

Review

Conventional and molecular cytogenetic diagnostic methods in stem cell research: A concise review

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Abstract

Regenerative medicine and cell therapy are emerging clinical disciplines in the field of stem cell biology. The most important sources for cell transplantation are human embryonic and adult stem cells. The future use of these human stem cell lines in humans requires a guarantee of exhaustive control with respect to quality control, safety and traceability. Genetic instability and chromosomal abnormalities represent a potential weakness in basic studies and future therapeutic applications based on these stem cell lines, and may explain, at least in part, their usual tumorigenic properties. So, the introduction of the cytogenetic programme in the determination of the chromosomal stability is a key point in the establishment of the stem cell lines. The aim of this review is to provide readers with an up-to-date overview of all the cytogenetic techniques, both conventional methods and molecular fluorescence methods, to be used in a stem cell bank or other stem cell research centres. Thus, it is crucial to optimize and validate their use in the determination of the chromosomal stability of these stem cell lines, and assess the advantages and limitations of these cutting-edge cytogenetic technologies.

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1. Introduction

Human adult and embryonic stem cells (hESC) in transplant programmes has supposed a considerable advance not only in regenerative medicine and cell therapy but also in basic biology. The potential therapeutic use of hESC derivatives requires guarantee of their quality, safety and traceability with the implementation of exhaustive quality control programmes. One of the main problems with stem cell lines of different source, mainly those of embryonic origin, is the possibility of chromosomal alterations and genomic instability which will explain, at least in part, their *in vivo* tumourigenic

potential (Ringden et al., 2003; Cowan et al., 2004; Draper et al., 2004; Menéndez et al., 2005a,b, 2006). Therefore, the introduction and the application of a strict cytogenetic programme is necessary. The study of processes such as cell-renewal, pluripotency, specific differentiation, undifferentiated associated markers, telomerase, mitochondrial, epigenetic and chromosomal stability must be considered and implemented in this emerging area of stem cell biology (Mandal et al., 2006).

The chromosomal stability in a cell line consists, mainly, of maintaining a normal karyotype both numerically and structurally, because hESC lines develop chromosomal aberrations after long-term culture indicating an unstable genomic status due to the *in vitro* culture after successive passages have been carried out (Maira et al., 2005; Calsander et al., 2006; Ludwig et al., 2006). Human ESCs may be prone to acquiring chromosomal anomalies while being cultured continuously *in*

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