Team Matches Small Molecule Drugs with Protein Target to Enhance Drug Delivery Efficiency for Colorectal Cancer

A research team led by Dr. Han-Chung Wu, a Research Fellow at the Institute of Cellular and Organismic Biology, Academia Sinica has successfully identified three novel peptides with high specificity and binding affinity to colorectal cancer cells that could vastly improve the efficacy of anti-cancer chemotherapeutic drug delivery systems. The research team used the peptides to develop a novel targeted liposomal drug, which showed marked cancer cell growth inhibition without any adverse effects in animal models. These significant discoveries were published in the journal *Science Translational Medicine* on June 3, 2015.

Colorectal cancer is one of the most commonly diagnosed cancers and a leading cause of cancer death worldwide. Traditional chemotherapy only has limited therapeutic efficacy due to non-specific delivery to tumor and non-tumor cells, and the development of drug resistance by cancer cells. Therefore, there is an urgent need to develop more tumor-specific targeted drug delivery systems that can more accurately and effectively deliver the anti-cancer chemotherapeutic drugs to the tumor sites.

In the study, Mr. Chien-Hsun Wu, the first author of the article, used phage display technology to identify three peptides that could bind to colorectal cancer cells with high specificity and binding affinity. Mr. Wu also found that these peptides could bind cancer cells obtained from the biopsy of colorectal cancer patients.

The research team then successfully concocted a targeted drug by conjugating these peptides to liposomes. This novel targeted liposomal drug combination could accurately deliver chemotherapeutics to tumors, resulting in a much higher dose of drugs being accumulated at the tumor site. This significantly increased the tumor inhibition abilities of these two types of chemotherapeutic drugs and effectively eliminated cancer without inducing any side effects for 150 days, with no trace of recurrence.

Professor Han-Chung Wu, the Principal Investigator of the group, said that small molecule drugs have the advantage of having higher tumor penetration abilities, but they are non-specific to tumors and have short half-life. The protein drugs are highly tumor-specific; however, they have lower tumor penetration abilities due to their large molecular sizes. The research team designed an effective targeted drug delivery system through an innovative approach by combining the potent small molecule drugs with highly specific protein targets, thus leveraging the benefits of the two therapeutic regimens while reducing their disadvantages. The efforts of the research team have led to the development of a new cancer treatment that increases the therapeutic efficacies of the drugs while reducing their side effects, thereby effectively curing cancer.

“Although there have been continuous discoveries of new cancer drugs,” said Dr. Ruey-Long

Hong; “most of the drugs have only limited efficacy against cancer with less than ideal effects on prolonging the lives of cancer patients. The research team ingeniously overcame the challenge of accurately delivering the drugs to the tumor sites by combining the liposomal drugs with peptides generated using phage display technology to design a new generation of targeted anti-cancer drug delivery system. The results from this study will provide significant contributions to cancer treatment.”

In addition to successfully designing a targeted drug delivery system against colorectal cancers, the group has also developed targeted drug delivery systems against lung, liver and breast cancers. In the future, these research results are expected to dramatically improve the quality of lives for cancer patients when applied to cancer therapy and early diagnosis.

The affiliations of the research team were Dr. Han Chung Wu, Research Fellow at the Institute of Cellular and Organismic Biology, Academia Sinica; Chien-Hsun Wu, a PhD candidate at the Graduate Institute of Life Sciences (a graduate school co-sponsored by National Defense Medical Center and Academia Sinica); Yi-Huei Kuo, a research assistant; and Dr. Ruey-Long Hong, an oncologist at the National Taiwan University Hospital.

The complete article entitled “α-Enolase–Binding Peptide Enhances Drug Delivery Efficiency and Therapeutic Efficacy Against Colorectal Cancer” can be found at the *Science Translational Medicine* journal website at: http://stm.sciencemag.org/content/7/290/290ra91.short?rss=1