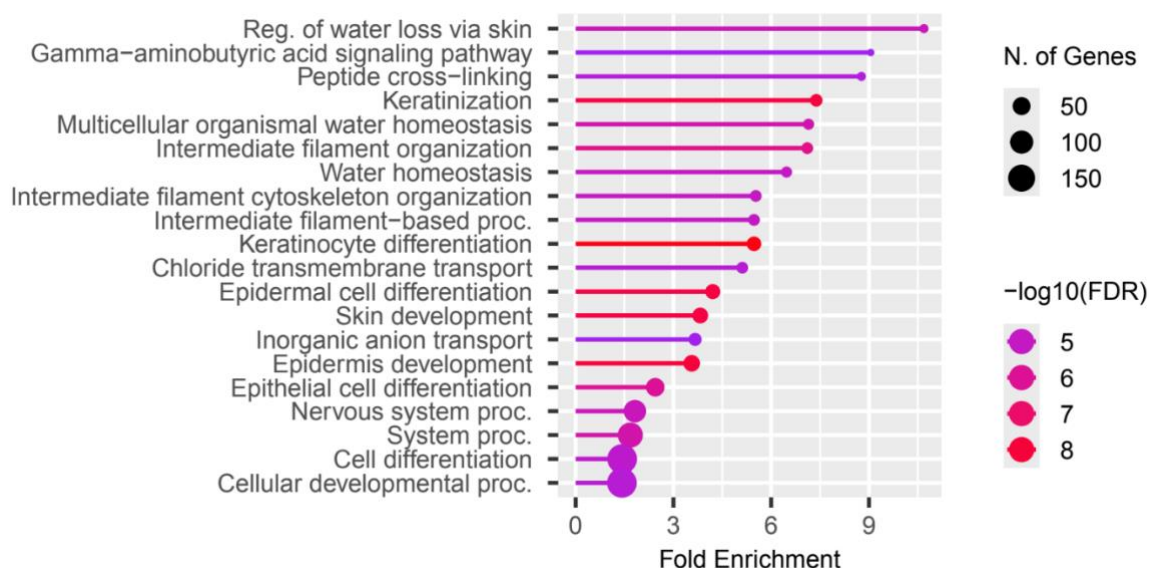


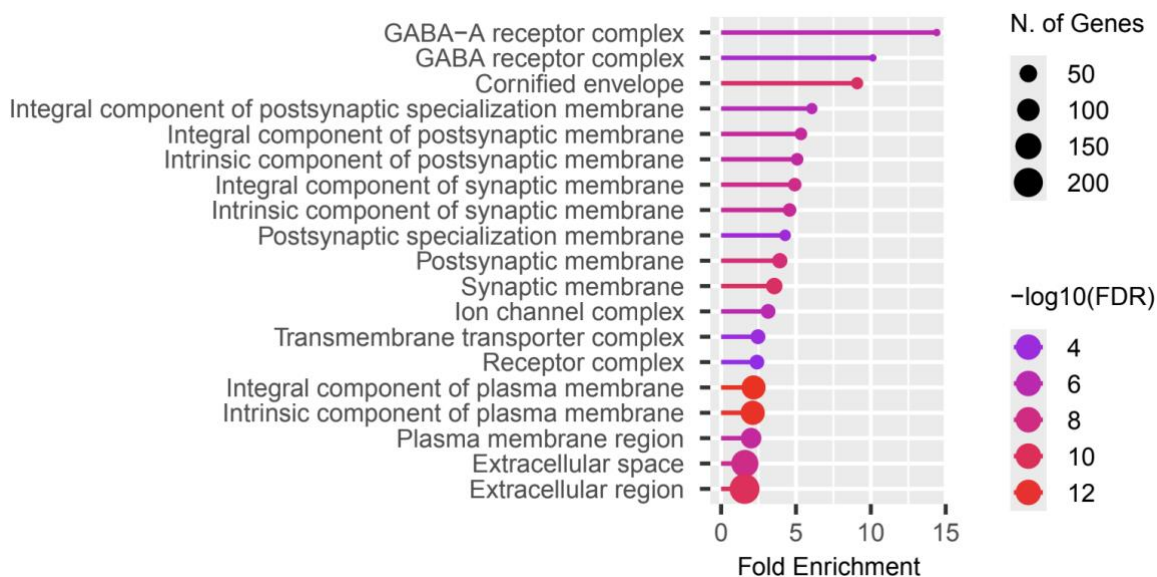
Figure S2: A total of 13 distinct P/PL variants were identified. The most frequently mutated gene was *BRCA1* (dark blue bars) present in 10 patients with 6 unique variants. The second most frequently affected gene was *BRCA2* (light green bars), present in 6 patients. *BARD1* (light blue bars) was mutated in 2 patients. All other variants were identified in a single patient each.

**Supplementary Figure S3: Functional Enrichment Analysis in Colombian women cohort**  
– Downregulated genes.

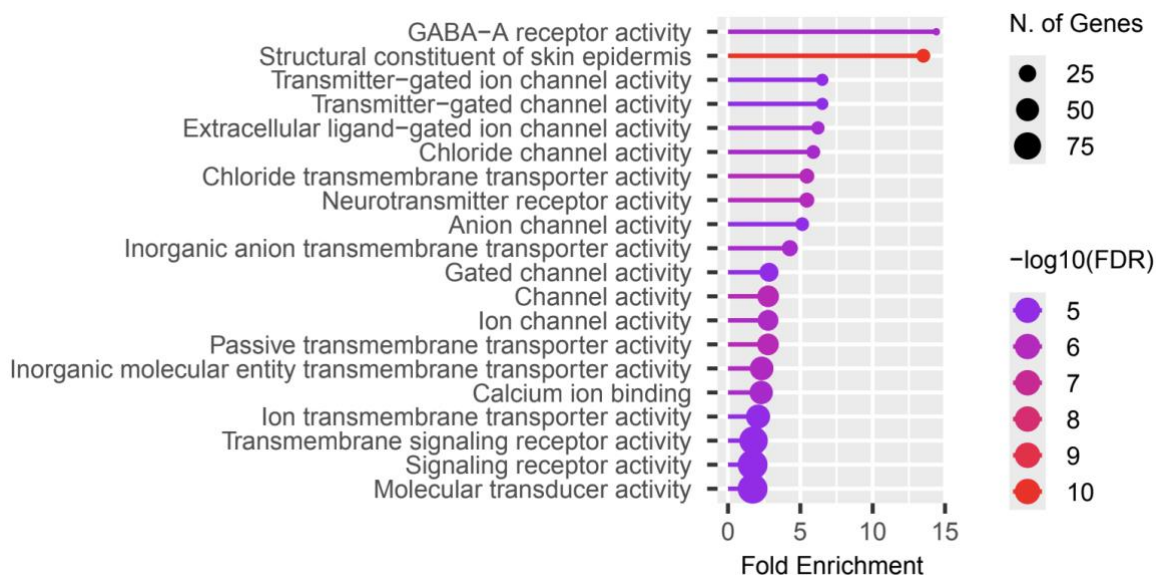
**2A: GO: Biological Process – Downregulated DEGs**



**2B: GO: Cellular Components – Downregulated DEGs**



## 2C: GO: Molecular Functions – Downregulated DEGs



## 2D: KEGG Pathways – Downregulated DEGs

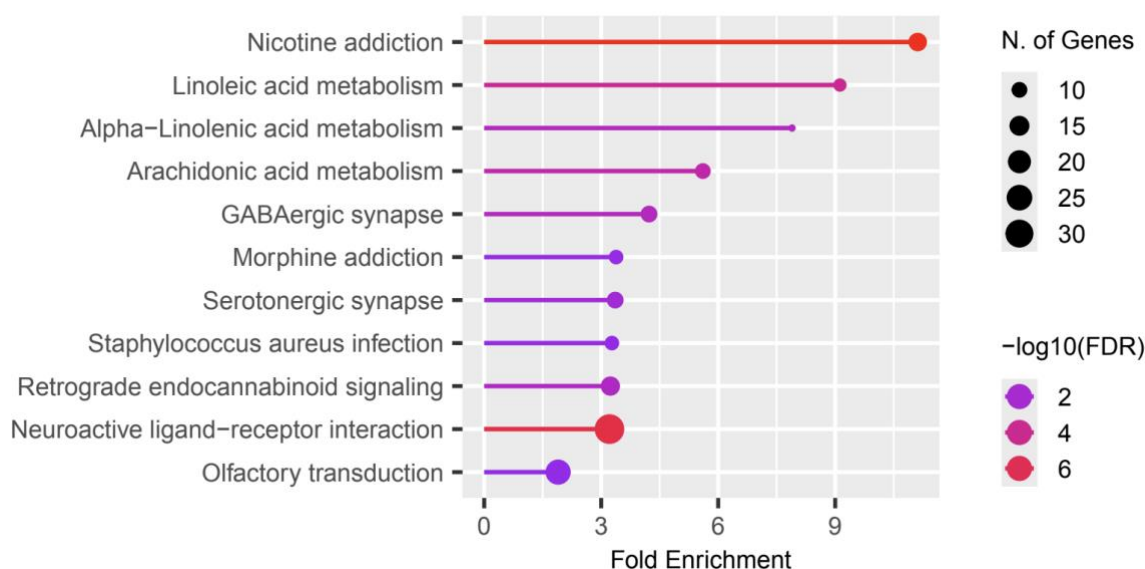


Figure S3. Functional enrichment compared H-TNBC vs S-TNBC. (2A) GO Biological Process. (2B) GO Cellular Component. (2C) Molecular Functions and (2D) KEGG Pathways. Each dot represents an enriched category, with size indicating the number of genes and color representing statistical significance.

**Supplementary Table S2:** Comparison of Immunophenoscore (IPS) between hereditary and sporadic TNBC in Colombian and TCGA cohorts.

| IPS                 | TCGA Cohort |          |                       | Colombian Cohort |            |                   |
|---------------------|-------------|----------|-----------------------|------------------|------------|-------------------|
|                     | H-TNBC      | S-TNBC   | <i>p value</i>        | H-TNBC           | S-TNBC     | <i>p value</i>    |
| <b>High IPS (%)</b> | 3 (37.5%)   | 4 (50 %) | <i>I</i> <sup>*</sup> | 6 (30%)          | 7 (16.7%)  | 0.32 <sup>*</sup> |
| <b>Low IPS (%)</b>  | 5 (62.5%)   | 4 (50 %) |                       | 14 (70%)         | 35 (83.3%) |                   |

<sup>\*</sup>Fisher exact test

**Supplementary Table S3:** Genes selected by LASSO logistic regression distinguishing hereditary from sporadic TNBC.

| Gene            | Coefficient |
|-----------------|-------------|
| <i>GSTA1</i>    | 0,421       |
| <i>FOXQ1</i>    | 0,352       |
| <i>NPTX2</i>    | 0,156       |
| <i>IL6</i>      | 0,128       |
| <i>FOXC2</i>    | 0,083       |
| <i>MMP13</i>    | 0,045       |
| <i>MSLN</i>     | 0,013       |
| <i>HLF</i>      | -0,258      |
| <i>AMPD1</i>    | -0,227      |
| <i>EPHA6</i>    | -0,221      |
| <i>CYP2E1</i>   | -0,188      |
| <i>B4GALNT2</i> | -0,183      |
| <i>AMH</i>      | -0,158      |
| <i>DSG1</i>     | -0,138      |
| <i>PLCH2</i>    | -0,130      |
| <i>ENDOU</i>    | -0,114      |
| <i>IL36RN</i>   | -0,099      |
| <i>EEF1A2</i>   | -0,089      |
| <i>CHIT1</i>    | -0,066      |
| <i>DDX25</i>    | -0,059      |
| <i>KRT9</i>     | -0,054      |
| <i>TPSD1</i>    | -0,029      |
| <i>BTN1A1</i>   | -0,028      |