Anti-carcinogenic Effect of Bowman-birk Protease Inhibitor (BBI) from Soy Beans

TOMOHIRO YANO, Ph.D.
Professor, Faculty of Life Sciences,
Toyo University

＜Abstract＞

Epidemiological studies indicate that diets containing high amounts of soybean products contribute to low cancer incidences and low mortality rates. Several components isolated from soybeans such as isoflavones and protease inhibitors are currently being intensively studied as possible cancer chemopreventive agents. Recently, protease inhibitors have been developed as a class of well-established cancer chemopreventive agents due to their strong anti-carcinogenic activities in model cancer systems (both *in vivo* and *in vitro*). The most predominant protease inhibitor in soybeans is the Bowman-Birk Inhibitor (BBI). BBI is a 71-amino acid protein (～8 kDa) which acts as a serine protease inhibitor and possesses both trypsin and chymotrypsin inhibitory activities. Interestingly, BBI is the only protease inhibitor derived from soybeans that displays chymotrypsin inhibitory activity. This chymotrypsin inhibitory activity may contribute to the anti-carcinogenic activity, but the trypsin inhibitory activity appears to not be essential. Although BBI has a broad spectrum of cancer-protective activities, knowledge of the exact mechanism(s) by which BBI exerts its anti-carcinogenic effects remains limited.

Among the different cell-cell interactions in mammalian cells, gap junctional intercellular communication (GJIC) is considered to be the only route allowing free and direct transfer of ions and hydrophilic molecules of up to 1000-1500 Da in size between cells, thereby maintaining electrical and metabolic cell homeostasis. The gap junction consists of juxtaposed transmembrane hemichannels (connexons) provided by adjacent cells, and each connexon consists of six individual transmembrane proteins called connexins (Cx). In general, it is well known that the Cx gene acts as a tumor suppressor gene by maintaining homeostatic control in multicellular organisms via GJIC. Additionally, it has been reported that important chemopreventive effects of several components depend on maintaining and/or restoring expression and function of the Cx gene during the carcinogenic process. Thus, it is reasonable to assume the Cx gene to be a logical target for cancer prevention. In our recent study, we reported that BBI suppresses the development of non-epithelial tumors such as sarcoma via elevated levels of the Cx43 protein. Furthermore, the up-regulation of Cx43 by BBI suppresses chemoresistance in non-epithelial tumors. Overall, it appears that BBI acts as a potential anti-tumorigenic agent in non-epithelial tumors in which Cx43 acts as a tumor suppressor gene and that BBI may be a promising agent to control chemoresistance.