Preface

Understanding basic cellular biology relies on research involving cell-based *in vitro* assays that are also used to model disease, test and screen compounds and assess the safety of chemicals. Most often, the investigation of such biological processes is based on studying homogeneous populations of mammalian cells cultured as monolayers on flat, two-dimensional (2D) polystyrene substrates. However, cells naturally exist within a complex three-dimensional (3D) tissue microenvironment composed of mixed cell populations, extracellular proteins and both physical and chemical signals from multiple sources.

It should be recognised that many important discoveries have been made from conventional 2D culture approaches. This reductionist view to understanding basic biological processes has value but is limited since cells growing on 2D substrates do not always reflect the true physiological behaviour of their native counterparts in real tissues. When forced to grow on a flat 2D substrate, cells adapt and radically change their shape, proliferate in an aberrant fashion and often lose their differentiated phenotype, resulting in abnormal cellular behaviour. It is widely appreciated that such structural modifications to the physical environment can result in changes to gene transcription and protein translation, remodelling of the cytoskeleton and irregular cell signaling.

Accordingly, the anatomy of a cell, i.e. its structure and form, are inextricably linked to its physiological function. Technologies are now becoming available that enable researchers to culture cells in 3D that in turn enhance the value of such cell-based assays and the generation of more accurate and physiologically relevant results. The growth of tissue-like structures in 3D in combination with media perfusion/circulation creates a dynamic system which advances cell-based models still further towards the recreation of more '*in vivo*-like' conditions.

Maintaining the natural 3D architecture of a cell is therefore considered one of the fundamental steps toward enhancing the value of cell-based assays. There are now several technologies available that promote solutions for 3D cell culture. In general, these fall into one of three categories: hydrogels (e.g. Matrigel™, collagen gels); cell aggregates (e.g. hanging drop methods, low adherence plates); and scaffolds (e.g. porous physical supports). There is no panacea and no one solution is suitable for all 3D culture needs. The availability of these technologies from commercial sources now allows the investigator to select the most appropriate method suitable for their experimental requirements. Moreover, 3D cell culture technology is often combined with new developments in dynamic media

perfusion, to further enhance cell growth and physiological relevance of the model. There are numerous advanced technologies that enable media perfusion encompassing cleverly designed devices and mini-benchtop bioreactors.

The aim of this text is provide the reader with a review of the types of technology available and examples of where such methods may be applied. This has been divided into descriptions of 3D cell culture technologies by certain commercial developers representative of these key areas and the users of such methods. The reader will learn about the options available to perform 3D culture, explore the options for media perfusion, from where such 3D technologies can be acquired, how they work and how they can be used. Any cell biologist considering 3D cell culture and aiming to enhance the physiological relevance of their cell-based assay should consult this text as a guide to getting started with such methods.

Key features

- A review of the current state-of-the-art technologies available for 3D cell culture and media perfusion models.
- Contributions from leading developers and researchers active in 3D cell technology and advanced cell-based assays.
- Instruction and guidance on performing specific 3D culture methods and media circulation systems.
- Examples of where such technologies have been successfully applied.
- Guidance on resources and technical support to help get started using 3D culture methods with options of dynamic media circulation.
- Relevance to multiple fields including stem cells, tissue engineering, cell-based screening assays, etc.
- Examples of advanced physiologically relevant *in vitro* models, including use of 3D culture and perfusion technology, organotypic models, co-cultures, etc.

Primary readership

Interest in 3D cell culture and the ability to create more tissue-like constructs are developing rapidly in the scientific community. Researchers recognise its value and are keen to apply such technology to their experimental systems. This book will be especially topical given the drive to improve the value of *in vitro* cell-based assays and generate more physiologically relevant data. A quick scan of the scientific literature will indicate that interest in this sector is developing rapidly. While many different approaches that enable 3D culture have been developed, most are based on research in academic labs and are published in scientific journals. While of value, they are not always technologies readily available to the majority of investigators interested in 3D cell culture. Several approaches to culture cells in 3D have now been commercialised. Numerous

small and large companies have undertaken the process of translating research into the creation of marketable products. These organisations are the pioneers of a new era in cell culture methods and have made such technology available to the greater scientific community through the development of bespoke products and applications. This was not possible until now and the time is right for this book to bring together the different approaches that are readily available and to support this rapidly growing sector of 3D cell culture.

Any cell biologist practising conventional 2D cell culture will be interested in this book as an opportunity to enhance the value of their cell-based assays and perform 3D culture methods. Specific sectors of interest include cancer cell biology, stem cells, tissue engineering, *in vitro* alternatives to animal use, liver toxicology, neuroscience and those requiring specialised cell culture models (e.g. co-culture, organotypic models). Cell culture as a technique is very general and is performed in academic, industrial and government laboratories worldwide. It is anticipated that many will benefit from this text as a comprehensive guide to technologies that are readily available, to act as a reference and assist in the selection of technology and guidance for use. Therefore the primary readership will be the practising bench scientists (postgraduate and postdoctoral students, research fellows, research scientists and the like). The secondary readership may be managers of cell culture facilities/departments, R&D heads of section, technical supervisors, advisors, etc. who would recommend methods to perform. Fringe interests include parties interested in cell biology in general and methods associated with the field.

The pharmaceutical industry is particularly interested in developing new approaches to enhance its ability to discover new compounds and has identified 3D culture as a priority area. Similarly, contract research organisations are now using 3D culture methods to provide additional information to their clients. Collectively, these are substantial opportunities. Societies interested in alternatives to animal research, cell biology, tissue engineering, cancer biology, etc. should all find this text of value.

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