Neuron Projection Guidance signature associates with tumor progression and changes in the tumor microenvironment in triple-negative breast cancer

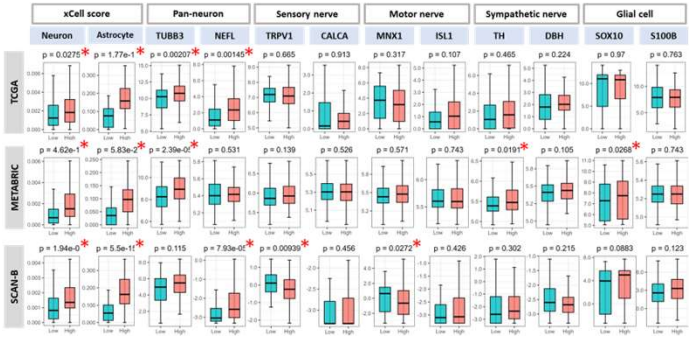
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Introduction

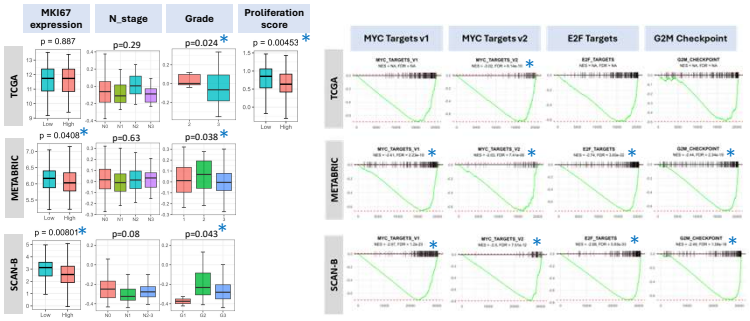
Background: Tumor-associated neurogenesis has emerged as poor prognostic indicators in various solid tumors. Recent studies have suggested that neurogenesis related molecules, particularly those involved in the neuron projection guidance pathway, may promote tumor growth, metastasis, and change the tumor microenvironment of triple-negative breast cancer (TNBC). However, their clinical relevance remains to be fully understood. We hypothesized that the "neuron projection guidance (NPG) score" may be associated with prognosis of TNBC patients. **Methods**: Transcriptomic and clinical data of 7948 breast cancer patient were obtained from 10 independent cohorts. The GSVA score of the NPG gene set from MSigDB was defined as the NPG score, and patients were divided into two groups by the median.

Results

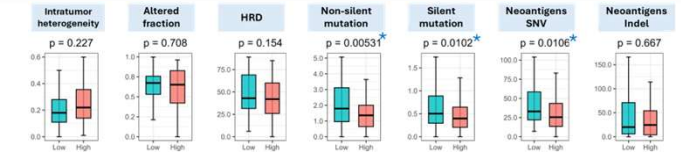
1. NPG score significantly associates with neuron-related score (xCell score) and neuron-related marker genes expression



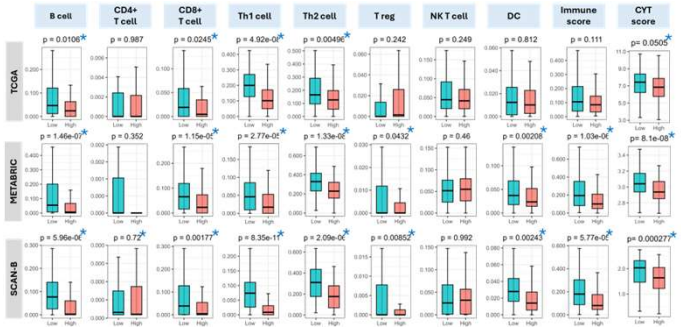
2.Proliferation negatively correlates with tumor proliferative activity

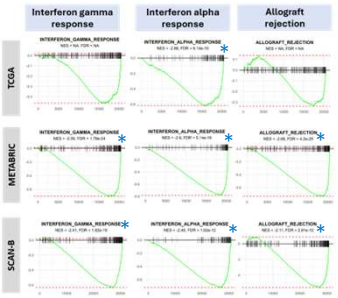


3. NPG score associates with lower tumor immunogenicity

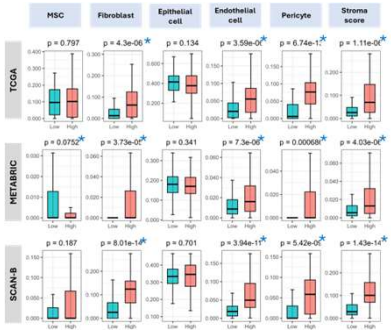


4. NPG score associates with reduced immune cell infiltration and immune activity

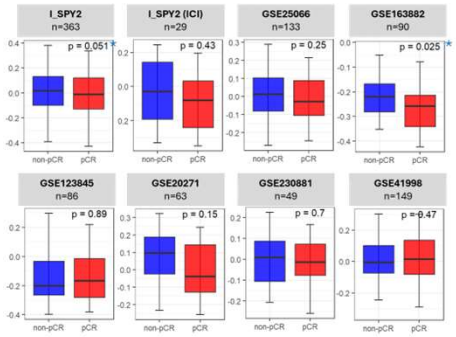




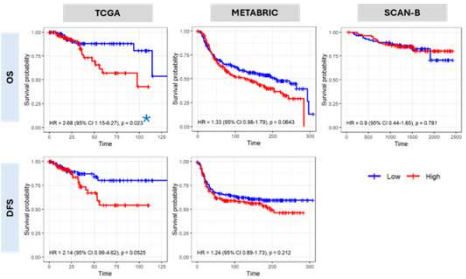
5. NPG score associates with enriched stromal cells



6. NPG scores were lower in pCR cases across neoadjuvant chemotherapy cohorts



7. Patients with high NPG score showed favorable prognosis



Conclusion

This study highlights the prognostic significance of neuron projection guidance score in TNBC. High scores were associated with cell proliferation-related gene sets, and an immunosuppressive tumor microenvironment. These results indicate that intratumoral neurogenesis may contribute to changes in tumor behavior and therapeutic response.

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