Hypoxia-induced epithelial-mesenchymal transition enhanced Glutathion-S-transferase expression in HT-29 cell line

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Colorectal cancer (CRC) is the most common type of malignancy in the gastrointestinal tract and drug resistance remains a major clinical problem in the current treatment of CRC. Cancer-associated epithelial-mesenchymal transition (EMT) has been found to play a critical role in drug resistance but the nature of these intrinsic links remains unclear. It has been suggested that oxidative stress (OS) had a direct role in promoting EMT and mesenchymal cells equibbed with flexible pathways in response to OS tend to gain resistance for chemotherapeutic drugs. The π and μ classes of Glutathione S-transferases (GSTs) play a regulatory role in cancer development. High levels of GSTs have been reported in some tumor types. Although there are some studies identified the resistance differences of EMT, the relationship between resistance profile differences of epithelial and mesenchymal forms in CRC is not yet been elucidated. Thus, the aim of the present study was to evaluate if OS generation by hypoxia inducing agent can have a role in EMT of CRC and to compare the expressions of GST isozyme levels for epithelial and mesenchymal phenotype. To determine the effect of hypoxia inducing agent on EMT, HT-29 cells were treated with 50-200 μM of cobalt chloride for 24 to 72 hours. The expression of the mesenchymal markers α-SMA, vimentin, and the epithelial marker E-cadherin was analyzed by real time qRT-PCR. The GST-π and μ isozyme levels of epithelial and mesenchymal forms were also quantified by qRT-PCR. As a result, vimentin and α-SMA expression increased whereas E-cadherin expression was decreased. The expression of GST-π in mesenchymal cells were significantly higher but no significant changes in GST-μ expression were observed. In summary, this study clearly demonstrated that GST-π had a functional importance in drug resistance of mesenchymal cells. Further studies for inhibition of GSTs in mesenchymal phenotype to overcome drug resistance will be conducted.