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Poster Sessions

Synergistic anti-cancer effects of PME-1 suppression and p53 activation on A549 cells

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Excessive phosphorylation of intracellular proteins is one of the causes of the development and malignant progression of cancer. Not a few molecular-targeted anticancer drugs have been developed to inhibit abnormal activation of limited number of kinases. Therefore, novel drugs development from this point of view is now facing difficulty. On the other hand, innovative drug discovery that targets "phosphatase activation", as a different angle of "kinase inhibition", has not been realized. Protein phosphatase 2A (PP2A) is an essential holoenzyme that is implicated as an important tumor suppressor based on its central role in phosphorylation-dependent signaling pathways. Protein phosphatase methyl-esterase (PME-1) catalyzes specifically the demethylation of PP2A catalytic subunit (PP2Ac). PME-1 also inhibits PP2A activity by directly binding to its phosphatase active site; the role as PP2A inhibitory protein. We revealed that PP2A inhibitory function, but not methyl-esterase activity, is important for tumor-promoting function of PME-1. We also found that PME-1 inhibition and p53 activation synergistically exert anti-cancer effects on human lung cancer cell line A549.