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EDITORIAL

Highlight report: quality control of stem cell-derived hepatocytes

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Recently, Godoy et al. (2018) published a comprehensive review about state-of-the art techniques to assess the degree of differentiation of hepatocyte-like cells derived from stem and precursor cells. The authors critically discuss that several studies relied on few selected markers to conclude that stem cell-derived cells are similar to real hepatocytes. These studies have created the wrong impression that the generation of almost fully differentiated hepatocytes from precursors can be considered as accomplished. However, this optimistic point of view has also been critically discussed (Godoy et al. 2013; Brulport et al. 2007; Hengstler et al. 2005). Upon the application of Omics technologies it has become possible to quantify the degree of differentiation based on an unbiased genome-wide expression analysis that can be performed by RNA-seq or gene array (Godoy et al. 2015; Cameron et al. 2015). The authors recommend an analysis pipeline that is applicable for all types of stem cell-derived cells (Godoy et al. 2018). One advantage is that a cell identity score can be obtained that quantitatively expresses the degree of similarity of the stem cell-derived cells to the intended target cell. Another aspect is that the transcription factors responsible for differences can be identified, which may serve as a basis for interventions to improve differentiation.

An interesting conclusion from these analyses is that differentiation may not only be incomplete but also unwanted differentiation may occur (Godoy et al. 2018). An example is that differentiation protocols intended to generate hepatocytes also induced genes typically found in colon and not in liver. Such problems are typically ignored in studies that base their conclusions only on analysis of a set of markers or functional readouts.

Hepatocyte in vitro systems represent a well established tool in toxicology (Doll and Hein 2017; Starokozhko et al. 2017; Parmentier et al. 2017; Cipriano et al. 2017; Ghallab 2017; Ehrhardt and Schmicke 2016; Ramboer et al. 2015; Elberry et al. 2016; Reif et al. 2017; Deharde et al. 2016). However, the availability of human hepatocytes represents a limiting factor (Grinberg et al. 2014; Schmidt et al. 2017). Generation of an unlimited supply of hepatocytes from stem cells would be urgently required. Nevertheless recent genome-wide studies demonstrate that there is still a long way to go until stem cell-derived 'hepatocyte-like cells' really deserve this name.

Compliance with ethical standards

Conflict of interest The author declares that she has no conflict of interest.

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