

# The advantages and applications of 3D cell cultures

Dr. Maddaly Ravi<sup>1</sup>

<sup>1</sup>Backstories

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Maddaly Ravi

Professor, Department of Human Genetics, Sri Ramachandra Medical College and Research Institute, Porur, Chennai, India.

This back-story is about the paper published in Journal of Cellular Physiology titled “3D cell culture systems: Advantages and applications” whose citation is as follows:

Maddaly Ravi, V. Paramesh, S.R. Kaviya, E. Anuradha, and F.D. Paul Solomon. 3D Cell Culture Systems: Advantages and Applications J. Cell. Physiol. 230: 16–26, 2014.

Cell cultures are important material of study for the variety of advantages that they offer. Both established continuous cell lines and primary cell cultures continue to be invaluable for basic research and for direct applications. Technological advancements are necessary to address emerging complex challenges and the way cells are cultured in vitro is an area of intense activity. An important advancement in cell culture techniques has been the introduction of three dimensional culture systems. This area is one of the fastest growing experimental approaches in life sciences. Augmented with advancements in cell imaging and analytical systems, as well as the applications of new scaffolds and matrices, cells have been increasingly grown as three dimensional models. Such cultures have proven to be closer to in vivo natural systems, thus proving to be useful material for many applications.

Cell lines, especially cancer cell lines, have contributed immensely in understanding the complex physiology of cancers. They are excellent material for studies as they offer homogenous samples without individual variations and can be utilised with ease and flexibility. Also, the number of assays and end-points one can study is almost limitless; with the advantage of improvising, modifying or altering several variables and methods. Literally, a new dimension to cancer research has been achieved by the advent of 3-Dimensional (3D) cell culture techniques. This approach increased many folds the ways in which cancer cell lines can be utilised for understanding complex cancer biology. 3D cell culture techniques are now the preferred way of using cancer cell lines to bridge the gap between the ‘absolute in vitro’ and ‘true in vivo’ and we continue our work using such in vitro models. The aspects of cancer biology that 3D cell culture systems have contributed include morphology, microenvironment, gene and protein expression, invasion/migration/metastasis, angiogenesis, tumour metabolism and drug discovery, testing chemotherapeutic agents, adaptive responses and cancer stem cells.

Our MSc in Human Genetics program includes a dissertation project component which the students pursue in their final semester of their 4-semester course. As a faculty member, I had 2 students assigned to me (the authors of the paper in discussion, Ms. S.R. Kaviya and Mr. V. Paramesh) and my role was to be their dissertation project mentor and guide. As was my field of interest, I chose to work with 3D cultures with the two students assigned. This time again, as how I always approached (and continue to approach) student projects, one of the first steps would be to make them understand the requirement for a thorough review

of literature before working on a project. Apart from making them understand the significance of thorough review of the available literature, I also emphasize on the importance of scientific manuscript writing and the manner in which manuscripts can be well prepared. Also, one of our research scholars Ms. E. Anuradha was working on designing scaffolds for tissue engineering applications at that time and was taken on board for the review along with our Head of the Department Prof. Solomon F.D. Paul.

Thus, the back story of the publication “3D cell culture systems: Advantages and applications” began and we set out to initially arrive at the components of the review; the aspects we wanted to cover in the review. Once we had the review outline frozen, we started off on collecting the literature available from all possible sources (the primary, secondary and the tertiary) and analyzing/collating the details. The details were filled into the components framework that we decided for the review manuscript and we could complete the “sections” of the manuscript.

After several revisions and editing, the net result was the comprehensive review on the advantages and applications of 3D cultures for studies involving differentiation, drug discovery for pharmacological applications, as tumor models for cancer research, for gene & protein expressions, for cell proliferation & cell-cycle analysis, for studies involving cytoskeleton, apoptosis, cell adhesion, cell signalling, cell motility, microenvironment, cell morphology, tissue architecture, drug response, and cell behaviour as co-cultures as the major components. Also, the various matrices and scaffolds used for 3D cultures were presented as a Table which gives the classification, properties, salient features, and the specific appropriate applications of the matrices and scaffolds.

We were happy that the manuscript took a good shape and turned out as one which deals comprehensively in this exciting area of science. All authors contributed equally for all aspects of manuscript preparation and submission. Ms. Kaviya’s contribution for the formatting, and the post-acceptance processes such as Galley proof corrections were exemplary as with Ms. Anuradha’s contribution to the Table on scaffolds and matrices. We thank the editors, the reviewers and the editorial/production team of Journal of Cellular Physiology for the entire process that happened from the manuscript submission till its acceptance and finally, the publication of the manuscript. We are also happy that the review continues to be among the top “most accessed” papers of the journal from the time it was published on-line. The review has obtained 106 citations till date (6th December 2017) in a little more than 2 years of its publication.

Now, the two PG students are well placed as research scholars and the research scholar Ms. E. Anuradha had obtained her Doctorate and is currently pursuing her post-doctoral career. Looking back at the story beginning, it sure gives a good feel that 2 MSc students could author a publication which was (and is) well received and they gained a firm footing/understanding of the steps involved in research methodology. Well, the three of us could author one more paper, this time, an original research paper titled “Culture phases, cytotoxicity and protein expressions of agarose hydrogel induced Sp2/0, A549, MCF-7 cell line 3D cultures” published in the Journal ‘Cytotechnology’ (Cytotechnology (2016) 68:429–441; DOI 10.1007/s10616-014-9795-z). The thorough review of literature sure helped us in what went into obtaining a second publication with the 2 students as co-authors.

The story is still on and I do continue to work with 3D cultures of cancer cell lines and I hope to contribute my miniscule bit to this area of science, in whatever way I possibly can.