ABSTRACT:

Summary. *Background*: Inorganic polyphosphate (polyP) elicits proinflammatory signaling responses in endothelial cells through interaction with two receptors, RAGE and $P2Y_1$. *Objectives*: The objective of this study is to understand the mechanism of polyP-mediated signaling pathway in breast cancer cells and to determine whether polyP exerts its proliferative and proinflammatory effect through activation of mTOR and Wnt pathways. *Methods*: mTOR activation by polyP in cellular model was monitored in the absence and presence of pharmacological inhibitors of specific signaling molecules. *Results*: PolyP effectively increases expression of cyclin D1, a key component of cell cycle regulation, at both mRNA and protein levels in simulated breast cancer cells by a Mtor- and Wnt/β-catenin-dependent mechanism. Moreover, using gel zymography, we showed that polyP significantly induced activation of matrix metalloproteases (MMP)-2 and 9 in MCF-7 cells. *Conclusions*: PolyP, through over-expression of cyclin D1 and activation of MMP-2 and -9 elicits proliferative and inflammatory signaling functions in breast cancer cells, respectively. These results clearly support the role of this molecule in the pathogenesis of breast cancer. Our findings suggest the clinical significance of administration of polyP inhibitors, alone or in combination with standard regimen, as a novel therapeutic approach in treatment of patients suffering breast cancer.

Keywords: Polyphosphate, mTOR, Wnt/ β-catenin, Breast cancer