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**Evaluation of a protein synthesis inhibitor for the treatment of nasopharyngeal cancer**

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**ABSTRACT**

There is an exceptionally high incidence rate of nasopharyngeal cancer (NPC) in the East Malaysian state of Sarawak, particularly in the Bidayuh ethnic community. Therefore, we decided to evaluate the role of silvestrol, a novel anti-cancer agent isolated from a species called Aglaia stellatopilosa endemic to Borneo, for the treatment of NPC. The molecular mechanism of NPC cell inhibition by silvestrol was investigated as a single agent and with a potent RNA Pol I inhibitor. The growth kinetics of NPC cells were dynamically monitored using a real–time impedance–based cell analyser; whereas dose–response profiles were generated using a colorimetric cell viability assay. Biological activities were studied via flow cytometry and Western Blot. Results suggest silvestrol mediated inhibition of NPC cell proliferation and there was a very strong synergistic interaction between silvestrol and an RNA Pol I inhibitor. Flow cytometry revealed that different cell lines differ in their sensitivity and responses to silvestrol for cell cycle perturbation. Western Blot showed that silvestrol alone or with an RNA Pol I inhibitor was able to partially or completely inhibit the synthesis of pro-oncogenic or pro-survival proteins. Interference in the expression of these proteins can disrupt indispensable processes upon which cancer cells have become dependent. Given that cancer cells are very sensitive to reductions in these proteins, a therapeutic window exists for silvestrol as an inhibitor of protein synthesis in conjunction with other agents that target the protein synthesis pathway.