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Frequency distribution of triple negative breast cancer subtype according FUSCC classification using immunohistochemistry

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Abstract

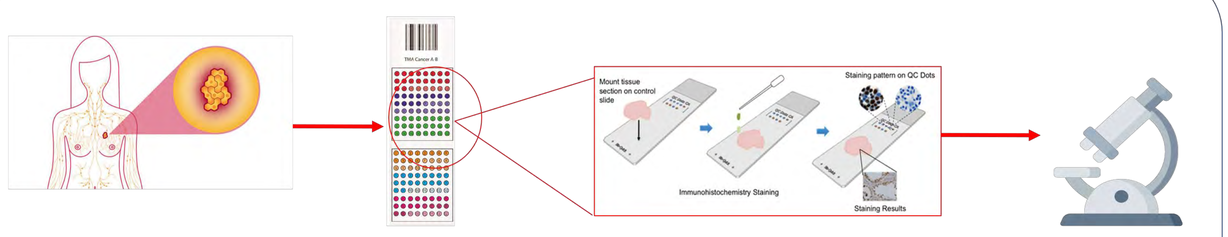
Introduction: Triple negative breast cancer (TNBC) is a heterogeneous disease and aggressive behavior. Recently, the molecular subtype of TNBC has been studied by transcriptome profiling identified into 4 subtypes by FUSCC classification as follow: luminal androgen receptor (LAR), mesenchymal-like (MES), basal-like immune-activated (BLIA), and immunomodulatory (IM) subtypes. The purpose of this study was to identify the expression of the subtype-specific-protein markers in order to classify the subtype of TNBC patients. **Method:** This study included patients diagnosed with TNBC at Songklanagarind hospital between 2016 and 2019. The tissue microarray was constructed and performed IHC stained for androgen receptor (AR), doublecortin like kinase 1 (DCLK1), cluster of differentiation 8 (CD8), and forkhead box C1(FOXC1) antibodies to classify the TNBC subtype regarding FUSCC classification. **Result:** We included 50 TNBC patients, with a mean age of 50 years old (33-77 years). The histological subtype was infiltrating duct carcinoma, not otherwise specified (NOS) (62.0%), and ductal carcinoma, NOS (32.0%). Most of the TNBC patients had high grade (grade 3 = 72.0%). The distribution of 50 TNBC samples according to FUSCC classification were classified as LAR subtype (AR positive, n = 9; 18.0%), MES subtype (DCLK1 positive, n = 3; 6.0%), IM subtype (CD8 positive, n = 14; 28.0%), BLIS subtype (FOXC1 positive, n = 23, 46.0%) and unclassifiable type (n = 1; 2%). **Conclusion:** This study revealed the distribution of TNBC subtype in southern Thai population. Molecular subtypes obtained may be beneficial for targeted therapeutic guideline in TNBC patients.

Keywords: triple negative breast cancer, molecular subtype, subtype-specific-proteins, tissue microarray, immunohistochemistry.

Introduction

- Triple negative breast cancer (TNBC) is a heterogeneous disease and found approximately 15–20% of all breast cancer. TNBC is a subtype of breast cancer that absence of estrogens receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor 2 (HER2).
- Many studies showed the racial variations of clinical behavior and the prevalence of TNBC, likely owing to the heterogeneous nature of the disease and differences in genetic background among those races (Ding et al., 2019). Moreover, TNBC subtyping based on the biologically and clinically relevant characteristics may contribute to the identification of therapeutic targets and prognostic prediction of this disease.
- The aims of this study was to evaluate the subtypes of TNBC based on protein expression using immunohistochemistry.

Method



* This is the result evaluated by one pathologist.

Result

Table 1: Patients' characteristics.

Characteristic	N = 50 (%)
Age (mean = 50)	
>50	24 (48.0)
≤50	26 (52.0)
Religion	
Buddhism	38 (76.0)
Muslim	11 (22.0)
NA	1 (2.0)
Diagnostic	
Infiltrating duct carcinoma, NOS	31 (62.0)
Ductal carcinoma, NOS	16 (32.0)
Intracystic carcinoma, NOS	1 (2.0)
Mucinous adenocarcinoma	1 (2.0)
Adenocarcinoma, NOS	1 (2.0)
Grade	
1	2 (4.0)
2	8 (16.0)
3	36 (72.0)
NA	3 (6.0)
T stage	
1	10 (20.0)
2	26 (52.0)
3	2 (4.0)
4	8 (16.0)
NA	2 (4.0)
N stage	
0	21 (42.0)
1	15 (30.0)
2	4 (8.0)
>3	6 (12.0)
M stage	
0	44 (88.0)
1	1 (2.0)
NA	5 (10.0)
Chemotherapy	
Yes	43 (86.0)
No	7 (14.0)
Radiation	
Yes	24 (48.0)
No	26 (52.0)
Hormone therapy	
Yes	4 (8.0)
No	46 (92.0)
Status	
Alive	32 (64.0)
Dead	18 (36.0)

- The representative microphotographs of each TNBC subtype are depicted in Figure 1.

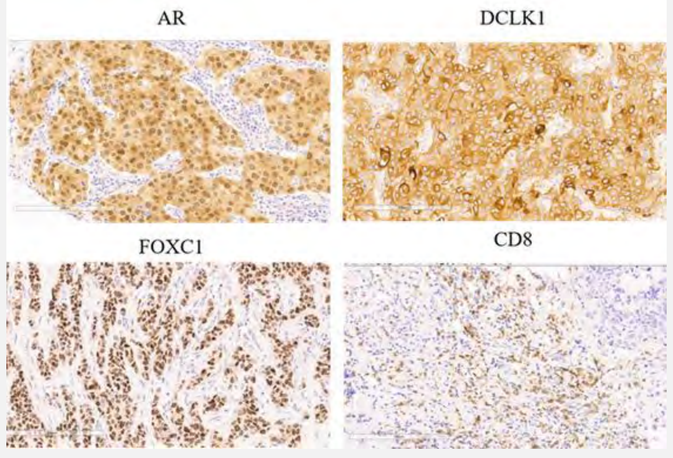
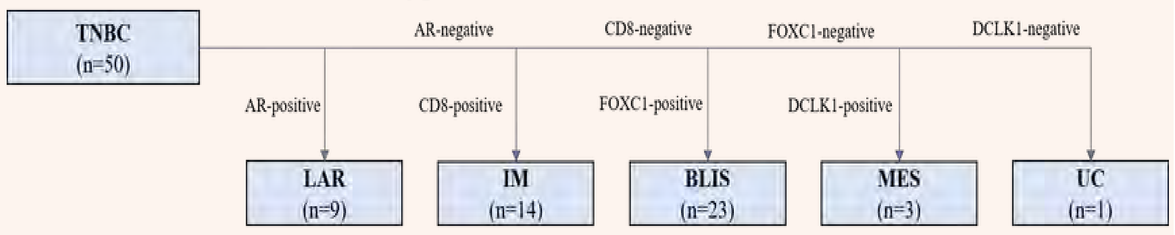
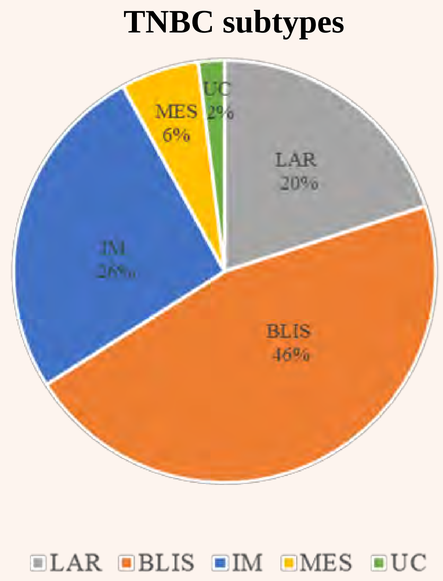


Figure 1: Microscopic images of a representative of each TNBC subtype.

- Classification of TNBC subtype.



- Distribution of TNBC subtypes defined by IHC surrogate markers. 49 cases were assigned to LAR, MES, and BLIS subtypes and 1 cases could not be classified into any subtype.



Conclusion

- This study revealed the distribution of TNBC subtype in southern Thai population.
- The distributions of TNBC subtype were classified into 5 subtypes based on proteins expression of IHC markers: LAR, IM, BLIS, MES, and unclassifiable subtype.
- The IHC marker may be useful for targeted therapeutic approaches in TNBC patients.

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