Mutations in PIK3CA Sensitize Breast Cancer Cells to Physiologic Levels of Aspirin

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Dear Editor

I read the paper by Turturro et al. (2016) concerning the potential predictive role of mutations in PIK3CA sensitize breast cancer cells to physiologic levels of aspirin PIK3CA, which appeared in the 156 (1) issue of Breast Cancer Res. Treat. Journal, with great interest. Mutations of PIK3CA gene are seen in hepatocellular, colon, brain, and BCa (Whitman et al., 1985; Gallia et al. 2006). PIK3CA mutations are found nearly 25-40 % in patient with BCa (Dirican et al., 2016). In 2014, we also determined 31% frequency of PIK3CA mutations in Turkish BCa patients (Dirican et al. 2014).

PI3K pathway plays a critical role in myriad of cellular actions that are necessary in both normal and cancer cell, for instance cell division, motility, growth, and survival [6]. In many cancer types, somatic mutations in PI3K pathway are recurrent. Oncogenic mutations in the PI3K pathway generally are evaluated in accordance to two different functions: activate mutation of the gene encoding PI3K (PIK3CA) or AKT (AKT1), and extinguish or reduce expression of PTEN. On the other hand, there are lots of studies about PIK3CA-PI3K relation with cancer treatment. These researches indicate that alterations of PI3K signal pathway are important to treat cancer. We know that there are different approaches for PI3K treatment such as trastuzumab, lapatinib, pertuzumab, anti-PI3K drugs, etc (Dirican et al., 2016).

In the study of Turturro et al. (2016) PIK3CA and KRAS are required for the greatest aspirin sensitivity in breast cancer, and that the GSK3β protein was hyperphosphorylated in aspirin-treated double knockin cells, but not in other clones/treatments. A more modest effect was observed with single mutant PIK3CA, but not KRAS alone. Their findings provide the first evidence that mutations in PIK3CA sensitize breast cancer cells to aspirin. Moreover, they used aspirin concentrations as high as 4 mM. But, they implied that it is important to note that lower daily aspirin doses may exhibit a more modest effect on proliferation and apoptosis. However, other researchers have reported that it is possible to safely reach serum levels of aspirin as high as 10 mM, indicating that their findings are clinically significant, as they are likely safe and feasible (Juarez et al., 2004).

In conclusion, Turturro et al. (2016) provide the first evidence that mutations in PIK3CA sensitize breast cancer cells to aspirin therapy. Therefore, we fully agree with suggestion of Turturro et al. (2006) that the prognostic or predictive role of PIK3CA should be emphasized. Besides, we believe that if such studies are carried out with increased number of populations that have PIK3CA mutations, it will provide a stronger rationale evidence for development of new therapeutic and diagnostic approaches for BCa patients.

References


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