Applications of Plant Lectins in Cholangiocarcinoma

Somsiri Indramanee¹,², Atit Silsirivanit³, Chawalit Pairojkul¹,², Chaisiri Wongkham¹,², Sopit Wongkham¹,³

Department of ¹Biochemistry, ²Pathology, ³Liver Fluke and Cholangiocarcinoma Research Center, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand, 40002

**Background and Objective:** Glycosylation was reported to be altered and associated with development and progression of many cancers. With the sugar-binding ability, lectins have been widely used in the study of glycans and glycoconjugates. Not only for detection of aberrant glycans in clinical samples, many lectins such as Concanavalin A (Con A) and European mistletoe (ML-I), have been applied as anti-cancer drugs. This study is aimed to determine the expression profile of glycosylation in cholangiocarcinoma (CCA) tissues using lectins. The possibilities of using lectin as a tool for detection CCA-associated glycans and the application of lectins in suppression cell growth in CCA were examined.

**Methods:** Fourteen lectins with different sugar preferences were screened by lectin-histochemistry staining in human CCA tissues. Lectins which differentiated CCA from normal bile ducts were selected for clinical application and functional analysis in CCA cell lines. Cell growth was analyzed using Sulforhodamine B colorimetric assay (SRB) staining suppress CCA cell growth.

**Results:** Using 14 different lectins, the lectin-histochemistry revealed different patterns of lectin staining in CCA tissues, only *Dolichos biflorus* agglutinin (DBA) exhibited negative staining with all histo-types CCA. Succinylated wheat germ agglutinin (sWGA), *Sophora japonica* agglutinin (SJA) and *Ulex europaeus* agglutinin (UEA-I) showed strongly positive staining with CCA but low reactivities with normal bile ducts, with 100% (53/53), 81% (43/53), and 64% (34/53) positive staining, respectively. The functional analysis revealed that sWGA could suppress growth of KKU-M139 and KKU-M214 to 42% and 32% compared with the non-treated controls. UEA-1 showed 36% growth suppression in KKU-M214 but not in KKU-M139, while SJA had no growth suppression effect and KKU-M055 was not suppressed by any lectin treatments.

**Conclusions:** The aberrant glycosylations in CCA were demonstrated using lectin histochemistry. sWGA and UEA-1 exhibited growth suppression on CCA cell lines. The aberrant expressed glycans are possibly used as the biomarkers for CCA. In addition, we have shown the potency of plant lectins to suppress CCA cell growth. This information emphasized the applicable of lectins in CCA diagnosis and treatment. The mechanism and role of these aberrant glycans in CCA are needed to speculate insight.

**Key words:** Cholangiocarcinoma (CCA), Glycosylation, Lectins