【Title】

[2P-0336]Secreting protein p53PAD7 induces apoptosis via the Hippo signaling pathway

【Author and Affiliations】

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【Abstract】

The tumor suppressor p53 gene is the most frequently mutated gene in human cancer. p53 is a transcription factor that activates numerous genes. The p53PAD7 gene is known as a target of p53 that suppresses cell proliferation, however, the molecular function of p53PAD7 is totally unknown. Here, we found that p53PAD7 is secreted to the cell culture medium and that recombinant p53PAD7 protein induces apoptosis. We hypothesized that p53PAD7 acts as a ligand that is received by specific receptors. To identify the candidate receptors, we performed immunoprecipitation and mass spectrometric analysis together with a heterobifunctional crosslinker and successfully identified protocadherin FAT1 and FAT4 as p53PAD7 receptors. Human FAT1 and FAT4 are homologs of Drosophila melanogaster Fat, which is a receptor of the Hippo signaling pathway that regulates cell proliferation. Consistently, we observed activation of YAP/TAZ when cells were treated with recombinant p53PAD7 protein. Taken together, our results suggest p53PAD7 is a novel secreting protein that extrinsically induces cell apoptosis via the Hippo signaling pathway.

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