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Anti-cancer Drug Screening of Dual Tubulin and Hsp27 Inhibitors with 2D and 3D Lung Cancer Cell Assays

Janine Maria Naim
Cleveland State University, J.NAIM@csuohio.edu

Rati Lama
Cleveland State University, R.LAMA71@csuohio.edu

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College of Sciences and Health Professions

Student Researchers: Janine M. Naim; Rati Lama

Faculty Advisor: Bin Su, Ph.D.

Abstract

Cancer is the leading cause of death worldwide. Metastatic lung cancer is the most common cancer among men and women in United States. National cancer society has estimated 1.6 million deaths and 2.2 million new cases of lung cancer in the United States in 2012. The current treatment options available for lung cancer are limited and have drawbacks such as poor bioavailability, numerous side effects, poor efficacy and drug resistance. Therefore, there is a need for development of new agents for anti-cancer therapy. Two-dimensional (2D) monolayer cell culture is most widely used for anti-cancer drug screening purposes. Three-dimensional (3D) cell culture models are symmetrical cellular aggregates that mimic *in vivo* tumor characteristics. It has been demonstrated that the 2D monolayer cell assay for drug screening is a very artificial model and cannot represent the characteristics of 3D solid tumors. The multi-cellular tumor 3D spheroid model is of intermediate complexity, and can provide a bridge to the gap between the complex in vivo tumors and simple in vitro monolayer cell cultures. A series of tubulin and Hsp27 dual inhibitors were developed in our research group, and have been preliminarily investigated for the anti carcinogenic activity with breast cancer cells. In the current project, the compounds were further screened with 2D monolayer lung cancer cell culture. Several compounds from the library were identified to have potent anti-tumorigenic activities. These compounds were tested on 3D lung cancer platform and the activities of the compounds on monolayer cell culture were compared with those in 3D tumor spheroids. Because of the pathophysiological resemblance of *in vitro* three-dimensional spheroids with tumors *in vivo*, the compounds with better activities in spheroid models can be expected to have better potency in animal models as well. Drug screening with 3D tumor spheroids eliminates the compounds that show artificial good potency in two-dimensional models. 3D model serve as a novel approach for drug screening purposes and the evaluation of compounds in the platform can help identify potent compounds for further *in vivo* xenograft studies.