

Discovery of the first vacuolar transporter responsible for the endogenous alkaloid accumulation

(Laboratory of Plant Gene Expression, RISH, Kyoto University)

Kazufumi Yazaki

Among a large number of plant secondary metabolites, alkaloids comprise one of the most important groups due to their strong and divergent biological activities, and some are applied for clinical use [1]. Alkaloids are defined as nitrogen-containing low-molecular-weight organic substances. They are often highly accumulated in particular organs of medicinal plants, which are called the ‘medicinal part’, whereas it is known that some alkaloids are translocated from source organs to such sink organs. The movement of biosynthetic intermediates from specific cells to other types of cells in tissue, and further detailed movement within the organelles in a cell is also suggested. However, little is known how alkaloids are transported across membranes and finally accumulated in specific organelles such as vacuole of the sink organ. Actually, vacuoles are the main subcellular compartment for the accumulation of alkaloids, and in many model experiments, vacuolar uptake of endogenous alkaloids have been reported [2]. However, no endogenous transporter molecule has been identified for the vacuolar transport of those alkaloids thus far.

As a representative of such alkaloids, we selected nicotine, a pyridine alkaloid, which is biosynthesized in root tissues, then translocated to the leaves, and finally accumulated in the leaf vacuoles in *Nicotiana* species. Recently, we have identified a novel multidrug and toxic compound extrusion (MATE)-type transporter in cDNA AFLP as a strong candidate of nicotine transporter in tobacco plant [3]. This gene, designated as *Nt-JAT1* (*Nicotiana tabacum* jasmonate-inducible alkaloid transporter 1) was co-regulated with nicotine biosynthetic genes following methyl jasmonate treatment of tobacco BY-2 cells. This MATE gene was expressed in the leaves, stems, and roots in tobacco plants. Biochemical analyses using a yeast cellular transport system and proteoliposome system suggested that Nt-JAT1 transported nicotine using the H⁺ gradient across the membrane as its driving force [4]. The location of Nt-JAT1 was shown to be the tonoplast. These data suggested that Nt-JAT1 plays an important role in the nicotine translocation by acting as a transporter responsible for the unloading of nicotine in the aerial parts of the plant and its deposition in the vacuoles. To our knowledge, this is the first identification of a vacuolar transporter for alkaloids in plant. A possible application of this alkaloid transporter for the production of valuable alkaloids is also discussed in the reference.

References

- [1] Shitan, N., Yazaki, K., Chapter 12. Membrane transport of plant secondary metabolites. In: Plant Membrane and Vacuolar Transporters (Eds. Pawan K. Jaiwal, Rana P. Singh, and OM Parkash Dhankher), CAB International, Oxfordshire, UK, pp. 283-300, 2008.
- [2] Shitan, N., Yazaki, K., Accumulation and membrane transport of plant alkaloids. *Curr. Pharm. Biotech.*, vol. 8, no. 4, pp. 244-252, 2007.
- [3] Yazaki, K., Sugiyama, A., Morita, M., Shitan, N., Secondary transport as an efficient membrane transport mechanism for plant secondary metabolites. *Phytochem. Rev.*, vol. 7, pp. 513-524, 2008.
- [4] Morita, M., Shitan, N., Sawada, K., Van Montagu, M., Inzé, D., Rischer, H., Goossens, A., Oksman-Caldentey, K-M., Moriyama, Y., Yazaki, K., “Vacuolar transport of nicotine is mediated by a novel multidrug and toxic compound extrusion (MATE) transporter in *Nicotiana tabacum*.” *Proc. Natl. Acad. Sci. USA*, vol. 106, no. 7, pp. 2447-2452, 2009.