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Enhancement in mitochondrial biogenesis by (-)-epigallocatechin gallate (EGCG) through conjugation with a methyl-branched carbonate chain

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(-)-Epigallocatechin-3-gallate (EGCG) is known as a mitochondria-targeted molecule that can prevent mitochondrial deterioration and induce mitochondrial biogenesis by modulating key regulators of mitochondrial metabolism. In this study, we tackled whether derivatization of EGCG could result in enhancement of its effects on mitochondrial biogenesis. EGCG, EGCG peracetate (AcEGCG), and its 4"-O-alkyl substituted congeners prepared by previously reported procedures were biologically evaluated. Interestingly, EGCG and AcEGCG were only marginally effective in inducing mitochondrial biogenesis, while AcEGCG congeners with an alkyl group at the 4"-O position showed significantly increased biological activity compared to their parent compound. Among these series, compound 3f with a methyl-branched carbonate chain at the 4"-O position of the AcEGCG scaffold showed the most enhancements in inducing mitochondrial biogenesis. Hepa1-6 cells treated with 3f exhibited increases in both mitochondrial mass (1.5 times) and relative mtDNA content to nDNA (1.5 times). As a mitochondrial biogenesis enhancer, 3f also increased expression levels of regulators for mitochondrial function, including PGC-1 α (4.0 fold), p-AMPK (2.5 fold), SIRT1 (4.2 fold), ERR α (1.8 fold), NRF-1 (1.6 fold), NRF-2 (1.7 fold), and mtTFA (2.0 folds). Investigation of oxidative phosphorylation by mitochondria in the presence of 3f revealed that 3f increased NAD⁺/NADH ratio, the amount of cytochrome C, ATP synthesis, and oxygen consumption in Hepa1-6 cells by 2.2, 1.4, 1.5, and 2.1 folds, respectively. Taken together, these results warrant extensive structure-activity relationship study for EGCG derivatives to develop novel mitochondrial biogenesis enhancers.

Biography

Youhoon Chong has completed his PhD from University of Georgia, and Post-doctoral studies from The Scripps Research Institute. He is the Chairman of the Department of Integrative Bioscience and Biotechnology, Konkuk University. He has published more than 140 papers in reputed journals.

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