biomarkers

107P Evaluation of RAD50 as a prognostic marker of survival in breast cancer patients

K.V. Havrysh[1], V.V. Filonenko[1], I.G. Serebriiskii[2], R.G. Kiyamova[3]

[1]*Cell Signalling, Institute of Molecular Biology and Genetics of National Academy of Sciences of Ukraine, Kyiv, Ukraine,* [2]*Molecular Therapeutics, Fox Chase Cancer Center, Philadelphia, PA, USA,* [3]*Institute of Fundamental Medicine and Biology, Kazan Federal University, Kazan, Russian Federation*

Background: Breast cancer (BC) is common and aggressive malignancy. Resistance to drugs often develops and is not fully understood. One of the possible reasons of this is increased activity of the DNA repair system in cancer cells. Since molecular disruption of RAD50, which implicated in DNA double-break repair, sensitizes breast tumor cells to cisplatin-based chemotherapy in cell culture, one may be hypothesized that level of RAD50 gene expression in breast tumors could be considered as a potential predictive and prognostic marker of BC. The aim of this investigation was to examine the impact of RAD50 gene features (level of expression and Copy Number Alteration (CNA)) on survival of BC patients taking into account their clinical characteristics: stage of disease and molecular subtype of tumors.

Methods: Data on the clinical behavior, RAD50 gene expression (RNA-Seq (V2)) and CNA (deletion, gain, amplification) of the BC patients were obtained from three independent studies (TCGA, Provisional (n = 1105); TCGA, Cell 2015 (n = 1105); TCGA, Nature 2012(n = 825) using the cBioPortal (www.cbioportal.org/). Cases with absence of necessary data were excluded, leading to data sets from 2359 to 1220 samples. Testing intergroup differences (ANOVA, Tukey's HSD, Wilcoxon tests and Spearman's correlation) and analysis of BC patients' survival (Kaplan-Meier and Log-rank test) were performed using RStudio.

Results: A pairwise comparison groups of BC patients showed that level of RAD50 gene expression fluctuates significantly in breast tumors of various molecular subtypes (except pair of Luminal A and B), between patients on 1st and 2nd stages of disease and patients with different CNA. The patients with high level of RAD50 gene expression had significantly reduced overall survival in comparison with the patients that had low level of RAD50 gene expression only among patients with CNA. Correlation analysis of CNA and level of RAD50 gene expression has shown that high level of RAD50 gene expression bonded with gain and amplification of RAD50 gene.

Conclusions: Our finding allows us to consider the gain and amplification of RAD50 gene as traits which are associated with poor survival of BC patients and RAD50 as potential prognostic marker of BC.

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