techman / September 13, 2013 02:19PM

[BioChemistry] Biological Chemistry Researchers Target XIAP/Caspase-7 Complex to Kill Drug-Resistant Cancer Cells

[BioChemistry] Biological Chemistry Researchers Target XIAP/Caspase-7 Complex to Kill Drug-Resistant Cancer Cells (Chinese Version)

Academia Sinica Newsletter (2013/08/30) Through collaboration of Prof. Po-Huang LIANG, a Research Fellow in the Institute of Biological Chemistry, Academia Sinica, and laboratory members with the members from Genomics Research Center, Academia Sinica, and two local Hospitals, by using drug-resistant cancers cells or the cancer cells that cause poor prognosis in cancer patients as subjects, the team has identified a small-molecule inhibitor I-Lys, which can activate Caspase-7 to selectively kill those cancer cells. This paper was published on-line by Journal of Clinical Investigation on August 27, and selected by the journal for special report.

The research team explains that Caspase-3 is a major executioner protein of proteolytic degradation during apoptosis. However, Caspase-3 down-regulation (CASP3/DR) has occurred, which enables cancer cells to survive cancer therapy-induced apoptosis, and expression of structurally and functionally similar caspase-7 is induced in these cancer cells for maintaining cellular homeostasis. The team thus thought that activating Caspase-7 in the CASP3/DR cancers might selectively kill those cancer cells.

Due to the inhibition of Caspase-7 via complexation with its endogenous inhibitor XIAP (X-linked inhibitor of apoptosis protein), the team designed and synthesized I-Lys for selectively binding to Caspase-7 to disrupt the protein-protein interaction of Caspase-7 and XIAP, thereby releasing Caspase-7 for executing apoptosis.

Prof. Liang explains that because the complex of Caspase-7 and XIAP only exists in the cancer cells, not in normal cells, and moreover, I-Lys disrupts the interaction of XIAP with Caspase-7, but not Caspase-3, the use of I-Lys to induce cancer cell apoptosis is effective and safe without side-effect, as also revealed by the animal studies.

From clinical samples, CASP3/DR and Caspase-7 accumulation have been found in many malignancies such as breast, lung and colon cancers, and correlate significantly with poor survival in patients. This phenomenon is also related to cancer metastasis and poor prognosis. Therefore, this paper provides a basis of developing a useful cancer targeted therapy.

Media Contacts:
Dr. Po-Huang LIANG, Institute of Biological Chemistry, Academia Sinica
phliang@gate.sinica.edu.tw (Tel) +886-2-2366-5539
Ms. Mei-hui LIN, Office of the Director General, Central Office of Administration, Academia Sinica
mhlin313@gate.sinica.edu.tw (Tel) +886-2-2789-8821 (Fax) +886-2-2782-1551 (M) 0921-845-234
Ms. Pearl HUANG, Office of the Director General, Central Office of Administration, Academia Sinica
pearlhuang@gate.sinica.edu.tw (Tel) +886-2-2789-8820 (Fax) +886-2-2782-1551 (M) 0912-831-188

Further Information:
Academia Sinica Newsletter 2013/08/30

National Science Council International Cooperation Sci-Tech Newsbrief
---

Edited 1 time(s). Last edit at 09/13/2013 02:22PM by techman.