New Potential Therapy for Ovarian Cancer: Stearoyl-CoA Desaturase-1 (SCD1) Inhibition with the Novel Compound SSI-4

Chehade, Yara (School: Allen D. Nease High School)

Purpose: The experiment identified Stearoyl-CoA desaturase 1 (SCD1) as a novel molecular target in Serous Ovarian Carcinoma determined the potential of SSI-4, an SCD1 inhibitor, as a novel molecular inhibitor. SCD1 catalyzes a double bond in the cis-delta-9 position of saturated fatty acids transforming them into monounsaturated fatty acids promoting membrane synthesis and cell proliferation. Following determination of specificity and efficacy of SSI-4, cell death mechanism was examined through protein analysis. Experimental Design: Four Serous Ovarian cell lines were examined for SCD1 expression through Western Blot. Specificity of SSI-4 was determined through the rescue of the phenotype (Oleic acid) after SSI-4 treatment. Efficacy was determined through proliferation assays. Finally, the apoptotic mechanism of cell death was examined through Western Blots. Results: These studies identify SCD1 expression in all four lines tested. The phenotypic rescue of SSI-4 treated drugs concludes that SSI-4 is specific to SCD1 and anti-proliferative results are not due to off target effects. The proliferation assay of various SSI-4 concentrations concluded SSI-4 treatment results in a dose-dependent decrease in cell proliferation. Protein analysis detected Endoplasmic reticulum stress binding immunoglobulin protein, as well as apoptosis proteins Survivin and Cleaved Caspase 3. Conclusion: SCD1 expression coupled with promising dose-dependency and specificity of SSI-4 in vitro indicates the drug's therapeutic potential as a small molecule inhibitor in Serous Ovarian Carcinoma. Protein analysis implicates apoptosis as the primary mechanism of cell death. As a small molecule inhibitor, SSI-4 could be used independently and alongside platinum and or taxol therapies currently in use.

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