ATP is a powerful signaling molecule that, acting through membrane bound P2 receptors, modulates important cellular functions of different cellular types. In the present work we investigated ATP modulation of intracellular calcium concentration ($[Ca^{2+}]_i$), mitogen-activated protein kinases (MAPKs) and phosphatidyl inositol 3 kinase/Akt (PI3K/Akt) signaling pathways and their relationship in MCF-7 breast cancer cells. The results show that ATP increases $[Ca^{2+}]_i$ due to cation release from IP_3-sensitive intracellular stores involving phospholipase C (PLC) activation. In addition, we observed a transient calcium influx sensitive to gadolinium and lanthanum, induced by the addition of vehicle after purinergic activation, named stress activated calcium influx (SAC influx).

ATP stimulated the phosphorylation of the MAPKs ERK1/2, p38 and p46 JNK in a time and dose dependent manner, and also induced the phosphorylation of p54 JNK with a different profile when compared with other members of this family of kinases. The phosphorylation of MAPKs by ATP was dependent both on the PI-PLC/IP_3/Ca^{2+} pathway and protein kinase C (PKC) but independent of Src kinase and of calcium influx from extracellular space. In addition, ATP induced the expression of the transcription factor c-Fos and the phosphorylation of ATF1, c-Jun and JunD transcription factors in MCF-7 cells. The participation of the MAPKs in c-Fos induction and in c-Jun and JunD phosphorylation by ATP was established.

Moreover, ATP induced the phosphorylation, in a PKC dependent manner, of Src at its tyrosine 416 and of Akt at serine. Opposite to what we previously saw for MAPKs, Src participated in the phosphorylation of Akt by ATP. Accordingly, PI3K participated in the phosphorylation of Akt but not in the phosphorylation of MAPKs by ATP.

Pharmacological characterization by the use of different purinergic agonists together with RT-PCR studies supported the expression of $P2Y_2$ and $P2Y_4$ receptor subtypes. The results presented here help to understand the mechanisms and signal transduction pathways activated by extracellular nucleotides, particularly ATP, in breast tumor cells.