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SF1, a Standardised Fraction from Clinacanthus nutans Modulates Notch1 Signalling in Cervical Cancer Stem-Like Cells

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Abstract Background: Aberrant activation of Notch1 signalling in Cervical Cancer Stem Cells (CCSCs) plays a key role in the disease development, progression, metastasis, recurrence, and chemoresistance. Thus, targeting Notch1 is crucial for CCSC eradication. SF1, a standardised fraction from Clinacanthus nutans (C. nutans), has shown potent cytotoxic effects against cervical cancer cells, including CCSCs. However, its mechanism is uncertain.

This study aimed to elucidate whether SF1 can inhibit Notch1 signalling in CCSCs. Methods: SF1 was isolated from *C. nutans* leaves using a bioassay-guided fractionation. For CCSC enrichment, the human cervical cancer cell line SiHa was grown as non-adherent cells in stem cell-conditioned media (cervospheres) and characterised using sphere formation assay and flow cytometric analysis of stemness markers CD49f, CK17, Sox2, Nanog, and Oct4. The cells were then subjected to SF1 treatment, and Notch1 activity was examined using Western blot and quantitative RT-PCR. Results: The study discovered that SiHa cervospheres were efficient at forming spheres and contained more Sox2-and Nanog-positive cells than SiHa monolayers. In addition, cervospheres exhibited elevated Notch1 activity, with higher levels of the active Notch1 intracellular domain (NICD) protein and Notch1 mRNA than their monolayer counterparts. Following SF1 treatment, NICD protein levels in the cervospheres were significantly reduced, while Notch1 mRNA levels increased. These findings indicate that SF1 modulates Notch1 signalling at the post-transcriptional or post-translational level. However, the precise mechanism remains to be elucidated. Conclusion: SF1 possesses antitumor effects against SiHa-derived CCSCs via modulation of Notch1-signalling, a pathway associated with Cancer Stem Cells stemness.

Keywords

Author Keywords: Clinacanthus nutans; cancer stem cells; cervical cancer; Notch1 signalling; stemness

Keywords Plus: UP-REGULATION; EXPRESSION; PROGRESSION; ACTIVATION; RESISTANCE

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