Control differentiation of embryonic stem cell to specific lineages

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Most of applications of embryonic stem (ES) cells require directing differentiation of ES cells to defined cell types. This currently remains a challenge for stem cell biologists though efforts and progresses have been made. The most commonly used method for differentiating ES cells is by initiating the differentiation via embryoid body (EB) formation, which resembles to a certain degree the early embryo development *in vivo*. However, individual cells in the EBs receive variable autocrine and paracrine signals according to their location in the EBs as well as the size of the EBs, which subsequently can lead to different cell fates. As a result, the differentiated cells by this approach are often heterogenous, possibly containing all three germ layers. In addition, it is difficult to dissect signalling pathways required for certain cell type differentiation with this method. Therefore, recent progresses have been made to differentiate ES cells in adherent culture conditions in chemical-defined media, which resulted in more enriched populations of desired cell types. We have previously differentiated human embryonic stem cells (hESCs) to neural progenitors in adherent culture with chemical-defined medium by blocking BMP signalling pathway. In the current study, we established an approach to efficiently differentiate hESCs to definitive endoderm, then to the hepatocytes. The differentiation process of hESCs recapitulates the liver development *in vivo* and hESC-derived hepatocytes are able to carry out a range of hepatocyte functions, particularly expressing several members of cytochrome P450 isozymes which are capable of converting the substrates to metabolites. Our results have provide evidences that hESCs can be differentiated efficiently to certain cell lineages in a more defined, controllable conditions, which will be useful not only for biomedical and therapeutic applications but also for elucidating molecular mechanisms of early embryo development.

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at Imperial College London as a lecturer/principle investigator. The research interests of her laboratory are in the field of embryonic stem cell biology, particularly on directing differentiation of human embryonic stem cells to neural and hepatic cell fates. The overall goals of our researches are to understand how the proliferation, cell fate determination and differentiation of human embryonic stem cells are controlled.