

Lysophosphatidylethanolamine in *Grifola frondosa* as a Neurotrophic Activator via Activation of MAP Kinase

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We found that *Grifola frondosa* extracts induced activation of mitogen-activated protein kinase (MAPK) in cultured PC12 cells, a cell line of rat pheochromocytoma cells. The active substance was isolated by a few chromatographic steps including high-performance liquid chromatography, and was identified to be lysophosphatidylethanolamine (LPE) from various structural analyses. LPE from *Grifola frondosa* (GLPE) was confirmed to induce activation of MAPK of cultured PC12 cells, and found to suppress cell condensation and DNA ladder generation evoked by serum deprivation, thus suggesting that the GLPE had anti-apoptotic effects. Moreover, GLPE caused morphological changes in and up-regulation of neurofilament-M expression of PC12 cells, demonstrating that the GLPE could induce neuronal differentiation of these cells. The activation of MAPK by GLPE was suppressed by AG1478, an antagonist of epidermal growth factor receptor (EGFR) or by U0126, an inhibitor of MAPK kinase (MEK1/2), but not by K252a, an inhibitor of TrkA or by pertussis toxin. These results demonstrate that LPE from *Grifola frondosa* induced activation of the MAP kinase cascade (EGFR-MEK1/2-ERK1/2) of PC12 cells, the activation of which induced neuronal differentiation and suppressed serum deprivation-induced apoptosis. This present study has clarified for the first time the involvement of the MAPK signal cascade in LPE actions.