1-SS-54 Student Sessions

The role of stathmin in the antiproliferative effects of eribulin in breast cancer cells

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Stathmin is a member of microtubule destabilizing proteins that modulate the dynamics of microtubule polymerization and depolymerization. Stathmin promotes microtubule depolymerization and the activity was regulated by its phosphorylation state. It has been reported that high stathmin expression is associated with poor prognosis in breast cancer patients. Eribulin, an analogue of the marine natural product halichondrin B, is a microtubule-depolymerizing drug that has been used in the treatment of patients with advanced breast cancer. In this study, we examined the involvement of stathmin in the antiproliferative activities of eribulin in breast cancer cells (MCF7 and MDA-MB-231). Eribulin induced phosphorylation of stathmin in both cells. The eribulin-mediated phosphorylation of stathmin was attenuated by the inhibitors of protein kinase A (H89) and Ca^{2+}/calmodulin-dependent kinase II (KN62). In addition, the phosphorylated stathmin was reduced by the protein phosphatase PP2A activator FTY720, whereas it was increased by the PP2A inhibitor okadaic acid. Of note, eribulin did not directly affect the phosphatase activity of recombinant PP2A, but the expression of PP2A subunits was reduced in eribulin-treated cells. Furthermore, the antiproliferative effect of eribulin was more efficient in stathmin-overexpressing cells compared to control. Together these data provide a novel mechanism of antiproliferative effects of eribulin which is mediated through stathmin dynamics in breast cancer cells.