Exploring Melanoma Dynamics: Insights from a 3D Cell Culture Model with Vemurafenib Treatment

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Background and aim
Malignant melanoma represents a difficult challenge in oncology due to its high mortality rates and frequent development of treatment resistance mechanisms. Phenotype switching, a recognized phenomenon in melanoma cells wherein they transition from a highly proliferative/low invasive state to a low proliferative/highly invasive state, is implicated in the development of treatment resistance. To enhance our comprehension of this dynamic process, elucidating the underlying mechanisms is imperative to identify optimal therapeutic targets for novel treatments.

Despite the necessity for effective treatments, the use of animal models in drug development is hindered by time constraints, high costs, and ethical considerations, underscoring the urgency for improved in vitro models. Utilizing 3D human tissue models presents a promising avenue to address these challenges, offering cost-effective and expedited experimentation while closely mimicking human physiology. Therefore, improving 3D in vitro human tissue models is pivotal in drug development and biomedical research in general.

For these models to be suitable for preclinical studies, it is important to thoroughly characterize and recognize their restrictions and applicability. Our study aims to establish a simple yet robust 3D melanoma model and employ multiple assays to investigate the dynamics of melanoma spheroids, facilitating their utility as a platform for drug screening, notably utilizing the MAPK inhibitor, vemurafenib, a key agent in melanoma therapy.

Methods
A viability assay and migration assay were performed on spheroids in suspension and spheroids in a collagen matrix, respectively, after 96-hour treatment with the MAPK inhibitor, vemurafenib. The viability assay was performed using a sensitive colorimetric assay, CCK-8. For the migration assay, images were obtained every 24 hours for a total of 96 hours, and the spheroid core and migrating cells were identified.
Volume measurements were performed in GFP-expressing human melanoma spheroids, after performing live-cell imaging of full thickness human melanoma skin models treated with vemurafenib for 72 hours, using confocal microscopy.

Results
Treatment with vemurafenib led to a significant reduction in spheroid viability and attenuated migration compared to untreated controls. Live cell imaging revealed a marked decrease in spheroid volume following 72-hour vemurafenib treatment

Conclusion
Our findings demonstrate the efficacy of vemurafenib treatment in 3D melanoma spheroids across multiple assays, highlighting the utility of this model in assessing diverse melanoma therapies.

Keywords:

Melanoma, cancer skin model,

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