

Abstract

Both p130Cas and PKN3 are important regulators of cellular signaling deregulation of which leads to malignant behavior of cancer cells. Recently we have found that SH3 domain of p130Cas mediates interaction with proline rich region of PKN3 suggesting their possible cooperation in regulation of these processes. In this work we have focused on the phosphorylation of p130Cas by PKN3 and identified serine 498 (S498) within the serine rich domain of p130Cas to be phosphorylated by PKN3 *in vitro*. Given that S498 is localized within the 14-3-3 binding motif and its phosphorylation is required for interaction of p130Cas with 14-3-3 proteins, we propose potential existence of novel PKN3/p130Cas/14-3-3 signaling axis. In the second part of the work we have studied this pathway in response to antiestrogen treatment in estrogen receptor positive breast cancer cell line MCF7. Although we have shown inactivation of PKN3 occurs as an early response to tamoxifen treatment, we do not rule out its possible role in further promotion of resistance to antiestrogens. Furthermore, understanding the signaling triggered by interaction of PKN3 with p130Cas and its possible downstream effects on promoting malignant growth of cancer cells would help in finding novel therapeutic targets.