

Three-dimensional *In Vitro* Models for Oral Cancer Research

Shankargouda Patil¹, Dominic Augustine², Roopa S Rao³

Contributors:

¹Associate Professor, College of Dentistry, Jazan University, Jazan, Saudi Arabia; ²Assistant Professor, Department of Oral and Maxillofacial Pathology, Faculty of Dental Sciences, MS Ramaiah University of Applied Sciences, Bengaluru, Karnataka, India; ³Professor and Head, Department of Oral and Maxillofacial Pathology, Faculty of Dental Sciences, MS Ramaiah University of Applied Sciences, Bengaluru, Karnataka, India.

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The oral cavity is the most predominant location in the head and neck region for primary malignant tumors. Oral cancers are the leading cause of morbidity and mortality among all cancers in India.

Cancer of the oral cavity is a major public health problem with approximately 300,000 new cases reported annually worldwide. Two-thirds of these occur in developing countries, the majority within the Indian subcontinent, where these account for up to 20% of all cancers. The majority present with locally advanced disease (Stage III and IV) with dismal 5-year survival rates of 20-50%. There are 145,000 deaths worldwide and 45,000 deaths in India a year.¹

The primary step in curbing the menace of progression and recurrence in oral cancer is research intended to understand genetic, epigenetic and cellular pathways, tumor transcriptional profiling, DNA methylation patterns, and anti-cancer drug trials.

Cancer researchers rely on the use of paraffin-embedded tissue samples, fresh specimens, cell lines, cell cultures of primary tumors and/or genetically engineered mice. Each of these models is used for diverse studies depending on research requirement like drug trial or genetic analysis since all studies are not feasible to perform in animals.²

Cell lines emerge as reliable alternatives to overcome these issues, being at the same time easy to manipulate and molecularly characterize.³

However, a major drawback is the lack of tumor microenvironment which can be recreated using three-dimensional (3D) models. 3D *in vitro* models help to understand the influence of the microenvironment on cellular proliferation, differentiation, gene expression, and apoptosis. Due to this promising potential 3D cultures are currently being adopted by a plethora of biomedical agencies with therapeutically orientated studies being the major focus of research.⁴

Lab animals such as transgenic/knockout mice have been used with appreciable success for cancer research. The hamster cheek pouch model is considered as an ideal model for oral cancer because of its tolerance.

However, major hurdles exist in India pertaining to use of animal models. Animal lab facilities in institutions are a challenge to maintain, and high costs in private laboratories to carry out animal experiments are a hindrance to research. Hence, 3D *in vitro* models can be used as suitable alternatives.

With the increasingly recognized fact that tissue microenvironment plays an important role in regulation of normal cell function, researchers need to develop models to understand genetic and biochemical clues provided by the tissue microenvironment that plays a critical role in suppression of tumorigenic phenotypes.⁵

A well-defined 3D *in vitro* cancer model mimics tumor structures closely found *in vivo* and allows for cell-matrix and cell-cell interactions has gained strong interest for a wide variety of diagnostic applications. It offers a promising insight for oral cancer research.

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