Câncer de mama TN: todos os tumores são iguais? A visão dos patologistas

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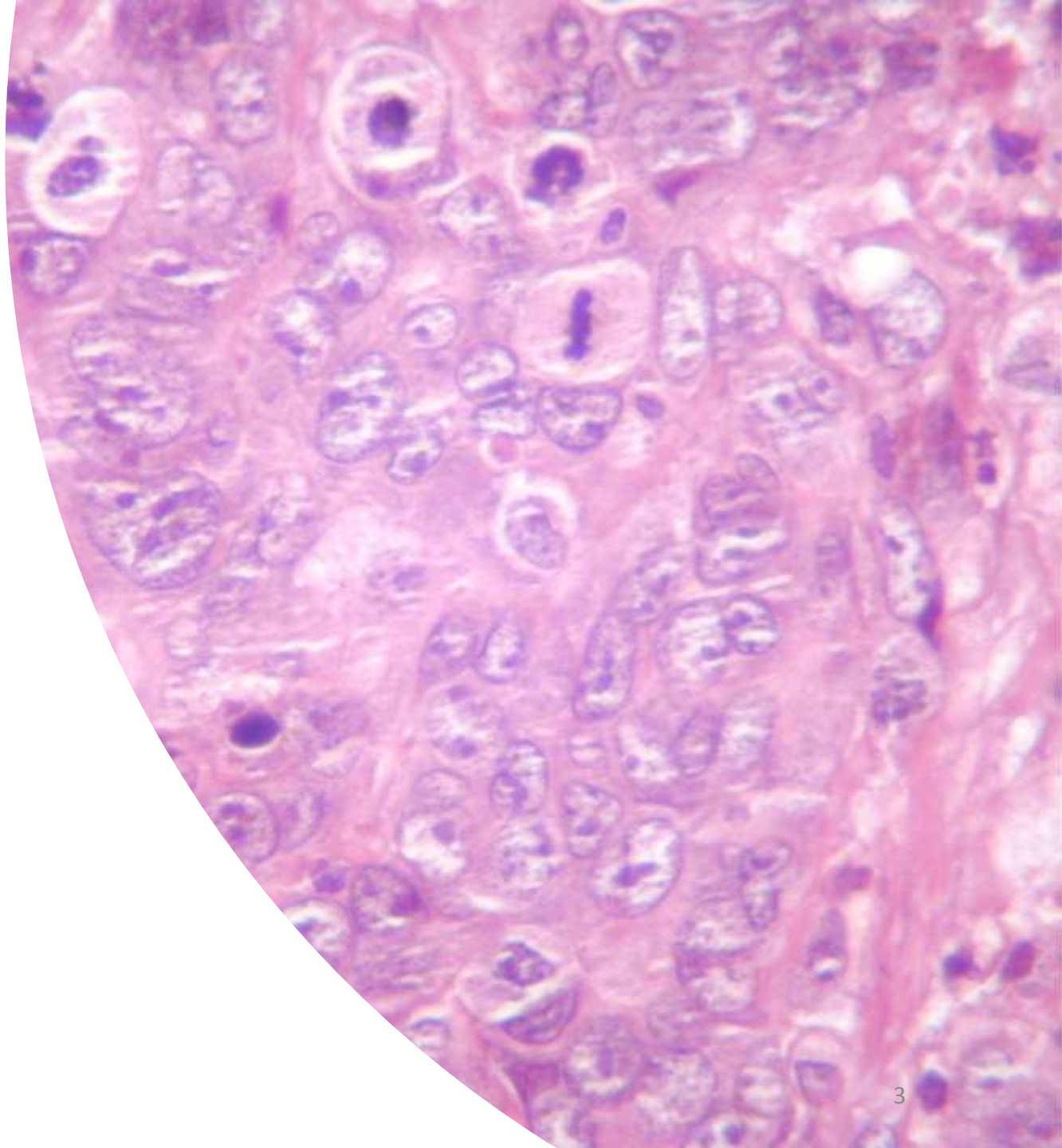
Não existe conflito de interesse nessa apresentação

There is no conflict of interest in this presentation

Carcinomas mamários TN

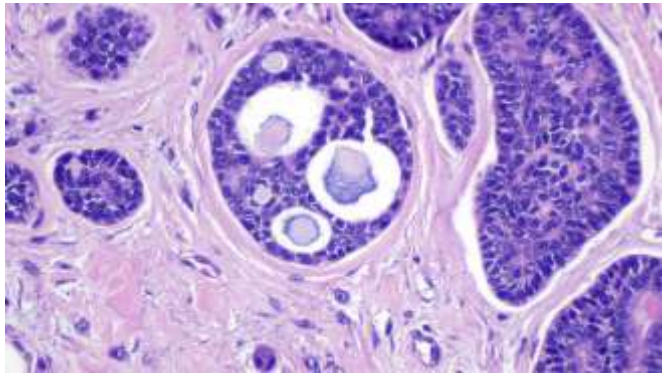
- Metástase/sítio extramamário
- Tipos histológicos especiais
- Tipo histológico não especial
  - Subtipos moleculares
    - Basal1
    - Basal 2
    - Mesenquimal
    - Luminal-androgênico
  - Modulação imune
  - Modulação estromal intratumoral



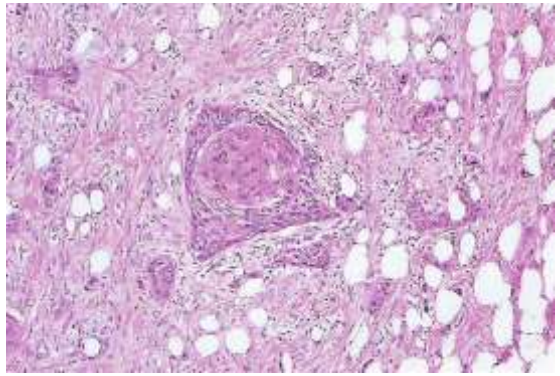
Carcinomas mamários TN: tipos histológicos especiais de prognóstico favorável e baixa atividade proliferativa

- Carcinoma adenoide-cístico
- Carcinoma adenoescamoso de baixo grau
- Carcinoma metaplásico do tipo fibromatose
- Carcinoma secretor

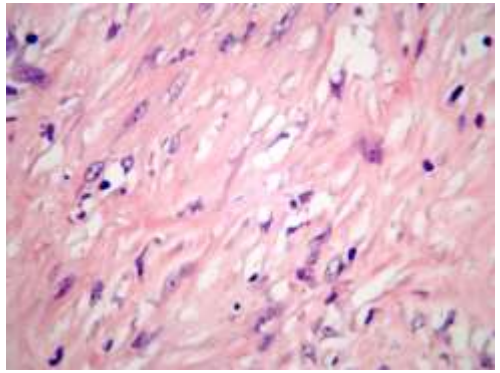
Adenoide cístico



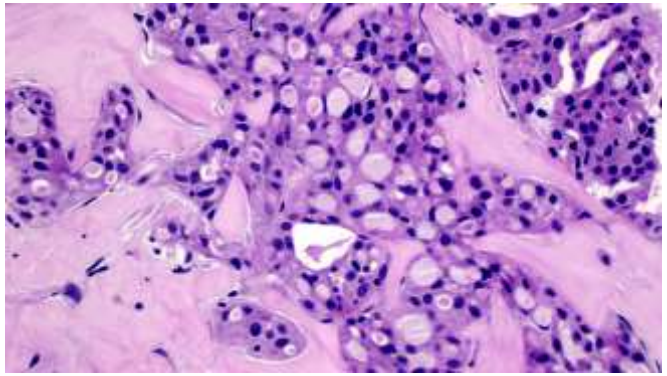
Adenoescamoso de baixo grau

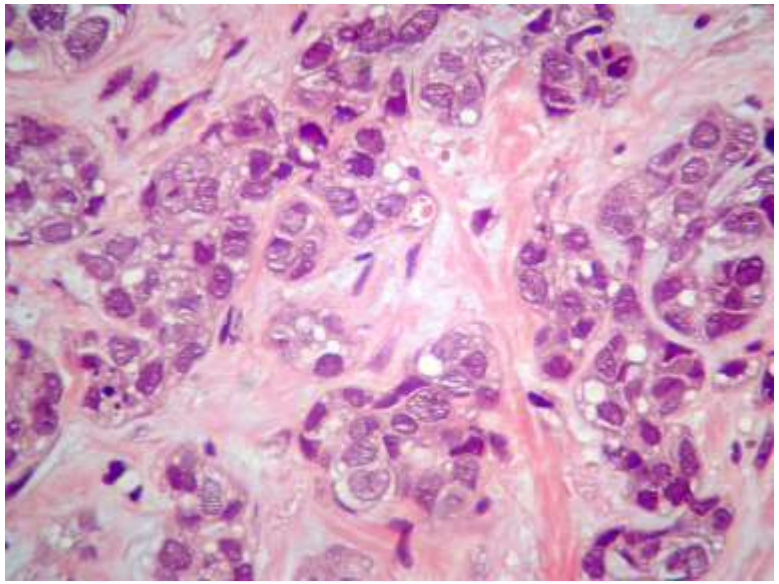


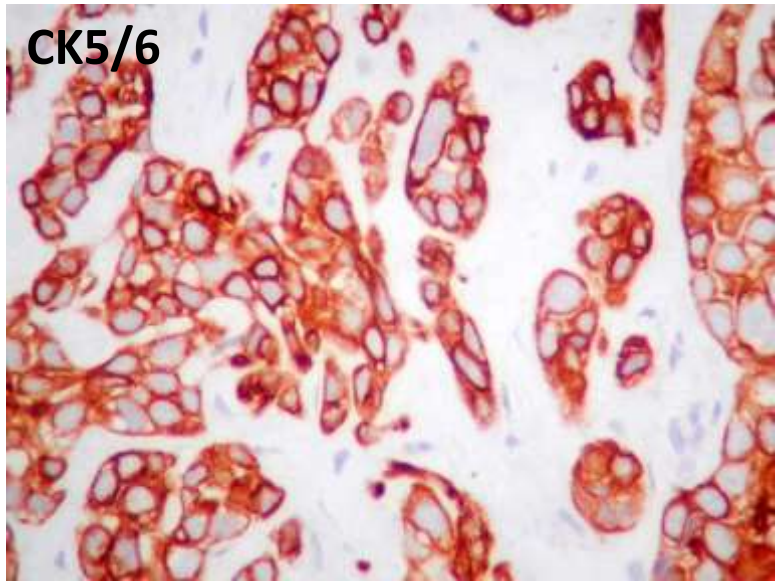
Tipo fibromatose

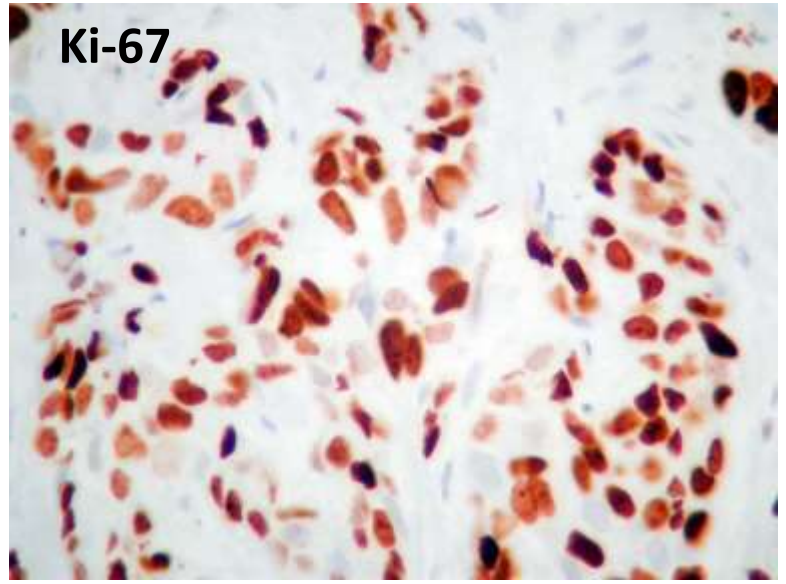


Secretor





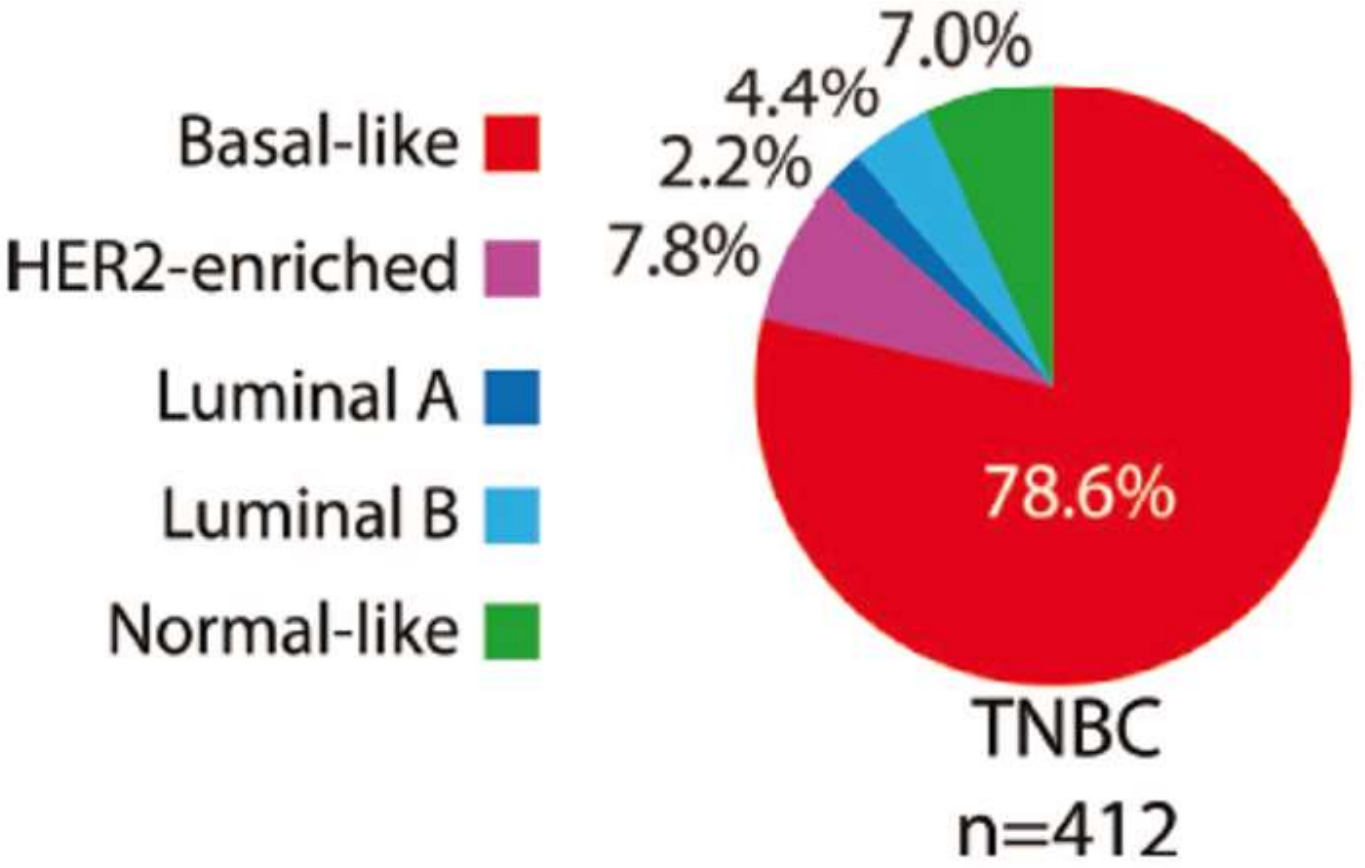




Heterogeneidade dos carcinomas TN

subtipos moleculares

Subtipos moleculares intrínsecos



Prat et al. The Oncologist 2013;18:123-133

Research article

Identification of human triple-negative breast cancer subtypes and preclinical models for selection of targeted therapies

Brian D. Lehmann,[1] Joshua A. Bauer,[1] Xi Chen,[2] Melinda E. Sanders,[3] A. Bapsi Chakravarthy,[4] Yu Shyr,[2] and Jennifer A. Pietenpol[1]

[1]Department of Biochemistry, [2]Department of Biostatistics, [3]Department of Pathology, and [4]Department of Radiation Oncology, Vanderbilt-Ingram Cancer Center, Vanderbilt University School of Medicine, Nashville, Tennessee, USA.

J Clin Invest 2011; 121:2750-67

BL1: genes relacionados ao ciclo celular e reparo do DNA

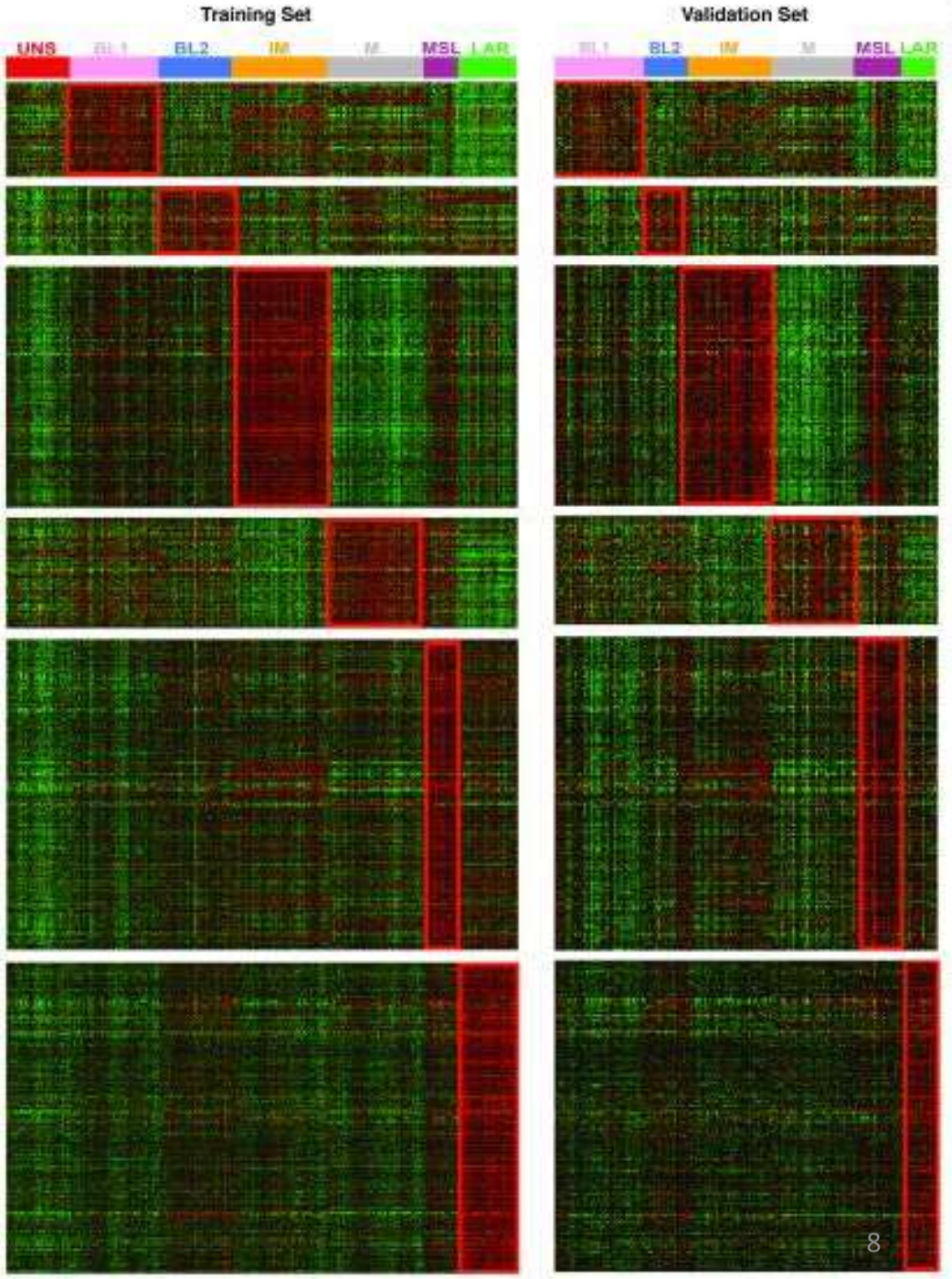
BL2: vias de sinalização de fatores de crescimento

IM: ativação imune

M: ativação TEM e vias de sinalização de fatores de crescimento

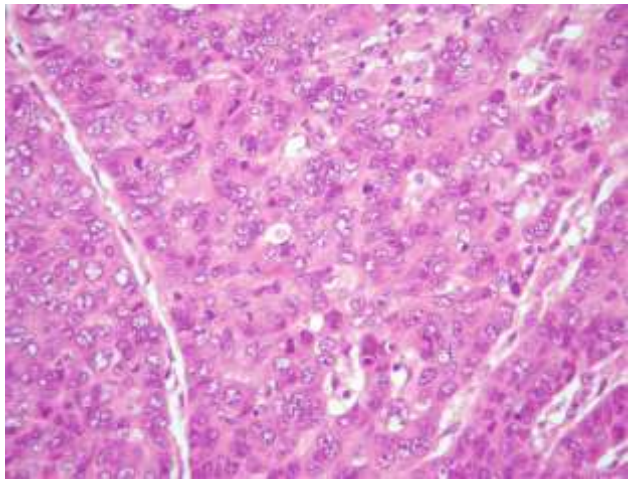
MSL: similar ao M , mas com redução na expressão de genes envolvidos na proliferação celular

LAR : via de sinalização do receptor de androgênio



Lehmann et al. J Clin Invest 2011;121:2750–67.

PLOS ONE



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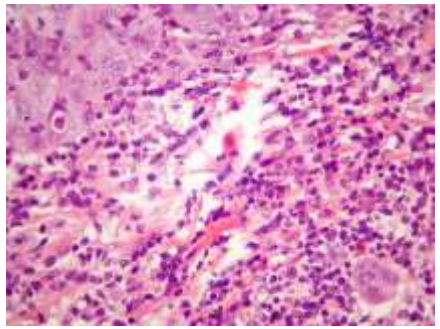
RESEARCH ARTICLE

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

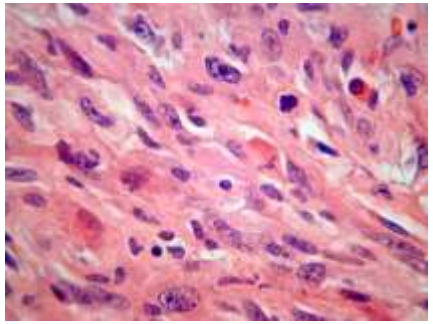
Brian D. Lehmann[1]*, Bojana Jovanović[2], Xi Chen[3,4], Monica V. Estrada[5], Kimberly N. Johnson[1], Yu Shyr[6], Harold L. Moses[7], Melinda E. Sanders[8], Jennifer A. Pietenpol[1,7]*

1 Department of Biochemistry, Vanderbilt University, Nashville, Tennessee, United States of America, 2 Department of Medical Oncology, Dana-Farber Cancer Institute, Harvard University, Boston, MA, United States of America, 3 Division of Biostatistics, Department of Public Health Sciences, University of Miami Miller School of Medicine, Miami, FL, United States of America, 4 Sylvester Comprehensive Cancer Center, University of Miami Miller School of Medicine, Miami, FL, United States of America, 5 Department of Medicine, Breast Cancer Research Program, Vanderbilt University, Nashville, Tennessee, United States of America, 6 Center for Quantitative Sciences, Division of Cancer Biostatistics, Department of Biostatistics, Vanderbilt University, Nashville, Tennessee, United States of America, 7 Department of Cancer Biology, Vanderbilt University, Nashville, Tennessee, United States of America, 8 Department of Pathology, Microbiology and Immunology, Vanderbilt University, Nashville, Tennessee, United States of America



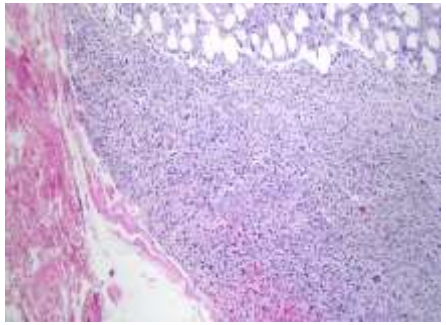
BL1

- N+ 32%
- pCR 49%



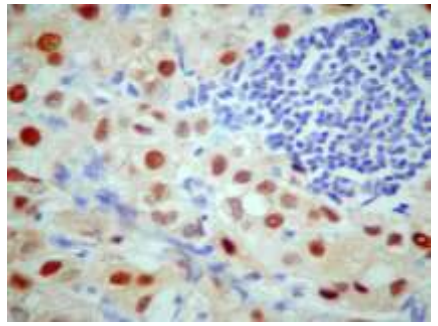
BL2

- N+ 33%
- pCR 18%
- Metaplásico



M

- N+ 21%
- pCR 36%
- Metaplásico
- Metastases pulmonares (46%)



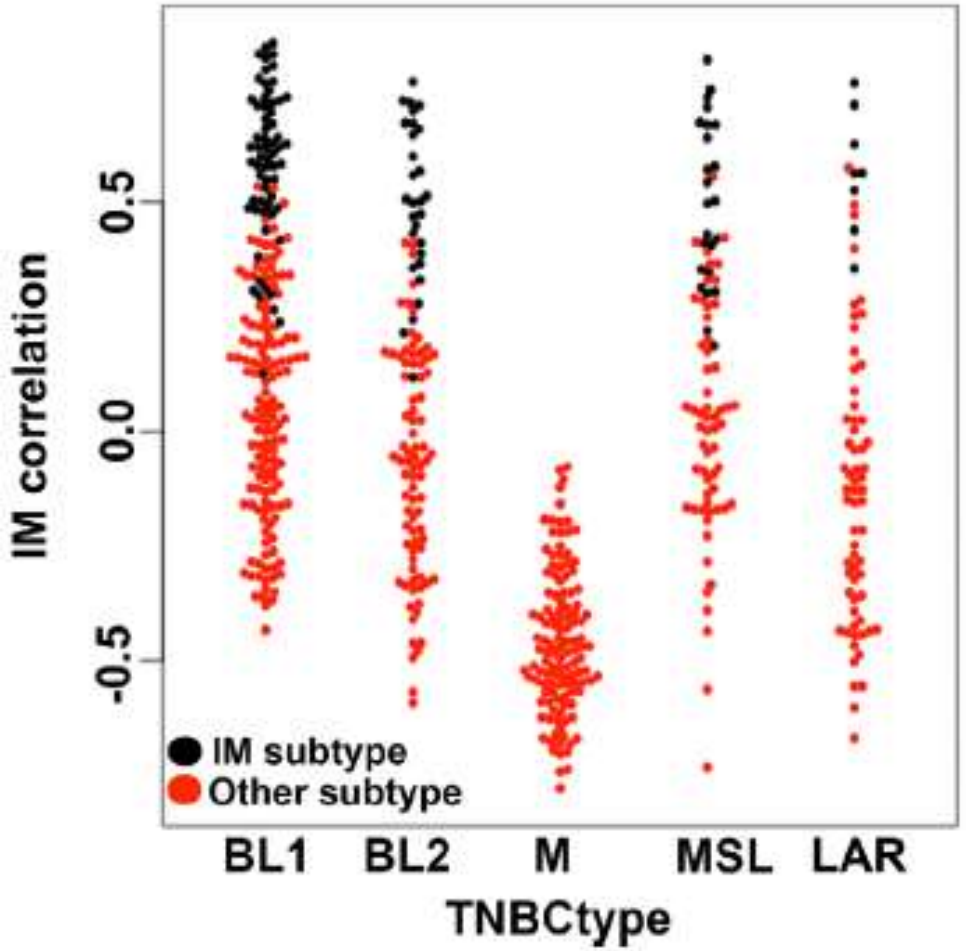
LAR

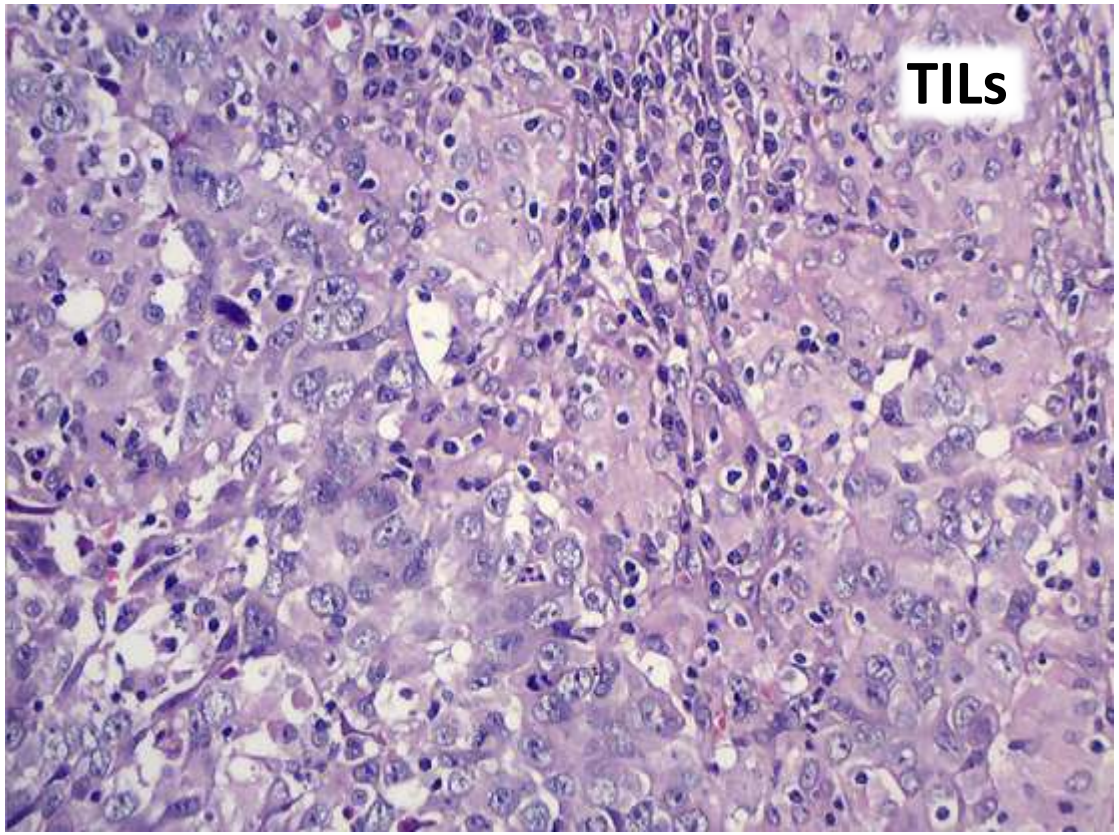
- N+ 47%
- pCR 29%
- Lobular
- Metastases ósseas (46%)

IM: TILs
MSL: células estromais associadas ao tumor

Lehmann et al. PLoS One 2016;11(6):e0157368

Características IM quanto aos subtipos moleculares





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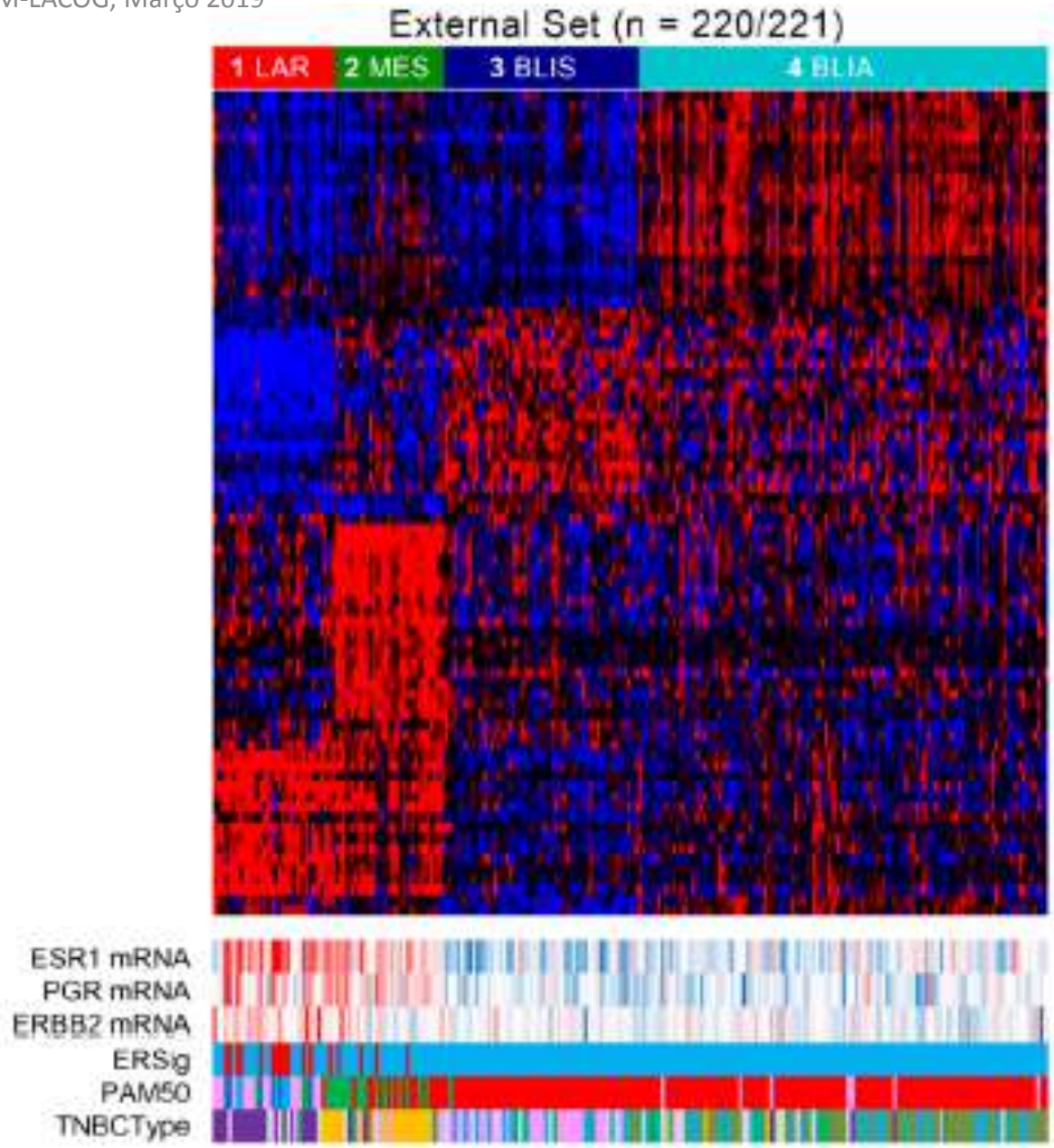
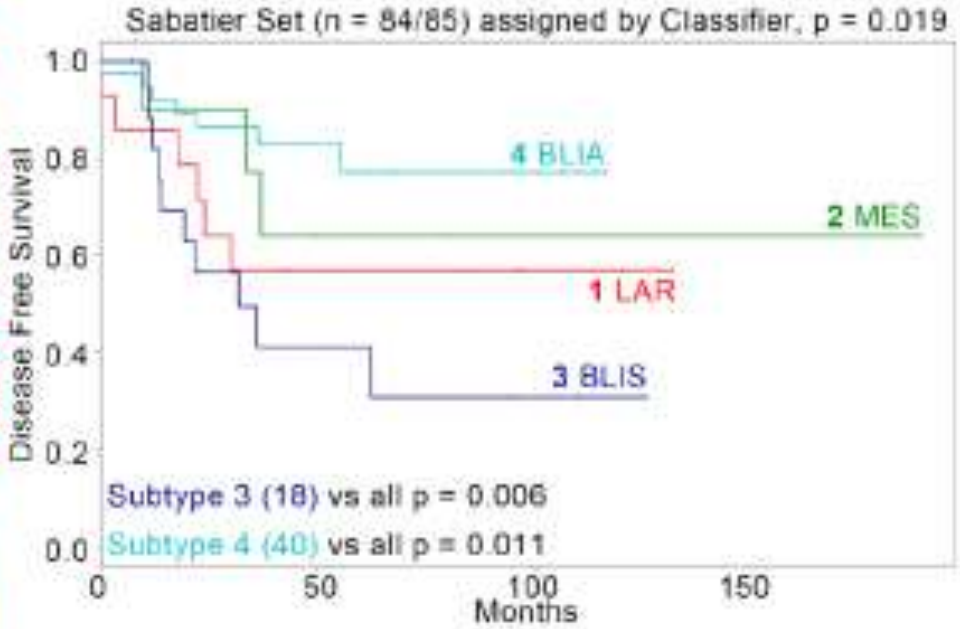
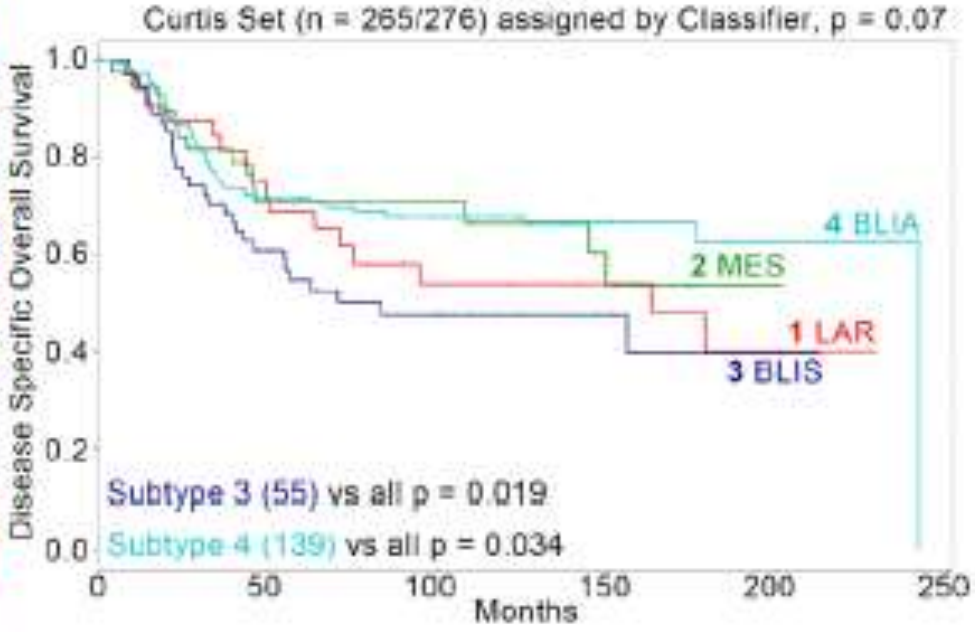


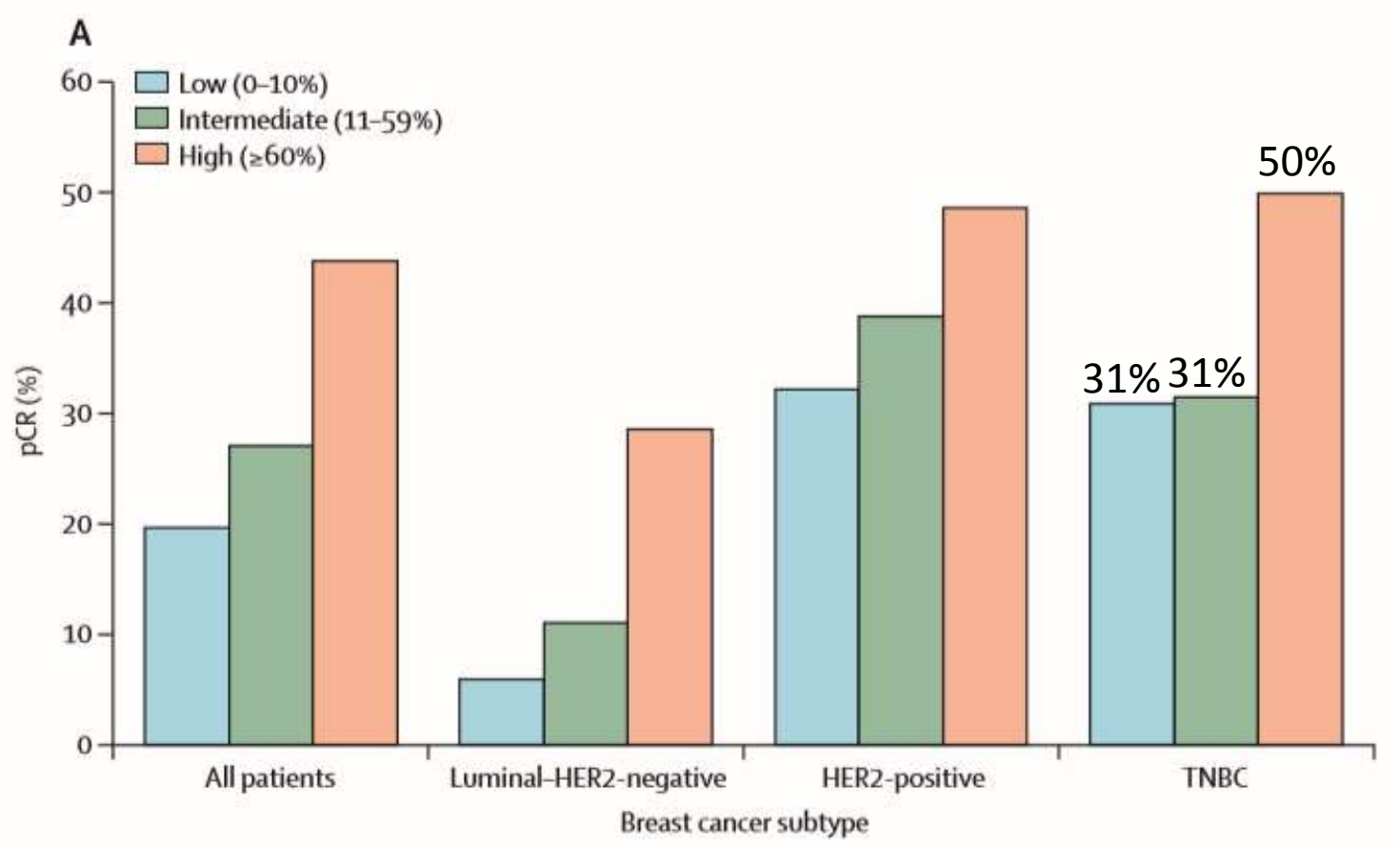




Burstein et al. Clin Cancer Res 2015;21:1688-98

TILs e carcinomas TN

- Seleção de pacientes de 6 ensaios clínicos do German Breast Cancer Group



Denkert et al. Lancet Oncol 2018;19:40-50

TILs e carcinomas TN

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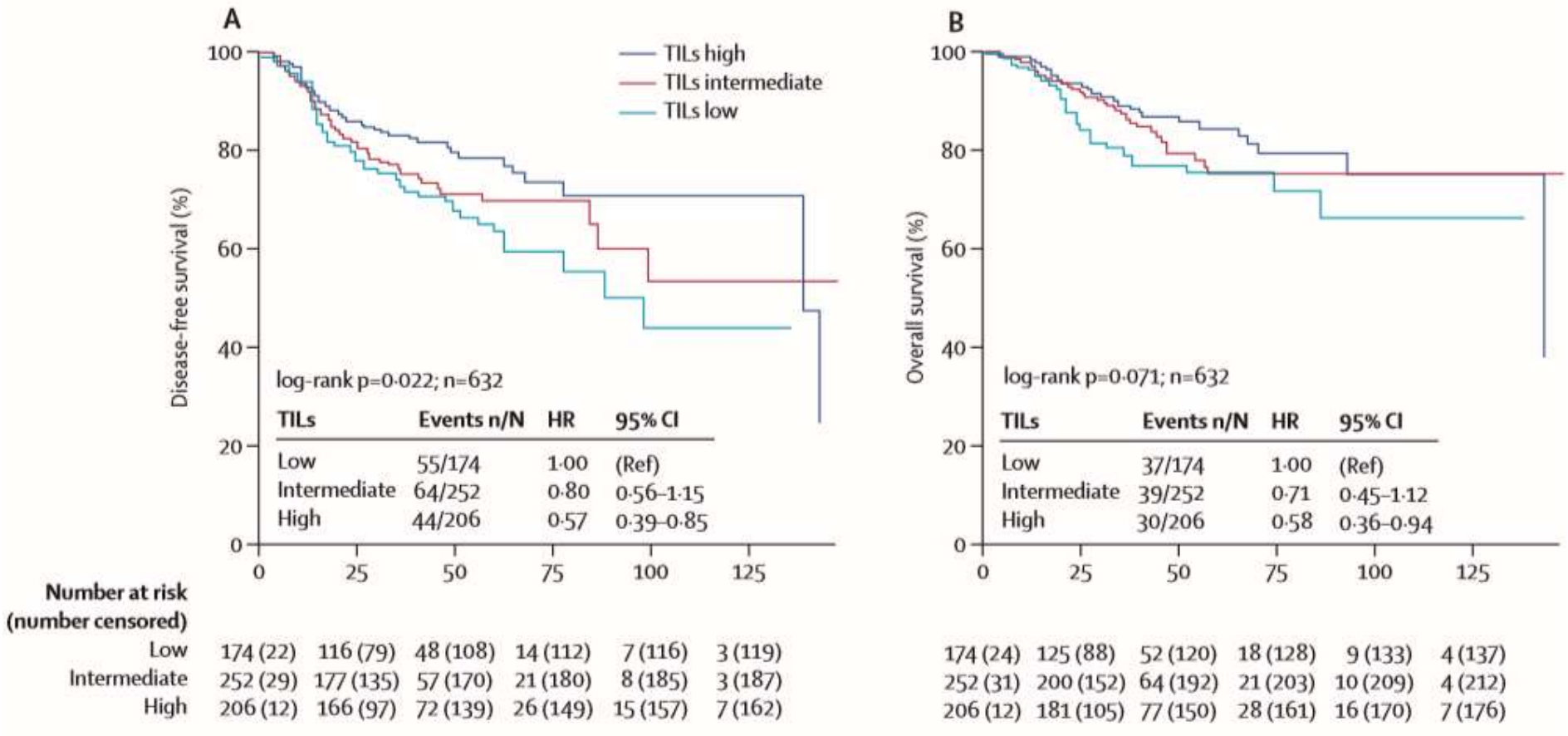


Denkert et al. Lancet Oncol 2018;19:40-50

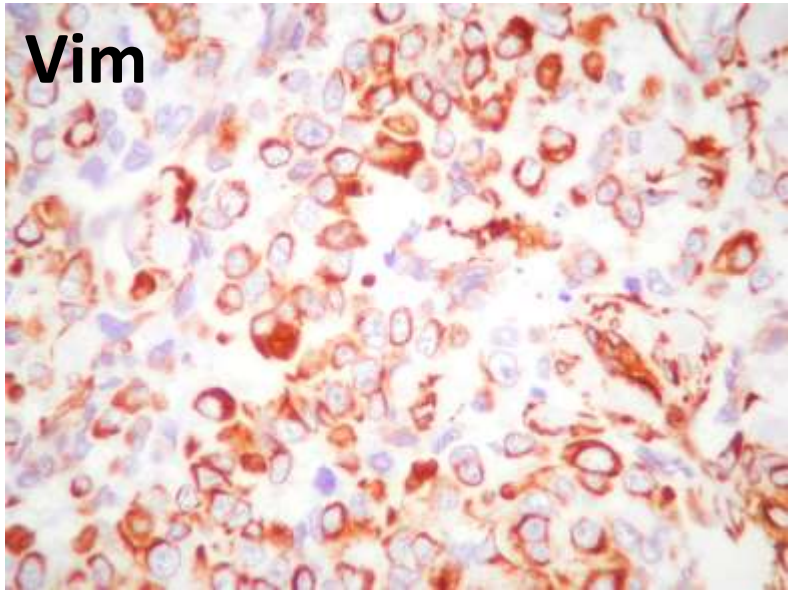
Carcinomas TN e espectro mutacional

- Grupo de maior heterogeneidade e instabilidade genômica
- Predisposição (mutações germinativas)
  - Relação com mutação *BRCA1*, *PALB2* e *FANCM*
  - Genes relacionados a vias de reparo do DNA (*PALB2, BARD1, BRIP1, RAD51C, RAD51D, RAD50*, e *XRCC2*)
- Progressão (mutações somáticas)
  - Maior frequência de *TP53* (80%)
  - Perda de genes supressores *BRCA1, PTEN*
  - Amplificação do oncogene *MYC* (26%)
- Variável nos diferentes subtipos moleculares

Shi et al. Molecular Cancer 2018;17:99

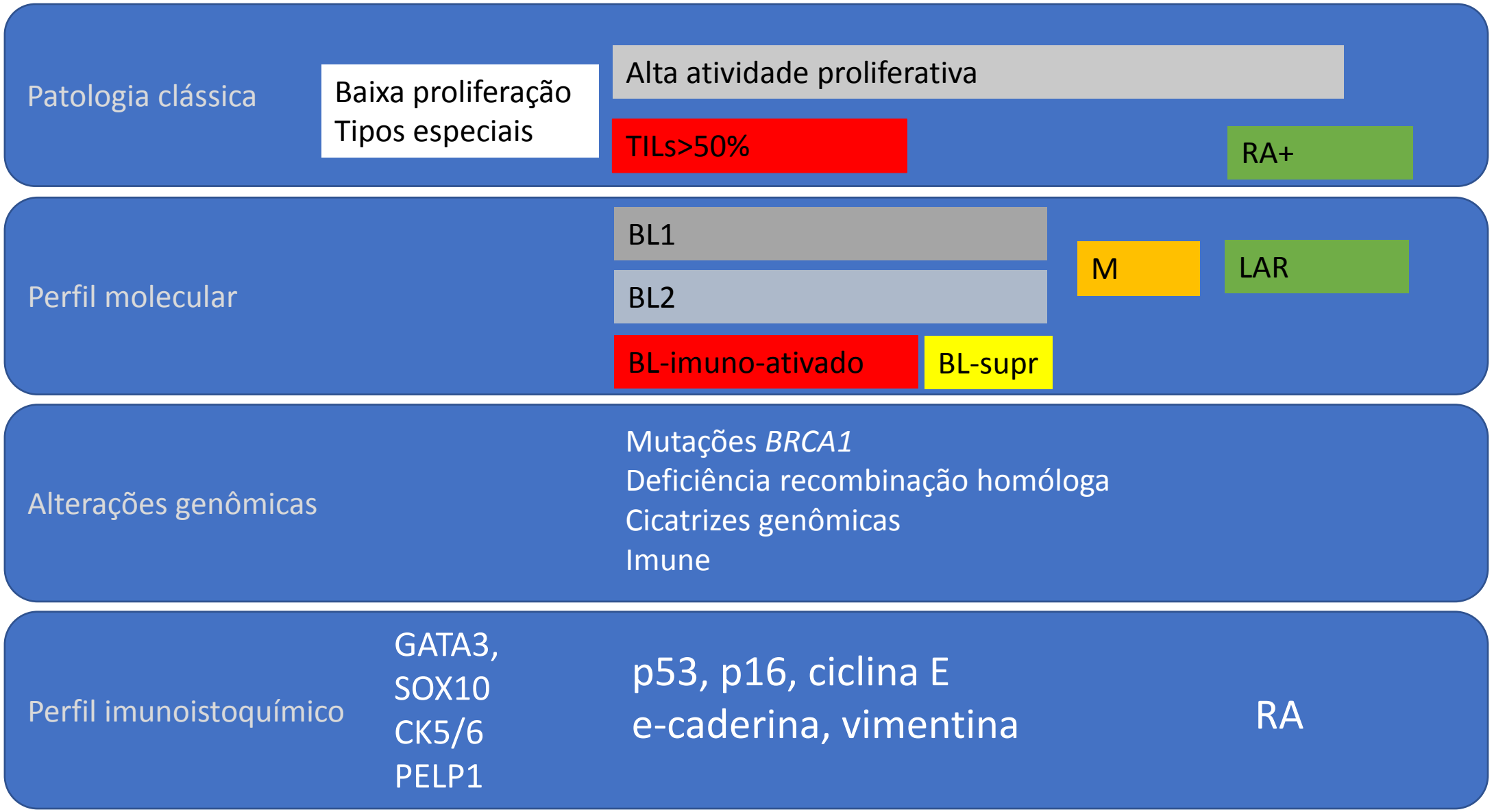
Heterogeneidade dos carcinomas TN: perfil imunoistoquímico

- Diferencial com metástases: GATA3, SOX10, PELP1, mamaglobina, GCDFP-15
  - Pulmão (napsina, TTF1)
  - Ginecológico (PAX-8, WT-1)
  - Gastrointestinal (CDX-2, CK20)
- Fatores prognósticos e/ou preditivos:
  - Receptor de androgênio
  - Perfil basal: citoqueratinas basais e EGFR
  - Reguladores do ciclo celular: p53, p16, ciclina E
  - Marcadores de TEM: e-caderina, vimentina



Peng et al. Arch Pathol Lab Med 2017;141:1033-51; Harbhajanka et al. Hum Pathol 2018;80:163-9; Maeda et al. Med Mol Morphol 2016;49:11-21

Carcinomas mamários TN



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