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Gβγ-mediated Signaling Pathway for Growth, Developmental Control and Toxin Biosynthesis in *Aspergillus nidulans*

Jeong-Ah Seo

Department of Food Microbiology and Toxicology, University of Wisconsin-Madison, 1925 Willow Dr., Madison, WI53706, USA

In the filamentous fungi, heterotrimeric G proteins play crucial roles in cell growth, asexual and sexual development, and pathogenicity and secondary metabolism. The basic unit of heterotrimeric G protein signaling is comprised of a seven-transmembrane domain G protein-coupled receptor, a heterotrimeric G protein consisting of α, β, γ and subunits, and downstream effector. In the model fungus *Aspergillus nidulans*, vegetative growth signaling is primarily mediated by FadA and SfaD, the α and β subunits, and a presumed Gγ subunit. To further understand heterotrimeric G protein signaling mechanisms in *A. nidulans*, we have identified and characterized the Gγ subunit GpgA and phosducin-like protein (PhLP) PhnA. Phosducin or PhLP is a positive regulator in Gβ function. Genome analyses in *A. nidulans* resulted in identifying a single Gγ subunit and three PhLPs, PhnA, PhnB and PhnC. Similar to Δ*sfaD*, deletion of each *gpgA* and *phnA* caused the restricted vegetative growth, defective sexual fruiting bodies (cleistothecia) in self-fertilization and severe impairment of outcrosses. Deletion of *phnA* resulted in asexual sporulation in liquid submerged culture, suggesting that PhnA is required for Gβ SfaD-mediated asexual development control. SfaD::GpgA (Gβγ) may function as a heterodimer in the growth and sexual development signaling pathways, but each component of heterodimer has somewhat different role in asexual development. Developmental defects caused by deletion of *flbA* encoding RGS (regulator of G protein signaling) protein negatively regulating FadA-mediated growth signaling were suppressed by deletion of *gpgA* and *phnA* respectively indicating that GpgA and PhnA function in FadA-SfaD mediated vegetative growth signaling. However, while FadA represses mycotoxin sterigmatocystin (ST) production, SfaD, GpgA, and PhnA are required for ST production. The Gβ SfaD is necessary for the expression of *aflR* encoding the transcriptional activator for the genes of ST biosynthesis. Over-expression of *aflR* is sufficient to restore ST production based on deletion of *sfaD* implying that SfaD-mediated signaling in ST biosynthesis may include transcriptional activation of *aflR*. Gβγ SfaD::GpgA and a positive regulator PhnA are required for normal vegetative growth, appropriate regulation of asexual sporulation, and the formation of sexual fruiting bodies. The identification of other G protein components and/or downstream effectors transducing SfaD::GpgA signals is critical for further understanding differential roles of G protein components associated with secondary metabolism and other physiological characteristics.

Curriculum Vitae

Name	Jeong-Ah Seo	Nationality	Korea
Affiliation	University of Wisconsin-Madison	Position	Assistant Scientist
Telephone	02-3661-5228	Faxmile	
E-mail	sja815@hotmail.com		
Education	1987 : Seoul National University, Department of Agricultural Biology (B.S.) 1990 : Graduate School of Agricultural Biology, Seoul National University, Plant Pathology Major (M.S.) 1994~1998 : Graduate School of Applied Biology and Chemistry, Seoul National University, Plant Pathology and Mycotoxicology Major (Ph.D)		
Experience	1999~2000 : USDA (NCAUR ARS), Peoria, Illinois, USA Mycotoxin Unit, Visiting Scientist 2000~2001 : University of Wisconsin-Madison Madison, WI, USA Fungal Molecular Genetics, Research Associate (Post-Doc) 2001~2006 : University of Wisconsin-Madison Madison, WI, USA Fungal Molecular Genetics, Assistant Scientist (Research Professor)		
Main Scientific Publication	Yu, J. H. , Mah, J. H. and Seo, J. A. 2006. Growth and developmental control in the model and pathogenic aspergilli. *Eukaryotic Cell* (in press) Seo, J.-A., and Yu, J. H. 2006. The phosducin-like protein PhnA is required for Gβγ-mediated signaling for vegetative growth, developmental control and toxin biosynthesis in *Aspergillus nidulans*. *Eukaryotic Cell* 5(2): 400-410. Seo, J.-A., Guan, Y., and Yu, J.-H. 2006. FluG-dependent asexual development in *Aspergillus nidulans* occurs via de-repression. *Genetics* 172(3): 1535-1544. Lafon, A., Han, K.-H., Seo, J.-A., Yu, J.-H. and d'Enfert, C. 2006. G protein and cAMP-mediated signaling in aspergilli: a genomic perspective. *Fungal Genet. Biol.* 43(7): 490-502. Seo, J.-A., Han, K. H., and Yu, J. H. 2005. Multiple roles of a heterotrimeric G protein g subunit in the filamentous fungus *Aspergillus nidulans*. *Genetics* 171(1): 81-89. Lafon A., Seo, J.-A., Han, K.-H., Yu, J.-H. and d'Enfert, C. 2005. The heterotrimeric G-protein GanB(α)-SfaD(β)-GpgA(γ) is a carbon source sensor involved in early cAMP-dependent germination in *Aspergillus nidulans*. *Genetics* 171(1): 71-80. Ni, M., Rierson, S., Seo, J.-A., and Yu, J.-H. 2005. The pkaB encoding the secondary protein kinase A catalytic subunit has a synthetic lethal interaction with pkaA and plays overlapping and opposite roles in *Aspergillus nidulans*. *Eukaryotic Cell* 4(8): 1465-1476. Seo, J.-A., and Yu, J.H. 2004. Toxigenic fungi and mycotoxins. pp. 689-721. Handbook of Industrial Mycology in Z. An (ed), Marcel Dekker, NY. pp.763. Yu, J.-H., Hamari, Z., Han, K.-H., Seo, J.-A., Reyes-Dominguez, and Y., Scazzocchio, C. 2004. Double-joint PCR: a PCR-based molecular tool for gene manipulations in filamentous fungi. *Fungal Genet. Biol.* 41(11): 973-981. Seo, J.-A., Han, K.-H., and Yu, J.-H. 2004. The gprA and gprB genes encode putative G protein coupled receptors required for self-fertilization in *Aspergillus nidulans*. *Mol. Microbiol.* 53(6): 1611-1623.		

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