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SOX9 And NANOG Expression as Predictive Markers for Chemotherapy Response in Triple-Negative Breast Cancer

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INTRODUCTION

- Triple-negative breast cancer (TNBC) poses a significant challenge in breast cancer treatment because of its heterogeneous nature and aggressive behaviour.
- This research aims to evaluate the roles of SOX9 and NANOG, two transcription factors in cancer stem cell dynamics, as potential predictive markers for chemotherapy response in patients with TNBC (Fig 1 and 2).

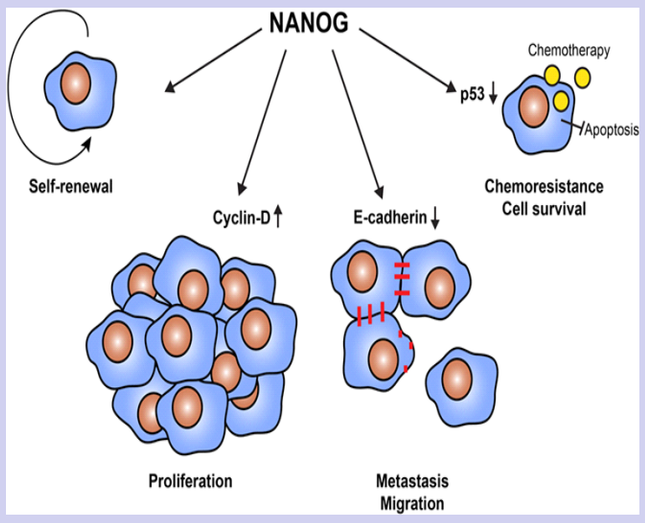


Figure 1. Cellular functions of NANOG in breast cancer stem cells.

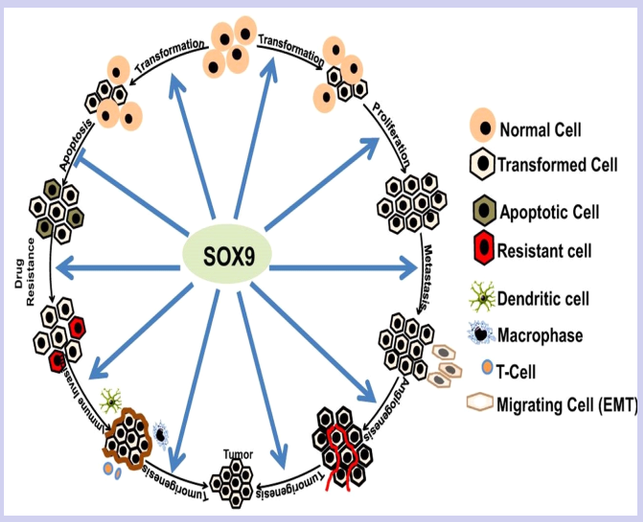
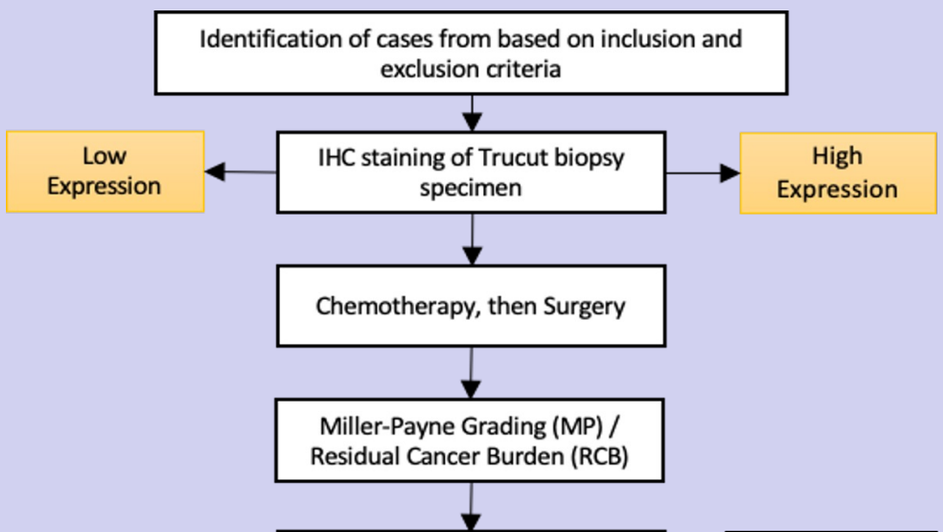


Figure 2. Cellular role of SOX9 in breast cancer progression.

METHODOLOGY

- Single-centre cross-sectional study at Universiti Kebangsaan Malaysia on TNBC patients (June 2016 - May 2023) (Fig 3).
- Objective: Association of SOX9 and NANOG expression levels with chemotherapy response, association with clinicopathological factors.
- Exclusions: second primary tumour, prior treatments, pregnancy.
- Semiquantitative assessment of SOX9 and NANOG expression, scored via IRS values, categorizied as low or high (Fig 4 and 5).



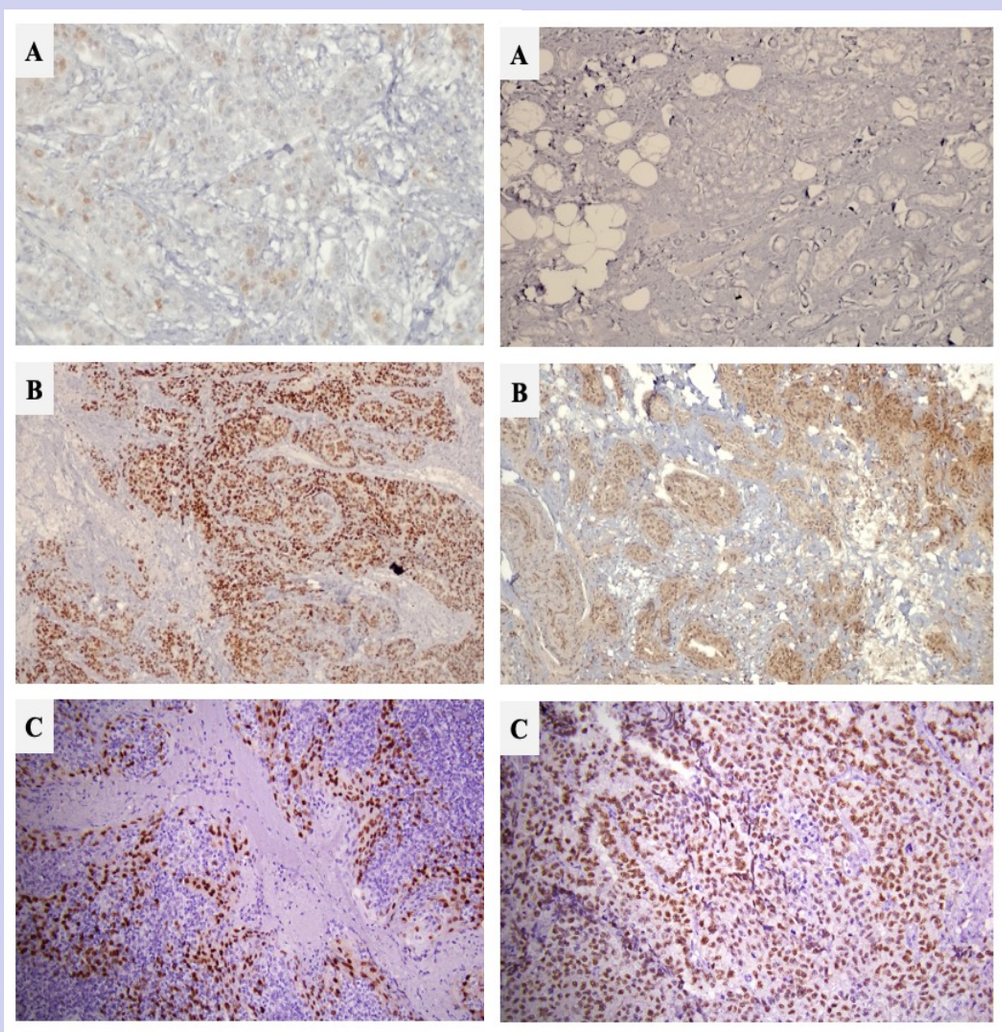


Fig 4. IHC staining of SOX9. Low expression of SOX9 proteins in TNBC (A) and high expression of similar proteins in B (magnification X10). Positive control of SOX9 protein (C) in tonsil tissue.

Fig 5. IHC Staining of NANOG. Low expression of NANOG proteins in TNBC (A) and high expression of similar proteins in B (magnification X10). Positive control of NANOG protein (C) in seminoma tissue.

RESULTS

- Non-responders were older than responders (54.07 vs. 45.07, p=0.049) with significant associations found with T stage, N stage, and lymphovascular invasion (p=0.001, p=0.005, p=0.007).
- SOX9 significantly decreased in responders post-chemotherapy (p=0.008), stable in non-responders.
- NANOG expression remained low pre- and post-chemotherapy (p>0.950).
- Post-chemotherapy SOX9 significantly associated with pathological response (p=0.022), not NANOG (p>0.950) (Fig 6).

Table 1. Demographic and treatment characteristics of the patients

Characteristics	n=28
Age in years (mean, SD)	49.57, 12.24
Diagnosis, n (%)	
Early and Locally advanced breast carcinoma	21 (75.0)
Metastatic breast carcinoma	7 (25.0)
Surgery, n (%)	
BCS with AC/SLNB	9 (32.1)
MAC	19 (67.9)

BCS: breast-conserving surgery, AC: axillary clearance, SLNB: sentinel lymph node biopsy, MAC: mastectomy

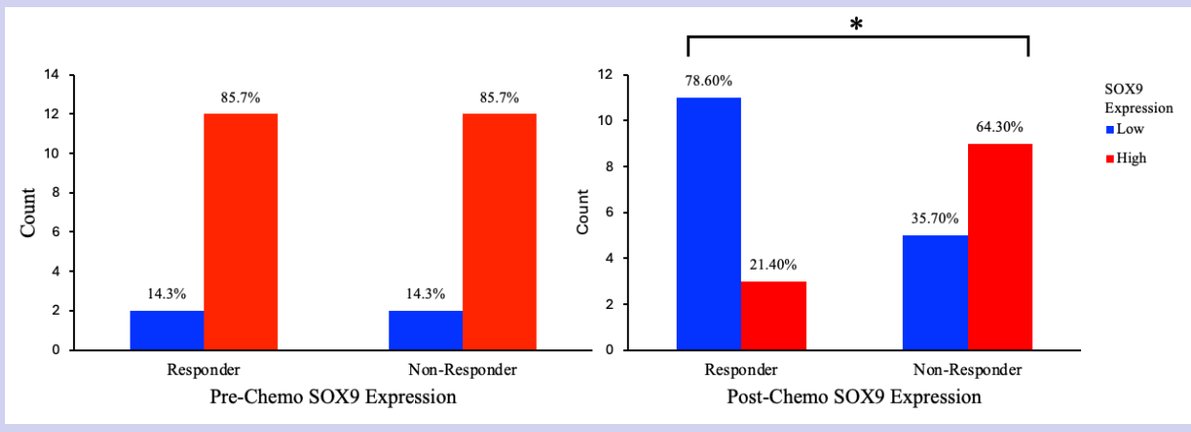


Fig 6. Pre- and post-chemotherapy SOX9 expression with outcome. (* = P <0.05 Pearson chi-squared test)

DISCUSSION

- Cancer stem cells influence breast cancer progression and therapy resistance, contributing to recurrence and metastasis.
- SOX9 linked to better chemotherapy response; regulates breast cancer cell survival and metastasis.
- NANOG showed no significant association; role in TNBC chemotherapy resistance is complex.
- Study limitations include interpretation bias and cross-sectional design.
- Future research should expand sample size and use molecular techniques.

CONCLUSION

This research highlights the specific role of SOX9 as a predictive marker for chemotherapy response in TNBC, demonstrating that lower expression leads to improved tumour response to chemotherapy. In contrast, the insignificant variation in NANOG expression limits its utility as a prognostic marker in TNBC.

REFERENCES

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