

From Genomes to Treatment: Personalized Therapeutics in a Pakistani Breast Cancer Cohort

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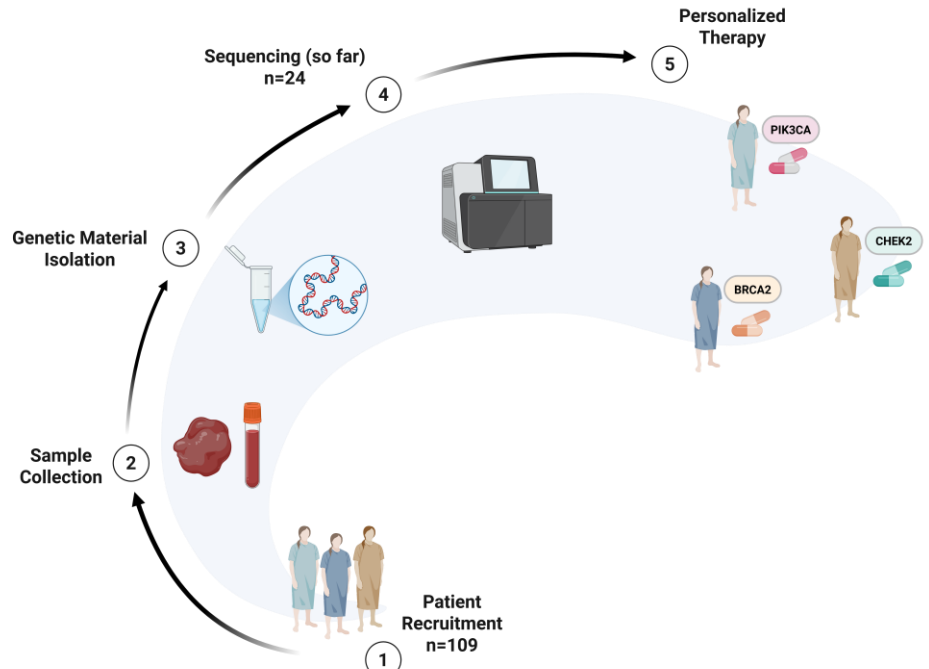
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Introduction

Breast cancer is a heterogeneous disease with variable treatment responses, underscoring the need for personalized therapeutic strategies. Although genomic profiling can identify personalized actionable targets, it is not routinely implemented in many settings, including Pakistan, highlighting the need to develop personalized therapeutic approaches.

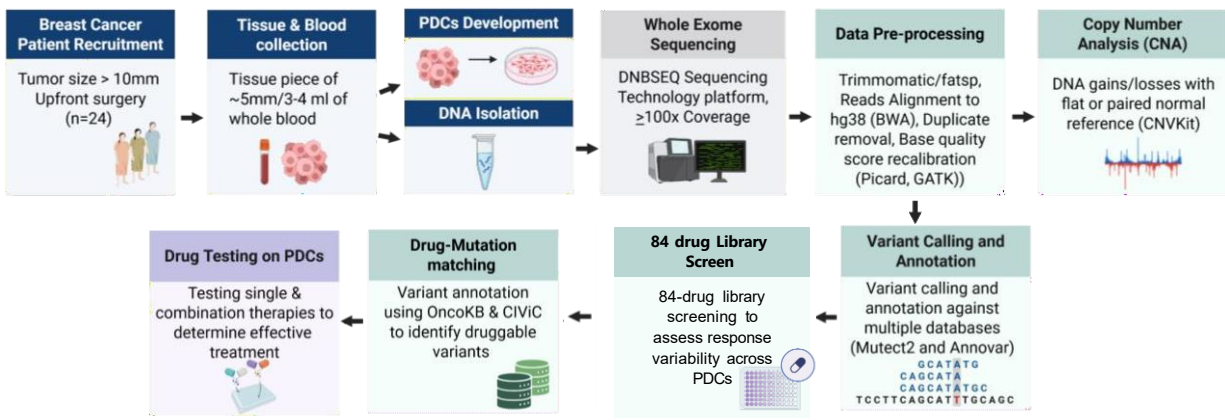
In this study, we adopt an integrated experimental and genomic approach. A total of 109 patients were enrolled, yielding 79 tumor samples and 55 patient-derived cell lines (PDCs). Genomic profiling was performed on 24 tumors (including 4 matched pairs), with RNA sequencing conducted for 22 samples. We first screened an 84-compound drug library across our PDCs to characterize the extent of therapeutic response heterogeneity. The screening revealed substantial variation in drug sensitivity, with some compounds showing strong activity against specific cell lines while others showed marked resistance, highlighting the potential for patient-specific treatment responses. In the next phase, genomic alterations identified through profiling were matched with mutation-specific therapeutic agents using established clinical knowledge resources, followed by experimental testing of selected drugs in the corresponding PDCs. This approach aims to link molecular alterations with functional drug responses and support a more precise, individualized strategy for breast cancer treatment.



Objectives

- Identify **genetic changes** in breast cancer patients
- Tailor therapies** for each patient according to their genetic profile

Methodology



Results

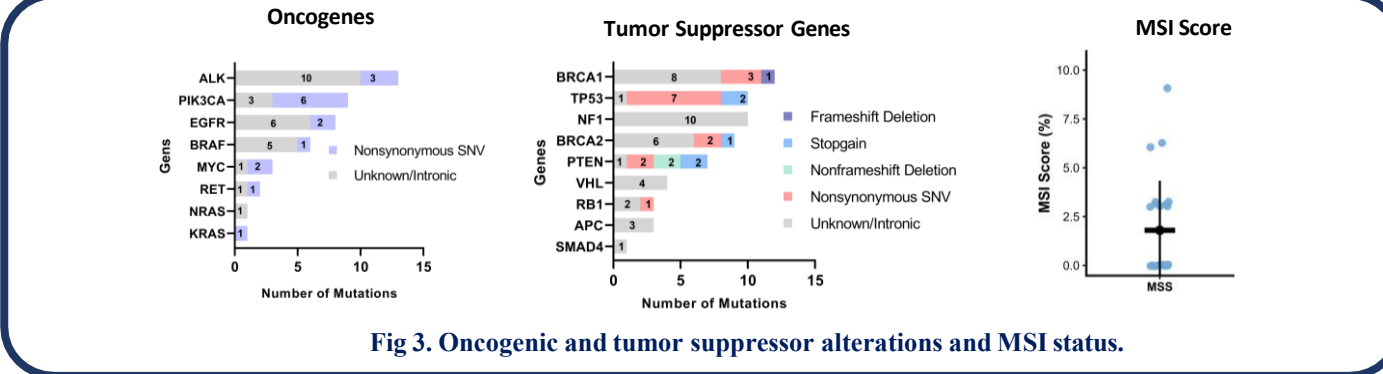


Fig 3. Oncogenic and tumor suppressor alterations and MSI status.

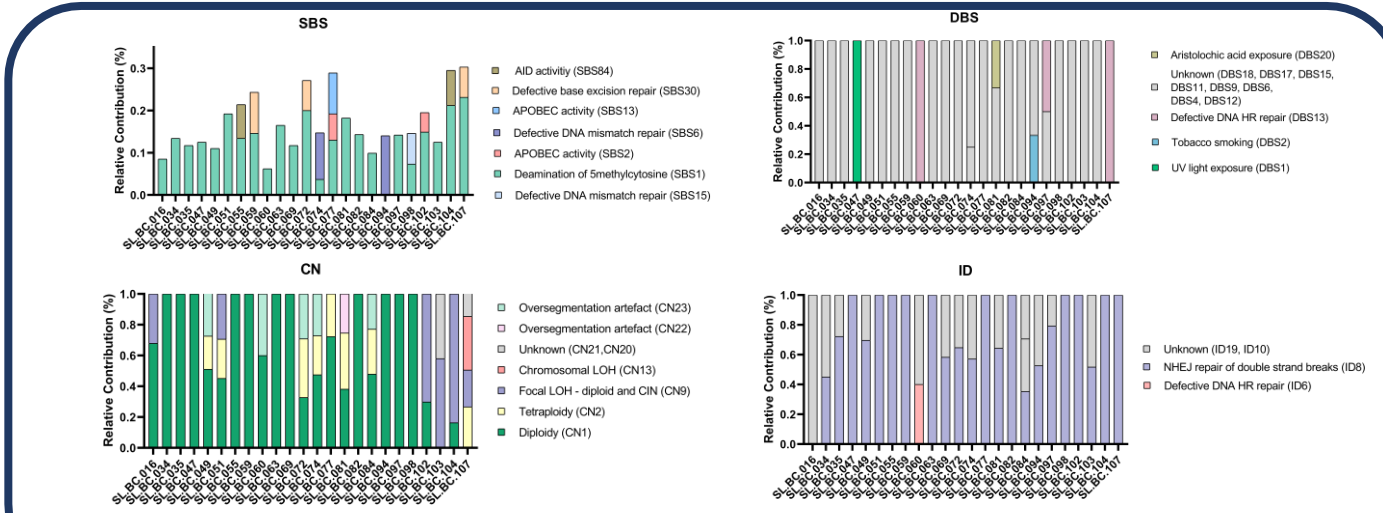


Fig 4. COSMIC mutational signature profile of the patients

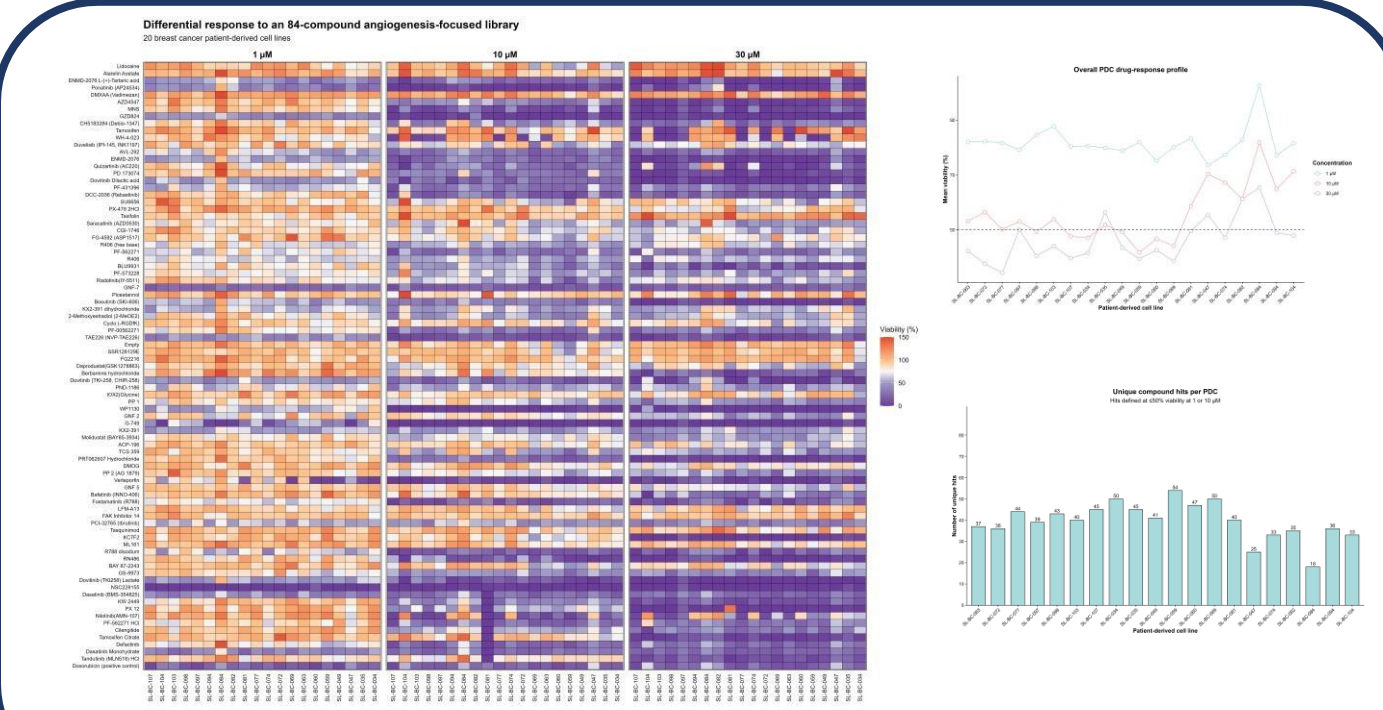


Fig 5. Heterogeneous responses and cell-line-specific hits across 84 drugs

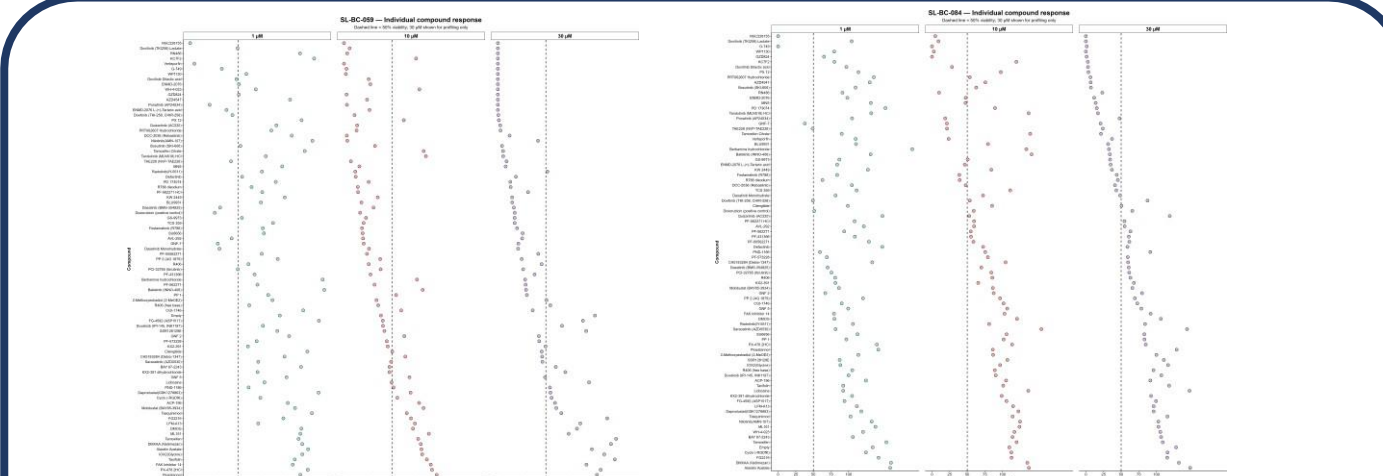


Fig 6. Most sensitive and resistant PDCs, highlighting the extent of response heterogeneity

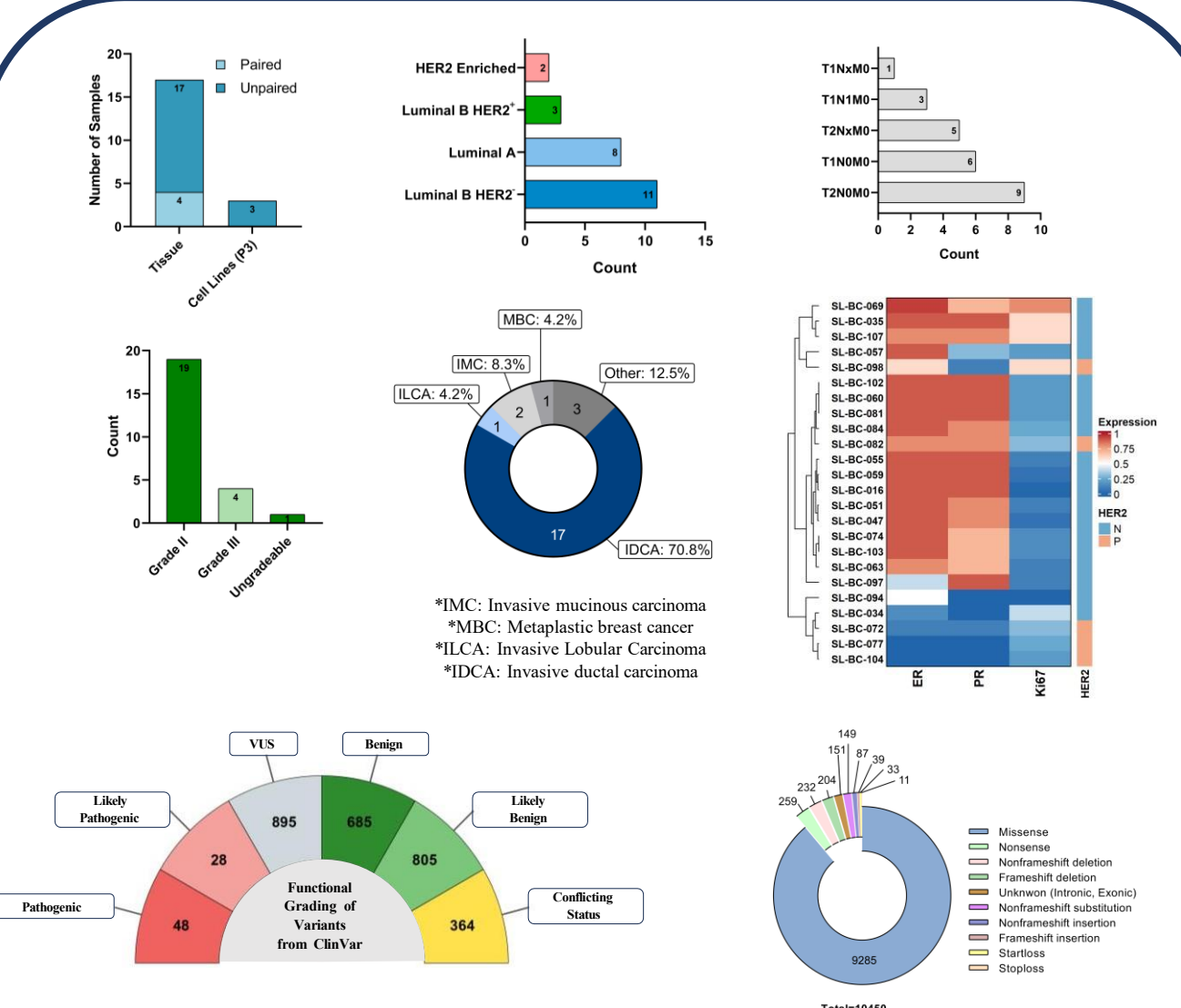


Fig 1. Patient Clinicopathological and Molecular Overview

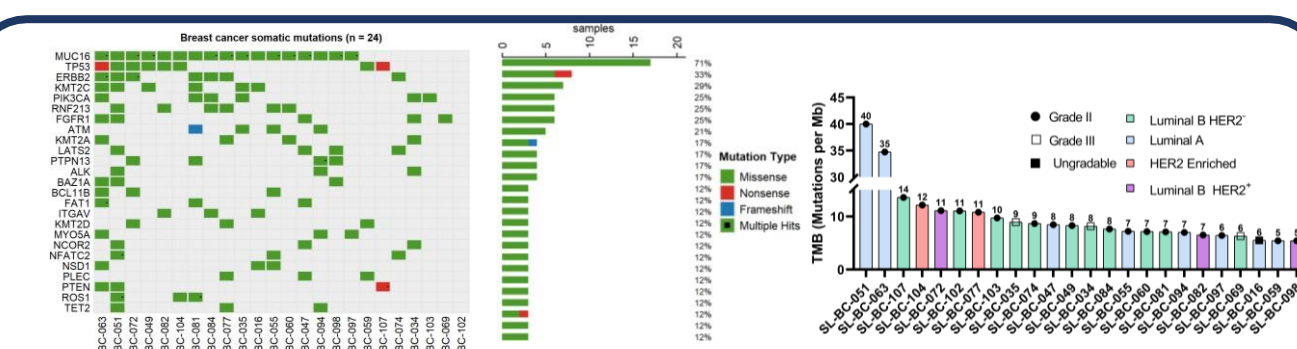


Fig 2. Mutational landscape and tumor mutational burden (TMB) of the breast cancer cohort



Fig 7. Clinically Actionable Alterations and Drug-Biomarker Associations

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