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Protein-protein Interaction of Heme Oxygeanse-1 and Caveolin-1 or -2 in Mouse Mesangial Cells

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Heme oxygenase (HO), catalyzes the first and rate-limiting step in catabolic oxidation of heme and yields equimolar amounts of carbon monoxide (CO), free iron and biliverdin. Among the 3 isoforms of HO identified in mammalian systems, HO-2 and HO-3 are expressed constitutively in selected tissues and HO-1 is expressed only upon stimulation by many stimuli.

In the kidney, mesangial cells are the resident macrophages of glomerulus and may respond to oxidative stimuli by induction of HO-1 upon contact with many harmful compounds like the metabolic products, toxic heavy metals like cadmium or other xenobiotics designated for urinary excretion.

Caveolins are integral membrane proteins present in caveolae, the small flask-shaped and detergent insoluble invaginations in plasma membrane and are implicated to function in the vesicular transport processes and the transduction of receptor generated signals.

The interaction of heme oxygenase-1 (HO-1) and caveolin in the cultured mouse mesangial cells (MMC) was investigated. In normal MMCs, high levels of caveolin-2 and low level of caveolin-1 at mRNA and protein level were observed without any detectable expression of caveolin-3. Upon treating the MMCs either with cadmium (Cd) or spermine NONOate (SPER/NO), expression of HO-1 mRNA and protein was increased. Caveolae rich membranous fractions from the MMCs treated with Cd or SPER/NO contained both HO-1 and caveolin-1 or caveolin-2. The experiments of immuno-precipitation showed complex formation between the HO-1 and caveolin-1 or caveolin-2 in the Cd treated MMCs. Confocal microscopic results also support co-localization of HO-1 and caveolin-1 or caveolin-2 at the plasma membrane. Co-localization of caveolins with HO-1 in caveolae suggested that caveolin could also play an important role in regulating the function of HO-1.