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Inhibitory effect of anti-HSV drug Acyclovir on cultured human cancer cells: A drug repurposing approach

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Drug repositioning has been growing in importance in the last few years as an increasing number of drug development and pharmaceutical companies see their drug pipelines drying up and realize that many previously promising technologies have failed to deliver as advertised. Current cancer therapy includes the use of chemotherapeutic agents, surgery and radiation therapy. It is estimated that four types of viruses [Human Papillomavirus (HPV), Hepatitis B (HBV), Hepatitis C (HCV) and Epstein-Barr virus (EBV)] alone could cause 12% of cancer cases worldwide. Investigation of the virus associated cancer serves as a unique platform for the development of novel strategies to prevent the development of infection that can predispose tumorigenesis. Studies on anti-viral drug treatments demonstrate promising results on the prognosis through the prevention of carcinogenesis. This concept triggered the idea of repurposing the antiviral drug Acyclovir (ACV) for breast carcinoma. The objective of the study was to repurpose Acyclovir by evaluating its morphometric, cell cycle arrest and migratory features on the breast cancer cell lines. The cytotoxicity studies were carried out with Acyclovir, Cisplatin and combination of Acyclovir+Cisplatin. The MTT assay results indicated the promising activity of the drugs/combinations tested against MCF-7 and MDAMB-231 cell lines. The Acyclovir showed IC50 of 3.16±1.10 µg/ml and 3.85±1.54 µg/ml, respectively with selectivity index of 33.46 and 27.46. To confirm the ability of the single cell to grow into a colony the clonogenic assay was performed. The platting efficiency was found to be 52.30% and the Survival Fraction (SF) in cells treated with drug at lowest concentration (0.25 µg/ml) was 1.31%. This indicates the potential anti-metastatic effect of the Acyclovir. The advanced studies like DNA fragmentation and cell cycle analysis were carried out. The accumulation of cells in at G2/M phase is an indication of cell death by apoptosis. To conclude, we present evidence that ACV has an anti-cancer effect on breast cancer cell line. The study shows that ACV was able to inhibit cancer cells proliferation, colony formation ability and cell cycle arrest at G2/M phase, while having no effect on the normal cells. These results provide new insights on the effect of antiviral agents on the tumorigenesis and metastasis. However, more research is necessary to identify the primary target of Acyclovir and maximize its potential as cancer drug.

Biography

Dr. Ashish Wadhwani completed his Ph.D from JSS University, Mysuru during 2010-2013. He worked as CSIR- Senior Research Fellow, Govt. of India (GoI). He was associated with National AIDS Research Institute (A unit of ICMR), Pune for his Post Doc joint proposal for HIV/AIDS and microbicides project. Dr. Wadhwani presented his research findings and won several awards at International conferences at Amsterdam, Malaysia, and USA, sponsored by Government National & International agencies. He has 23 research papers, one chapter in a book and two ongoing projects from GoI to his credit. He is former DST-IRF and QoL-Member of the Kyushu University, Japan, Technical Expert for Molecular Diagnostic Unit of National Institute of Biologicals, GoI, Member of Antimicrobial Resistance committee for drafting antibiotics policy for Pharmacy Council of India and Mentor of Change by ATL an initiative of GoI. Recently He received "Antiviral-Research-Fellow-2017" Award by Antiviral Research Society, India.

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