

# The Roles of Activin-A and Its Antagonists in Early and Late Stages of Colon Cancer: In vitro Study

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Colorectal cancer (CRC) is the third most common malignancy worldwide and is associated with a high rate of treatment failure. Although Activin-A and its antagonist Follistatin expressions in CRC were stage-dependent, there is a gap in understanding the roles of these proteins in CRC biology. This study aimed to measure effects of Activin-A at 100 ng and /or different concentrations of Follistatin at 25, 50, 100 and 200 ng single and combined novel treatments. This was accomplished on cell cycle progression and apoptosis in the SW480 and SW620 CRC cell lines, representing early and late malignancy stages, respectively. Cell cycle and apoptosis were assessed following the different treatments,  $n = 3$ , by a flow cytometry, western blot was used measure the protein expression of apoptosis and necroptosis markers (Casp-3, MLKL), followed by ANOVA or Kruskal-Wallis tests for data analysis. Both Activin-A and Follistatin at 100ng increased SW480 cell numbers in Sub-G1 phase, 7% for both;  $p < 0.05$ . Follistatin at 200 ng showed the maximal increase in cell apoptosis,  $p < 0.05$ . Both Activin-A and Follistatin increased the expression of Casp-3. In contrast, Follistatin at 200ng disclosed the highest increase in the SW620 cell counts in Sub-G1 phase, as well as cell death, at 10%, but was associated with increasing the expression of MLKL compared to the untreated cells. These findings provided evidence that both proteins had an effective impact on CRC cells, suggesting that they could represent a potential therapeutic target and/or develop new therapeutic approaches by modifying their concentrations.