OS04-2 Metabolomic identification of the target of the natural product glucopiericidin A

◯Masaya IMOTO[1]
[1]Keio University

In the course of the screening for the inhibitor against the filopodia formation, we found that one cultured broth of *Streptomyces* sp. #1869-19 showed the strong inhibition. Isolation of the active substances from the cultured broth of this strain showed that two substances, glucopiericidin A (GPA) and piericidin A (PA) synergistically inhibited the filopodia when they were co-treated. So far, the mode of action of GPA has not yet been clarified. However, because we found that glycolysis inhibitor 2-deoxyglucose as well as GPA could synergistically inhibit the filopodia formation with PA, GPA would be an inhibitor of glycolysis. Indeed, metabolome analysis revealed that GPA decreased the cellular level of final products of glycolysis by inhibiting either the step of glucose uptake into cells or the subsequent step of glucose phosphorylation. Because GPA inhibited Glucose Transporter-mediated uptake of ^{3}H-labeled 2-deoxyglucose, it was indicated that GPA suppressed glycolysis via inhibition of Glucose Transporter. On the other hand, PA is known as the inhibitor of mitochondrial respiratory chain complex I, and co-treatment of GPA and PA decreased cellular ATP levels synergistically. Because the filopodia formation is the ATP-energy dependent, depletion of cellular ATP induced by GPA and PA might be a cause of inhibition of filopodia formation.