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http://doi.org/10.1631/jzus.B2200113

# Luminal androgen receptor (LAR) subtype of triple-negative breast cancer: molecular, morphological, and clinical features

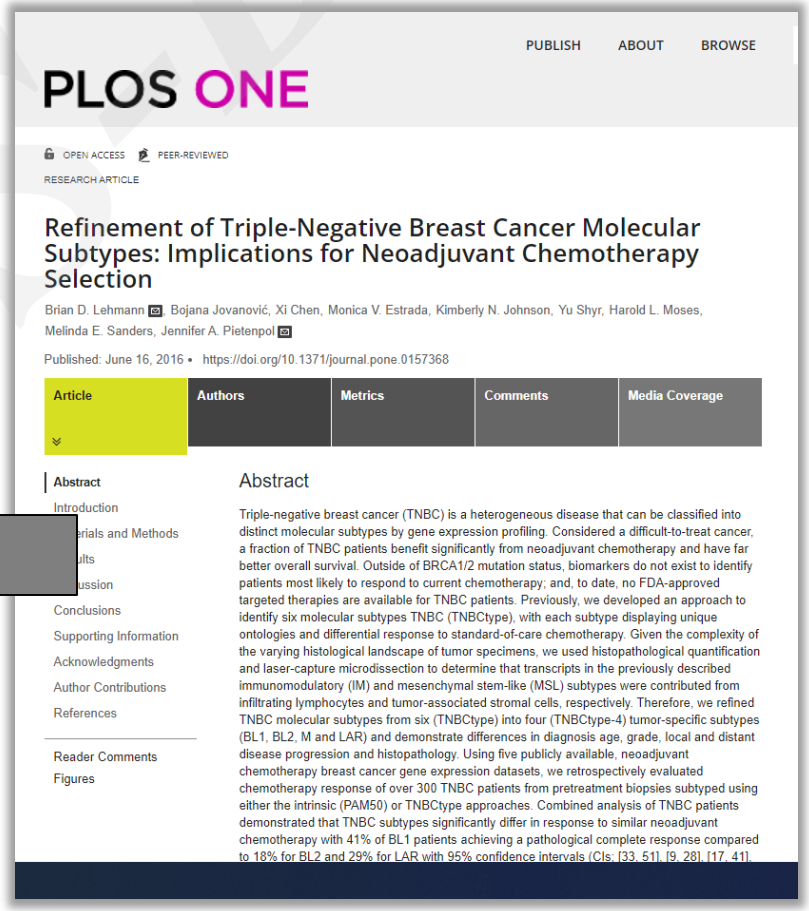
**Key words: LAR subtype; Triple negative breast cancer (TNBC); Androgen receptors; Prognosis**

# Research Summary

This review is devoted to the analysis of the relevant literature, reflecting the main results of studies on the molecular properties and clinical features of the disease course of LAR-type TNBC carcinomas

**According to the classification presented by Lehmann B.D. (2016), TNBC is a heterogeneous group of malignant tumors with 4 specific subtypes:**

- basal-like subtype 1
- basal-like subtype 2
- mesenchymal subtype
- luminal androgen receptor (LAR) subtype



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RESEARCH ARTICLE

Refinement of Triple-Negative Breast Cancer Molecular Subtypes: Implications for Neoadjuvant Chemotherapy Selection

Brian D. Lehmann, Bojana Jovanović, Xi Chen, Monica V. Estrada, Kimberly N. Johnson, Yu Shyr, Harold L. Moses, Melinda E. Sanders, Jennifer A. Pietenpol

Published: June 16, 2016 • https://doi.org/10.1371/journal.pone.0157368

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Abstract

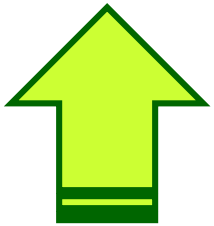
Triple-negative breast cancer (TNBC) is a heterogeneous disease that can be classified into distinct molecular subtypes by gene expression profiling. Considered a difficult-to-treat cancer, a fraction of TNBC patients benefit significantly from neoadjuvant chemotherapy and have far better overall survival. Outside of BRCA1/2 mutation status, biomarkers do not exist to identify patients most likely to respond to current chemotherapy; and, to date, no FDA-approved targeted therapies are available for TNBC patients. Previously, we developed an approach to identify six molecular subtypes TNBC (TNBCtype), with each subtype displaying unique ontologies and differential response to standard-of-care chemotherapy. Given the complexity of the varying histological landscape of tumor specimens, we used histopathological quantification and laser-capture microdissection to determine that transcripts in the previously described immunomodulatory (IM) and mesenchymal stem-like (MSL) subtypes were contributed from infiltrating lymphocytes and tumor-associated stromal cells, respectively. Therefore, we refined TNBC molecular subtypes from six (TNBCtype) into four (TNBCtype-4) tumor-specific subtypes (BL1, BL2, M and LAR) and demonstrate differences in diagnosis age, grade, local and distant disease progression and histopathology. Using five publicly available, neoadjuvant chemotherapy breast cancer gene expression datasets, we retrospectively evaluated chemotherapy response of over 300 TNBC patients from pretreatment biopsies subtyped using either the intrinsic (PAM50) or TNBCtype approaches. Combined analysis of TNBC patients demonstrated that TNBC subtypes significantly differ in response to similar neoadjuvant chemotherapy with 41% of BL1 patients achieving a pathological complete response compared to 18% for BL2 and 29% for LAR with 95% confidence intervals (CIs: [33, 51], [9, 28], [17, 41]

# *Research Summary*

**AR+ TNBC** ≠ **LAR type TNBC**

AR+ TNBC are breast carcinomas with an appropriately confirmed molecular genetic profile, and they are characterized by the presence of positive AR IHC expression in the tumor

The LAR subtype is defined as a variant of TNBC, which includes not only the presence of an indicator of AR-positive expression, but also many other morphological, molecular and genetic characteristics



The LAR subtype is of particular interest, since the literature on such tumors presents different and even contradictory data concerning the disease course and prognosis

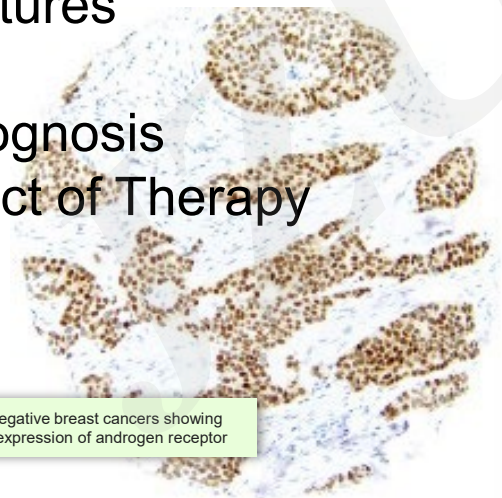
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# Research Summary

## LAR type TNBC

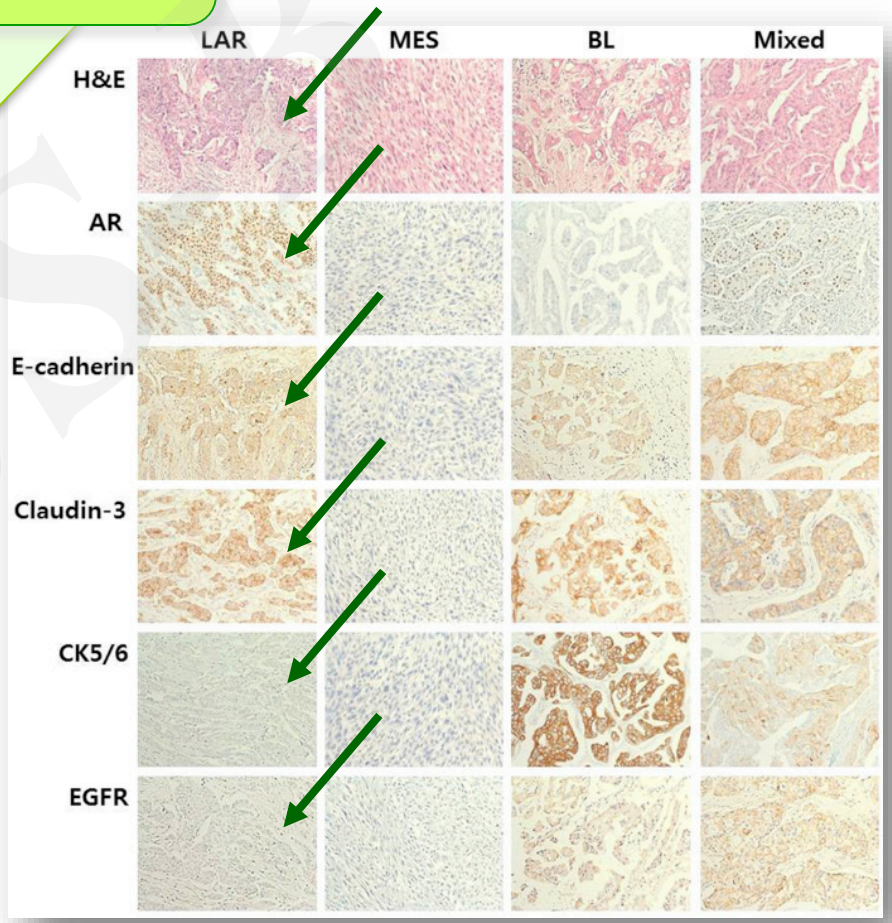
**Review contain data about:**

- Morphology features
- Molecular features
- Genetic features
- Metastasis
- Disease prognosis
- Clinical effect of Therapy



Triple-negative breast cancers showing nuclear expression of androgen receptor

Tung N, Garber JE, Hacker MR, et al. Prevalence and predictors of androgen receptor and programmed death-ligand 1 in *BRCA1*-associated and sporadic triple-negative breast cancer. *NPJ Breast Cancer.* 2016;2:16002. Published 2016 Feb 24. doi:10.1038/npjbcancer.2016.2




Kim S, Moon BI, Lim W, Park S, Cho MS, Sung SH. Feasibility of Classification of Triple Negative Breast Cancer by Immunohistochemical Surrogate Markers. *Clin Breast Cancer.* 2018;18(5):e1123-e1132. doi:10.1016/j.clbc.2018.03.012

# *Research Summary*

This review unveiled that the clinical, morphological and molecular genetic features of the LAR subtype of TNBC presented in the literature clearly indicate the existing differences and tumor heterogeneity of similar breast carcinomas. Numerous studies devoted to the various biological markers as potential factors for assessing the course and prognosis of the disease demonstrate significant differences from each other, and sometimes even completely opposite results.

## LAR type TNBC

The presented review demonstrates the need for a clear understanding of which tumors can be isolated as the LAR subtype of TNBC, what key criteria can be determined for their identification, which typing method can act as the main technique and what additional components can be used for detailing the subtype of carcinoma in cases of TNBC. Only such clearly defined approach will allow us to accurately define the LAR subtype of TNBC group patients, in order to form possible options for therapeutic strategies.