

BH₄/DH₄ deficiency in *Dictyostelium*: *spr* gene disruption

Young-Sik Park

School of Biotechnology and Biomedical Science, Inje University, Korea

BH₄ (L-erythro-tetrahydrobiopterin) has well-known cofactor functions for aromatic amino acid hydroxylation and nitric oxide synthesis in higher animals. BH₄ is also ubiquitous in lower eukaryotes including fungi. *Dictyostelium discoideum* is peculiar in its synthesis of a D-threo isomer of biopterin, named dictyopterin. The tetrahydro form of dictyopterin (DH₄) is synthesized during aggregation of spores together with a lower amount of L-erythro form and both are known to interfere with GTP binding to G protein. However, the biosynthesis of DH₄ as well as the cellular function have not been defined.

We created a mutant deficient in sepiapterin reductase (SPR), a crucial enzyme for BH₄ synthesis, by gene targeting. The *spr* mutant generated spores of poor viability and fruiting bodies of a larger size. The cellular content of BH₄ and DH₄ decreased much but not completely, supporting that a salvage pathway is working as in human SR deficiencies. We also created overexpression transformants of SPR in *spr* mutant as well as in wild type.

Further characterization of the mutants will be useful for elucidating the synthesis of DH₄ and the physiological function of BH₄/DH₄, probably related to nitric oxide, which might be applicable to neurological problems caused by BH₄ deficiency.