## S46-1 Microsomal prostaglandin E synthase-1: a novel therapeutic target?

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Prostaglandin $E_2$ ($PGE_2$) is the most common prostanoid produced by a variety of cells and tissues, and has a broad range of biological and physiological activities. $PGE_2$ is formed from arachidonic acid by cyclooxygenase (COX)-catalyzed formation of $PGH_2$ and further isomerization by PGE synthases (PGES). To date, two COX izozymes, COX-1 and -2, and three PGES isozymes, microsomal mPGES-1 and -2 and cytosolic cPGES have been identified. Among these PGES, only mPGES-1 is markedly induced by proinflammatory stimuli, down-regulated by anti-inflammatory glucocorticoid, and functionally coupled with COX-2 in marked preference to COX-1.

By our studies from disruption of the mPGES-1 gene in mice, we have previously found that mPGES-1 plays an important role in inflammatory reactions. Furthermore, the involvement of mPGES-1 in carcinogenesis and Alzheimer's disease pathology has been recently found. mPGES-1 deficiency suppressed chemical carcinogen-induced colon carcinogenesis and amyloid β-dependent neuronal cell death and behavioral deficits. These findings indicate that mPGES-1 is a potential target for the development of therapeutic agents for treatment of several diseases. On the other hand, we recently found that mPGES-1-derived $PGE_2$ might be involved in gastric cytoprotection using a mouse model. In this lecture, I will discuss the potential benefits and risks of mPGES-1 inhibitors.