FGF2 TRIGGERS RHO-A-MEDIATED-SENESCENCE IN RAS-TRANSFORMED MOUSE TUMOR CELL LINES.

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FGF2 (Fibroblast Growth Factor 2) is considered potentially oncogenic for being both mitogenic and angiogenic. However, the specialized literature contains contradictory data on this subject that remains unsolved. Recently, we have reported that FGF2 stimulates quasi-physiological cell proliferation, but blocks malignant growth. Thus, recombinant-FGF2(18kDa) triggers senescence in mouse Y1 adrenocortical tumor cells (bearing K-Ras-GTP high levels) and H-rasV12-transformed Balb3T3 fibroblasts, restraining cell proliferation in culture and tumor growth in Balb/c-Nude mice. This FGF2-triggered senescence is dependent on RhoA activity, but not on Rock-kinase. On the other hand, proliferation of parental immortalized Balb3T3 fibroblasts and of Y1 adrenocortical cells, with enforced low levels of K-Ras-GTP, is stimulated by FGF2. In conclusion, our results show that FGF2 can evoke previously unsuspected mechanisms to initiate senescence in Ras-transformed malignant cells, but not in immortalized non tumorigenic cells. This surprising phenomenon characterizes a FGF2-stress response that could be harnessed to curb resistance of malignant cells to programmed cell death.

Key words: FGF2-triggered senescence; Ras-transformed tumor cells.

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