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Abstract (600 word limits)

Molecular mechanisms for LZ-8 to bind on multiple RTK via targeting to N-glycan motif for promoting endosomal degradation of RTK

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Target therapies aiming at oncogenic receptor tyrosine kinase (RTKs) for prevention of hepatocellular carcinoma (HCC) progression were hampered by drug resistance due to co-expression of multiple RTKs raising compensatory secondary signaling after drug treatment. One potential strategy for reducing drug resistance is the comprehensive blockade of multiple RTKs via perturbing the N-glycan motif on RTKs. Most growth factor receptors, including EGFR and TGF β receptor (TGFβR) are N-glycosylated. N-glycans are essential for maintaining multiple RTKs on cell surface via multivalent association with galectin-3, one of the endogenous lectin on cell surface. Moreover, the role of *N*-glycans on RTK in tumor progression was emerging recently. Previously, interfering the N-linked glycosylation pathway has been used to reduce drug resistance in cancer therapy. However, this approach suffers from concern about systemic toxicity. Alternatively, the use of an anticancer agent capable of simultaneously binding the universal *N*-glycans on oncogenic RTKs is promising. The medicinal peptide LZ-8 (also known as Ling-Zhi 8 purified from Ganoderma lucidium) was known to be one of fungal immumodulatory peptides (FIP) and also an anti-tumor agent. Previously, LZ-8 was known to be a lectin-like peptide capable of binding carbohydrate motif on surface glycoprotein to modulate immune function. Our recent study suggested LZ-8 was able to suppress migration of HCC413, a patient derived HCC cell line, via binding N-glycan on multiple RTKs including EGFR, c-Met and Her3 to inhibit the downstream signaling. To fully elucidate the underlying mechanisms by which LZ-8 suppress HCC progression, we are investigating whether binding of N-glycan by LZ-8 may interfere the association of N-glycan with galectin-3 leading to disruption of N-glycan-galectin 3 lattice and facilitate endosomal degradation of RTK. Our study will benefit establishing strategies for anti-HCC progression by targeting the specific N-linked glycosylation site on multiple RTKs using LZ-8 and other lectin–like FIP.

Biography (200 word limit)

Wen-Sheng Wu is a professor in Department of laboratory medicine and biotechnology, college of Medicine, Tzu Chi University. After graduated from institute of biochemistry Taiwan University, he carried postdoctoral research at department of research, veteran general hospital Taipei and department of Medical technology Kaohsiung, Taiwan.

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