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Phosphatase activity of soluble Epoxide Hydrolase (sEH)

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Soluble epoxide hydrolase (sEH) is an enzyme with multiple functions that has two distinct enzyme activities: epoxide hydrolase (C-terminal domain) and phosphatase (N-terminal domain). The endogenous substrates of epoxide hydrolase are epoxyeicosatrienoic acids (EETs) that are hydrolyzed by sEH to corresponding diols, dihydroxyeicosatrienoic acids (DHETs). The N-terminal domain metabolizes lysophosphatidic acids (LPAs). In this study, I investigated the catalytic activity of sEH isolated from *Xenopus laevis* and the metabolism of lysophosphatidic acids (LPAs) by allelic variants of human sEH. Firstly the catalytic activities of both N/C terminal domains of sEH were investigated. *Xenopus* sEH cDNA was isolated from embryos of *Xenopus laevis*. The *Xenopus* sEH was expressed in *Escherichia coli* and was purified. The purified *Xenopus* sEH did not show phosphatase activity toward 4-methylumbelliferyl phosphate (4-MUP) or several LPAs although it had EH activity. The epoxide hydrolase activity of sEH seemed to be similar to that of human sEH, while *Xenopus* sEH did not have phosphatase activity toward several substrates that human sEH metabolizes. In contrast, to elucidate the sEH phosphatase activity that metabolizes LPAs, the human sEH were used. A purified wild-type (WT) and six allelic variants of sEH (K55R, R103C, C154Y, R287Q, V422A, and E470G) were used in this study. The R103C and R287Q variants revealed significant lower activity than WT sEH. The kinetic study indicated that R103C and R287Q variants had lower *V*max/*K*m ratio toward stearoyl-LPA than other variants. Regarding the effect of sEH allelic variants on VEGF expression, all variants except V442A revealed suppressed *VEGF* mRNA levels in Hep3B cells. These results suggest that the R103C and R287Q variants have lower phosphatase activity, however, all allelic variants except V442A have similar effect to the VEGF suppression.