Introduction

The promise of many cell-based regenerative medicine products is premised on the inherent biological properties of the cellular component, such as the high rates of proliferation, migratory ability, plasticity, and capacity for self-renewal of many types of cells. These same properties may also pose safety concerns, such as the potential for tumor formation following administration, which should be identified and minimized prior to first-in-human clinical testing. However, designing a preclinical testing program to evaluate the tumorigenic potential of cell-based regenerative medicine products can be challenging for several reasons, including: i) the heterogeneity and biological complexity of this product-class; (ii) the lack of a complete understanding of product attributes that are reliably predictive for tumorigenicity; and (iii) the difficulty of translating preclinical results to the clinical scenario.

Materials and Methods

In a continuing effort to maximize the safety of new therapies, ensure regulatory review practices continue to reflect the best available science and foster innovation by providing a more predictive and transparent regulatory pathway, FDA/CBER/OCTGT conducted a retrospective review of tumorigenicity studies for cell-based regenerative medicine products that were submitted between 2006-2011 as part of regulatory submissions. Data were analyzed to quantify product-specific risk factors and identify effective preclinical animal models, endpoints, and study designs for the evaluation of tumorigenicity.

Results

FDA/CBER/OCTGT received over 115 original regulatory submissions to initiate clinical investigations for cell-based regenerative medicine products during this time period. The cellular components of these products spanned a wide spectrum of cell types and tissue sources (Figure 1). The submissions contained studies that evaluated tumorigenic potential by direct testing of the product (in vitro or in vivo studies) (43%) or through consideration of product attributes, the scientific literature, and/or previous clinical experience (57%). Appropriate tumorigenicity study designs were product-specific and spanned a wide spectrum.

Discussion and Conclusions

The heterogeneity and biological complexity of cell-based products highlights the difficulty of developing and adopting a standardized, prescribed set of preclinical studies that are uniformly appropriate. Thus, a well-designed preclinical testing program is one that is: a) product and indication-specific; b) incorporates a tiered approach that is risk-based (as determined by comprehensive product characterization); and c) takes into account the limitations of both in vitro testing and available animal models. This presentation will explore the challenges to evaluating the tumorigenic potential of cell-based regenerative medicine products and identify important considerations for designing preclinical testing programs, including common approaches to optimize data interpretability.

Disclosures

The author has nothing to disclose.