The Notch ligand DLL1 exerts pro-carcinogenic effects in human breast cancer luminal A MCF-7 cells

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Background: Breast cancer (BC) is the most common cancer in women and has a high rate of relapse and death. The Notch signaling pathway plays an important role in normal breast development and homeostasis. Dysregulation of Notch receptors and its ligands Jagged1, Jagged2, and DLL4 has been detected in BC and implicated in tumor development, progression, drug resistance, and recurrence. The Notch ligand DLL1 has emerged as a player in BC as its expression is undetectable in normal breast tissues, but moderate to high in BC. In this study, we examined the role of DLL1 in BC luminal A MCF-7 cells. Methodology: DLL1 siRNA and recombinant DLL1 protein were used to evaluate the effects of DLL1 in MCF-7 cells. Gene expression was analyzed by qRT-PCR and immunobloting. Cell growth and proliferation were assessed by trypan blue exclusion and the MTT methods. Microscopy and scratch wound-healing assays were used to evaluate colony formation and cell migration. Findings: In MCF-7 cells, DLL1 downregulation reduced proliferation, colony formation efficiency, and migration. On the other hand, treatment with recombinant DLL1, which activates the Notch signaling pathway, increased MCF-7 cell proliferation and migration, confirming that DLL1 contributes to these processes in these luminal A BC cells. Conclusion: These findings provide evidence that DLL1 contributes to the pro-carcinogenic effects of luminal A MCF-7 cells by promoting clonogenic growth, cell proliferation, and migration.

Biography

Gabriela Silva holds a PhD in Biology from the Instituto de Biologia Experimental e Tecnológica, Portugal. From 2002 to 2008 she worked as Post-Doctoral fellow in the Instituto Gulbenkian de Ciência, Portugal, on projects that contributed to the understanding how HO1-1 protein affords cytoprotective and anti-inflammatory effects in various diseases. After that, she developed research in cancer. First on the role of HDAC inhibitors on hematologic malignancies and then on the mechanisms by which p16 protein exerts anti-oncogenic effects in osteosarcoma and on the mechanisms underlying the stromal fibroblast transformation in breast cancer. Since 2014, she has been a scientist at Instituto de Biologia Experimental e Tecnológica, Portugal, where she works on projects in the fields of biopharmaceutical process development and oncology. Her main scientific interests relate to the mechanisms underlying cancer development and therapy.

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