TCGA RNA-seq data analysis in breast invasive carcinoma

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ABSTRACT

KEYWORDS Keyword; Keyword2; Keyword3; ...

Introduction

Breast cancer is the most common malignant cancer affecting women and is the second leading cause of cancer death worldwide(Rosa 2015). This disease has more than 1,300,000 cases and 450,000 death each year around the world(Network 2012). This disease is widely heterogeneous, having a large and diverse set of molecular, histological and clinical behaviours depending of the tumour(Rosa 2015). In addition, the response to specific treatments it is also very different between patients. For this reason, breast cancer was been classified in different subtypes in order to achieve a better understanding of these disease. Traditionally, the classification has been based on clinicopathological features such as tumor type and size, lymph node status and histological grade(Rosa 2015). Actually, nowadays this disease is an entity difficult to classify due to the wide range of classifiers that we can take into account: histological, immunopathological, transcriptional, genomic, miRNA-based, epigenetic, microenvironmental, macroenvironmental, longitudinal and other classifiers(Bertos and Park 2011). However, we have an actual classification based on simple molecular characteristics(Network 2012)

- **Estrogen receptor (ER) positive:** The most numerous and diverse, with several genomic tests to assist in predicting outcomes for ER+ patients receiving endocrine therapy.
- **HER2 or ERBB2 amplified:** Great clinical success because of effective therapeutic targeting of HER2, which has led to intense efforts to characterize other DNA copy number aberrations.
- **Triple negative:** Lacking expression of ER, progesterone receptor (PR) and HER2. It is also known as basal-like breast cancers, are a group with only chemotherapy options, and have an increased incidence in patients with germline BRCA1 mutations or of African ancestry.

The more frequently mutated genes in breast cancer are BRCA1, BRCA2, PALB2, ATM, TP53, PTEN, PIK3CA, AKT1, GATA3, CDH1, RB1, MLL3, MAP3K1, CDKN1B, between others(American Cancer Society 2016). If we focus in their functionalities, these genes are linked with DNA repair, control of cell cycle, apoptosis, cell proliferation and gorwth. BRCA1 and BRCA2 mutations are the most common cause of hereditary breast cancer(American Cancer Society 2016). In addition, women with these mutations also have higher risk of developing other cancers, mainly ovarian cancer(American Cancer Society 2016). In case of BRCA1 mutations, the risk compared with the population is about 60% meanwhile in BRCA2 mutations is about 45%(American Cancer Society 2016).

Anyway, as we describe above, each tumour has a high specific profile with a lot of different variables difficulting the establishment of simple classifiers. In the last decades, molecular knowledge advances have allowed to initialize personalized medicine. In this way, we can use targeted drugs to very specific tumour types with a high percentage of effectiveness. The main problem of this personalized medicine is the very reduced number of tumours in which we can observe a remission. This is due to the very high specificity of the treatments, useful only for a tumour with a concrete molecular characteristics.

In this way, new technologies focused not only in mRNA expression profiling, DNA copy number analysis and massively parallel sequencing but also in detecting abnormalities in DNA methylation, miRNA and protein expression provides a wider range of information(Network 2012). Therefore, we can use all these tools in order to get a deeper understanding about tumor molecular mechanisms resulting in advances towards personalized medicine.

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American Cancer Society, 2016 http://www.cancer.org/cancer/breastcancer/detailedguide/breast-cancer-risk-factors.

Bertos, N. R. and M. Park, 2011 Breast cancer - one term, many entities? J Clin Invest **121**: 3789–96.

Network, C. G. A., 2012 Comprehensive molecular portraits of human breast tumours. Nature **490**: 61–70.

Rosa, M., 2015 Advances in the Molecular Analysis of Breast Cancer: Pathway Toward Personalized Medicine. Cancer Control **22**: 211–9.