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The regulation of human carbonyl reductase 3 (CBR3) in epithelial cell lines

Regulace lidské karbonylreduktasy 3 v buněčných liniích epithelu

Abstract

The enzymatic reactions carried out by enzymes from the short-chain dehydrogenase/reductase (SDR) superfamily can be grouped mainly as NAD(P)(H)-dependent oxidoreductions acting on a highly diverse set of substrates. The SDR superfamily has several members capable mediating carbonyl reduction and therefore affecting endogenous processes of both xenobiotic and endogenous ligands. Two monomeric carbonyl reductases, namely carbonyl reductase 1 (CBR1) and carbonyl reductase 3 (CBR3), have been found in humans. Whereas substrates and gene regulation of CBR1 have been described, CBR3 is poorly characterized. Despite the high similarity of CBR3 with CBR1 in amino acid level, both isoforms seem to play distinct roles. In the present study, the five colon carcinoma cell lines (Caco-2, HCT-116, SW-480, HT-29 and TC-7) and one lung carcinoma cell line (A-549) were used to investigated the regulation of CBR3. The constitutive level of CBR3 mRNA was clearly distinct in all cell lines tested. HT-29 cells turned out to be the best model for investigations of CBR3 regulation from all cell lines used. Several lines of evidence suggest the regulation of CBR3 expression via Nrf2-antioxidant response element (ARE) pathway. Next, TNF-a induced the CBR3 mRNA level in HT-29 cells. Further, natural product guggulsterone was shown to induce CBR3 mRNA level in Caco-2 cells, but the underlying mechanism of effct of this promiscuous steroid receptor ligand could not be elucidated.