Bi-Functional Human Selenoprotein P, Selenium-Rich Plasma Protein

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Selenoprotein P (SeP; the "P" denotes its presence in plasma) is the major selenoprotein in plasma. All selenoproteins so far reported contain one selenocysteine (Sec) residue per molecule except SeP, which is assumed to contain ten Sec residues. We have reported that human SeP is capable of reducing synthetic phosphatidylcholine hydroperoxide (PCOOH) in the presence of glutathione (Saito, Y. *et al., J. Biol. Chem.,* **274,** 2866). First, we will report the further enzymatic characterization of SeP: (1) thioredoxin is the most preferable electron donor for SeP; (2) the SeP N-terminal fragment (containing one Sec) exhibits the enzymatic activity; and (3) SeP reduces naturally occurring substrates, PCOOH and cholesteryl ester hydroperoxide (CEOOH), in oxidized low density lipoprotein (OxLDL). The latter findings suggest that SeP functions to prevent OxLDL formation in atherosclerotic lesions. Second, we will show evidence that SeP functions as a Se transporter. We found that the Se content and Se-containing enzyme (cGPx, PHGPx and TR) activities in the Jurkat cells decreased rapidly when cultured with a medium containing SeP-deficient human serum, but not eGPx-deficient or control serum. Addition of purified SeP or its C-terminal fragment (Sec-rich) to a medium resulted in increases in the Se-containing enzyme activities in the cells. Thus, SeP functions as not only an enzyme but also a Se transporter.