GENE EXPRESSION MODULATE BY NUCLEAR CALCIUM

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Many hormones, growth factors and cytokines regulate cell proliferation through transient Ca^{2+} increases. Since many of these cascades promote Ca^{2+} signals within the nucleus we used a protocol of Rapid Subtraction Hybridization (RaSH) to investigate the influence of nuclear calcium on the expression of genes involved in the regulation of cell proliferation. An adenoviral construct containing parvalbumin, a Ca^{2+} buffering protein, fusioned to a nuclear localization sequence was used to buffer Ca^{2+} specifically in the nucleus. Another construct containing a parvalbumin mutated in two of its calcium binding sites was used as a control. This procedure allowed for the selection of genes which are specifically altered by small alterations on nuclear calcium concentration. RaSH identified that higher calcium concentrations induce the expression of the legumain gene. This gene encodes an endopeptidase highly expressed in several types of solids tumors. This protein facilitates the establishment of metastasis by elevating the migratory and invasive capacity of the tumor. Lower nuclear calcium concentrations induced the expression of the gene ARID 1A which belongs to a DNA binding protein family and is involved in diverse cellular events such as cell growth, differentiation and development. The results of the present expression analysis suggest that nuclear calcium have an important role on regulating genes involved in cellular proliferation.