Regulation of TIF1β Phosphorylation in Colorectal Cancer

Larina Tzu-Wei Shen¹, Han-Yi Chou² and Mitsuyasu Kato¹,³

¹ Department of Experimental Pathology, School of Integrative and Global Majors, University of Tsukuba, Japan
² Graduate Institute of Oral Biology, School of Dentistry, National Taiwan University, Taiwan
³ Faculty of medicine, University of Tsukuba, Japan

Dynamic state of post-translational modifications has been postulated to take part in a wide range of processes in cancer. Notably, deregulating the balance between kinases and phosphatases leads to change protein phosphorylation status which has amply reported in cancer progression. As a multifunctional protein, Transcription intermediary factor 1 beta (TIF1β) is reportedly subjected to multiple protein posttranslational modifications, including phosphorylation. TIF1β is an intermediary factor of transcription and epigenetic modulator of gene expression in several physiological processes including embryonic development and cell differentiation as well as in establishment and/or progression of some cancers. Interestingly, serine 473 residue of TIF1β affects the binding between TIF1β and heterochromatin protein 1 (HP1) which could serve as a molecular switch to regulate chromatin remodeling and epigenetic modulation. However, gaps exist in our knowledge of how TIF1β phosphorylation at Ser473 cross-talks with cancer progression and what the biological consequence is. I use colorectal cancer to investigate the molecular mechanisms regulating phosphorylation/de-phosphorylation of TIF1β in cancer progression. Here I present evidences that TIF1β phosphorylation is correlated with intestinal epithelial cells proliferation/differentiation, cancer progression, could be induced by epidermal growth factor (EGF) stimulation as RAS-MEK-ERK signaling pathway and dephosphorylated by protein phosphatase 4 (PP4). Furthermore, immunohistochemistry data on different pathologic grades of colorectal cancer show low phosphorylated TIF1β with high expression of protein phosphatase 4 catalytic (PP4C) subunit provide a link that PP4C may involve in de-phosphorylation of TIF1β in colorectal cancer progression. Taken together, my results suggest a novel role for TIF1β phosphorylation at Ser473 may be involved in cellular proliferation/differentiation as well as cancer progression through homeostatic balance between PP4 and ERK signaling pathway.