Chemotherapy: Open Access
ISSN: 2167-7700

Liu and Wang, Chemo Open Access 2017, 6:2
DOI: 10.4172/2167-7700.1000234

Commentary Open Access

# Discovery of a Small Molecule in the Treatment Development of Pancreatic Cancer

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**Received date:** March 15, 2017; **Accepted date:** May 23, 2017; **Published date:** May 29, 2017



**Keywords:** Pancreatic cancer; *KRas* gene; Binding affinity; Patients

## Commentary

Researchers at the State Key Laboratory of Electroanalytical Chemistry, Changchun Institute of Applied Chemistry (CIAC), Chinese Academy of Sciences, have identified a promising small-molecule APY606 in the treatment development of pancreatic cancer *via* attenuating the Ras-mitogen-activated protein kinase (Ras-MAPK) signaling cascade. This work collaborated with researcher at State University of New York, Stony Brook has been published in the scientific journal PLoS ONE [1].

*KRas* gene is the most essential oncogene in human cancer, and the oncogenic mutations are found in approximately 90% of patients with pancreatic cancer. However, effective therapies for these patients are unavailable currently. In general, multiple cellular processes are affected by the oncogenic Ras mutants *via* exploiting their extensive signaling, in which the Ras-MAPK signaling cascade exerts important roles. Thus, targeted-Ras therapies are beneficial for the treatment of pancreatic cancer. Using an innovative SPA (Specificity and Affinity) drug screening strategy (which searches for potential lead compounds reaching the maximization of the performances on the binding affinity and binding specificity predictions), which begun four years ago, the CIAC researchers have identified a core of 26 small-molecule agents targeted KRas oncoprotein from NCI/DTP Open Chemical Repository [2]. From these agents, the researchers were interested in focusing on APY606 since the fact was uncovered that in pancreatic cancer, "its anti-cancer property is the most promissing", explained Dr. Zuojia Liu, a researcher at CIAC. In the studies, the researchers assessed the effect of APY606 on antitumor activity against human pancreatic cancer cell lines, Capan-1 and SW1990, and on the Ras-MAPK and apoptosis-related signaling cascades. The combined data suggest that APY606 exerts extensive antitumor activities for the therapeutic intervention in pancreatic cancer through attenuating the Ras-MAPK signaling cascade.

Accordingly, APY606 treatment of both cancer cells resulted in an inhibition of cancer cell viability at a dose- and time dependent manner. In addition, APY606 exhibited strong inhibitions in tumor cell invasion and migration and significant decrease of mitochondrial membrane potential by altering the expression levels of several apoptotic indexes. "What is most important is that inhibition of KRas activity brings about a great reduction in the cell viability and growth in the pancreatic cancer. Thus, the results present this agent as a new small molecule targeted KRas oncoprotein should be directed", the researcher added.

"The next step will be the identification *in vivo*. This step is critical, as not all patients are with mutated KRas; therefore xenograft models who may finally benefit from this treatment must be better defined", concluded the CIAC researchers.

## Acknowledgement

Supported by National Natural Science Foundation of China (81573448) and Natural Science Foundation of Jilin Province (20150101009JC) for anticancer drug discovery program.

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