Introduction

Validation of cell lines

Otto-Wilhelm Merten & Ian Freshney

There are two reactions when one introduces the topic of cell line validation, one from industrial and commercial enterprises, who accept, with resignation, that they must take this into account, and one from the academic field, where, by and large, the reaction is that the topic is too pedantic, and serious consideration of the problems is placed on the “to do” list a long way below writing the next paper or grant application. The purpose of this collection of papers is to underline that, regardless of location, anyone involved in cell culture must take seriously the words of caution that they contain.

Consider as an analogy, three climbers tackling a steep rocky ascent. Climber A looks carefully at all the approaching problems and decides that the climb is too risky and should not be attempted. Climber B looks quickly at the ascent, sees no problems, and scales up the face rapidly without any precautions, only to peel off two thirds of the way up. Climber C assesses the difficulties of the climb, picks equipment and route carefully, and completes the ascent. For anyone who does not see the analogy, A is overwhelmed by the potential problems of maintaining safe aseptic technique, monitoring for mycoplasma and viral contamination, and authenticating the origin of the cells in use, and feels that the using animals might be simpler (forgetting that this would increase the validation problems by an order of magnitude). B feels that the problems are trivial and that such validation procedures are for the more prosaic and not compatible with cutting edge research. B would not be the first scientist to be impaled on this cutting edge! C appreciates the potential problems, but realises that the technology is available to handle them, either in house, or by contracting out, and that a more valid and sustainable result will be obtained if a few simple precautions are observed.

In an attempt to help address the problems facing cell culturists in assessing and tackling problems of cell line validation, a symposium was held within the ETCS 43rd International Meeting, held in Granada, Spain, in September, 2001. A short list of speakers was enlisted to deal with the topics of mycoplasma and viral contamination, cross-contamination and authentication, and the more general aspects of cell line provenance. Although successful within the context of an excellent and well-attended meeting, it was felt that these topics deserved greater exposure. Accordingly, against the normal practice of ETCS meetings, it was decided to generate a publication from these invited presentations, supplemented with an additional paper on prion contamination.

The principles of good cell culture technique are similar to good laboratory practice, in that due care must be taken in ensuring that proper safety and aseptic procedures are observed. These topics are not dealt with here as they are already dealt with extensively elsewhere. For the same reason, the problem of overt contamination by micro-organisms is also not covered. The emphasis of this publication is on the more cryptic aspects of contamination, those that are not always obvious in routine examination of microscopic appearance or culture behaviour. The two keys are (1) proper sourcing of materials from reliable sources, and (2) routine diagnostic testing in spite of a consistently (you hope!) negative outcome.

It is hoped that these presentations will help readers to obtain a reasonable perspective of both the scale of the problems and of the solutions that are available. It is not meant as a practical manual, as most of the diagnostic procedures mentioned are available elsewhere and duly referenced, but more as an assessment of the current position and an alert to those actively involved in cell culture to take heed and apply both the requisite diagnostic techniques and precautionary measures. No validation means, both literally and scientifically, that any results that are obtained are invalid. Not to take heed is, at best, poor science, and, at worst, plain deceit.