DNA Replication-Initiation Proteins as Novel Anticancer Targets

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Professor Liang obtained his BSc in Chemistry from Zhongshan University in 1982, MSc in Chemistry from Miami University (Ohio, USA) in 1988, and PhD in Biology from Brown University (USA) in 1993. After his PhD study, he worked as postdoctoral researcher from 1993-1998 at Cold Spring Harbor Laboratory (USA), the world-renowned biological research institute. He then joined the Hong Kong University of Science and Technology in 1998 and has been leading a research lab to study DNA replication and cancer in the Department of Biochemistry.

His major scientific contributions are in the DNA replication in budding yeast and humans and molecular cancer detection and anticancer drugs research and development. He has been performing cutting edge research in the field, having published two research papers each in *Cell, Genes Dev* and *PNAS*. Together with other high quality papers in *J Cell Biol, Mol Cell Biol, Cancer Res, J Mol Biol* etc., the total journal impact factors of his papers from 1993 to 2004 is over 180, and his papers have been cited over 620 times.

Initiation of DNA replication is controlled by the cis-acting DNA elements called replicators and the trans-acting replication-initiation proteins that interact with the replicators. While obligatorily expressed in cancer cells, some initiation proteins are not expressed in non-proliferating normal cells. Therefore, these proteins are attractive targets for anticancer detection and intervention. By using antisense oligodeoxynucleotides and small interfering RNA molecules targeted to the mRNA encoding DNA replication-initiation proteins, hCdc6p, hMcm2p and hCdc45p, we have shown that silencing of the target genes resulted in inhibition of DNA replication and cell proliferation in cultured human cells. Furthermore, silencing of these genes resulted in apoptosis in cancer but not normal cells, as cancer cells entered an abortive S phase while normal cells mainly arrested in G1 phase. Our studies suggest that inhibiting the expression of selective replication-initiation proteins is a novel and effective anticancer strategy (Feng et al., *Cancer Res.* 63:7356-7364, 2003). Furthermore, we have established an anticancer drug screening platform by using the reverse yeast two-hybrid system coupled with the yeast two-hybrid system and human cancer cell cultures. Using our screening system, we have identified several extracts, fractions and pure compounds from Chinese medicinal herbs that are not cytotoxic to yeast cells yet can induce apoptosis of human cancer cells. This may lead to the development of effective anticancer drugs with few side effects.

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