

## **NOVEL VIRTUAL PATIENT TECHNOLOGY FOR PERSONALIZING SINGLE-AGENT AND COMBINATION THERAPIES OF CHEMOTHERAPEUTIC AND TARGETED DRUGS: VALIDATION IN XENOGRAFTED BIOPSIES OF A MESENCHYMAL CHONDROSARCOMA PATIENT**

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**Introduction:** Lack of tools for predicting response of individual patients to pharmacotherapy is a significant impediment to providing improved, personalized medical treatments. The Virtual Patient (VP) is a predictive biosimulation technology, comprising computer-implemented mathematical algorithms of key physiological, pathological and pharmacological processes in the body of the patient. Calibrated with available patient-specific data, the VP can accurately retrieve preclinical and clinical reality and predict short- and long-term drug *in vivo* effects. **Materials & Methods:** Growth curves of untreated human tumor xenografts, derived from a lung metastasis of a mesenchymal chondrosarcoma (MCS) patient and histopathological results of this metastasis, were used to calibrate the VP's solid tumor model. Published data were used to model PK/PD of three targeted therapies (Bevacizumab, Sunitinib, Sorafenib), as well as PK of four chemotherapeutic drugs (Docetaxel, Gemcitabine, Doxorubicin and Irinotecan) in mice. In vitro proliferation assays of the patient's tumor cells were employed for establishing patient-specific concentration-effect curves for the chemotherapeutics. The virtual drugs were then 'administered' to the virtual MCS xenograft as single-agents and in combinations, and short-term tumor growth dynamics were simulated under different regimens. Results were compared to corresponding experimental growth curves of treated and untreated tumors for evaluating prediction accuracy. **Results:** Predictions indicate several therapies, namely, Bevacizumab +Docetaxel combination, Sunitinib, to be significantly superior to others, notably Gemcitabine, in the MCS patient's xenografts. Over the simulated treatment period of up to 41 days, combinations with Bevacizumab are predicted to greatly enhance the treatment efficacy in comparison to the corresponding monotherapies. The average accuracy of the VCP's predictions is 82%. **Conclusions:** The Virtual Cancer Patient's showed high precision in predicting the growth pattern and response of xenografted MCS patient's tumor cells to various mono- or combination therapies. Our results suggest that treatments involving anti-angiogenic drugs greatly improve this patient's tumor growth inhibition. These results support the use of the Virtual Cancer Patient as a powerful tool for personalizing patients' treatment, especially when the application of new drugs is anticipated or when treatment of patients with rare diseases is considered.