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# Can a Cancer Cell Turn into a Normal Cell?

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HepG2 cells, a human liver cancer cell line (hepatocellular carcinoma), are being considered as a future model for bioartificial liver studies. They have the ability to differentiate and demonstrate some features of normal liver cells. Our previous studies focused on examination of the morphological and functional properties of these cells under different extracellular environmental conditions. We have created a culture model that these cells demonstrate remarkable changes after 30 days. These changes include an increase in the cytoplasmic organelles, formation of bile canaliculi, occurrence of junctional complexes between the adjacent cells, existence of microvilli on the apical surfaces, accumulation of glycogen particles in the cytoplasm, an increase at the density of albumin labeled areas and a rise at the Na-K ATPase level on cellular membranes. In addition to these changes, reproduction rate decreases which is another important difference between cancer cells and normal cells. All these changes demonstrate that these liver cancer cells have tendency to change their features and behave like "healthy-normal liver cells". In other words, they become "specialized" or "mature". These findings have made us think that if a cancer cell has ability to turn into a healthy cell again. The next step was to investigate the changes on the expression of 84 key genes involved in the progression of hepatocellular carcinoma. The genes in the array included those involved in DNA damage, cell growth, cell-cell adhesion, apoptosis, angiogenesis, epithelial to mesenchymal transition, proteolysis, and immune response. Specifically, EGFR, Flt-1, KDR, which are growth factor receptors, were highly expressed on 30$^{th}$ days of the experiment, Similarly, growth factors HGF, IGF2 and VEGFA were markedly higher in these cells. Cell adhesion molecules; CDH1 and CDH13 were significantly upregulated. GADD45B, which is a p53 target gene and known to get induced during growth arrest, was more expressed. On the other hand, the genes that were downregulated included cell cycle regulators and apoptosis genes, such as BIRC5, CCND1, CDKN2A, E2F1, LEF1, MSH2, and TERT. Experiments related with the changes on the expression of some other genes, which are important for carcinogenesis, are also in progress. Behaviors of other cancer cell types under the same cultural conditions and importance of cancer stem cells in differentiation process are other questions to be answered. In future, differentiation of cancer cells *in vivo* and finally making them behave like "healthy cells" might be another therapeutic approach for cancer treatment.