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Artificial Peptides Dispose of Virus Proteins into Cellular Trash Can

Peptide aptamers are able to bind with high specificity to target proteins in the cell and block their functions. Scientists of a research group headed by Professor Felix Hoppe-Seyler of the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) have elucidated a new working mechanism of aptamers.

Peptide aptamers that are directed against proteins of hepatitis B viruses or of carcinogenic human papillomaviruses block viral multiplication or development, respectively. Cell-biological investigations have shown that they cause the virus proteins, which are normally dissolved in the cytoplasm, to clump together. The cell subsequently disposes of these protein aggregates in special bodies close to the nucleus called aggresomes. Scientists presume that the cell uses these “trash cans” to protect itself from the possibly toxic effects of defective and clumped proteins. This working mechanism of aptamers had been unknown to date.

Peptide aptamers consist of approximately 20 protein building blocks (amino acids) which are integrated into a supporting protein which stabilizes their structure. To obtain aptamers that precisely bind to a specific protein, molecular biologists use randomly generated gene libraries in yeast cells, which are read and translated into peptides. With the target protein as “bait”, they search for suitable binding partners.

Because of their ability to specifically shut down the function of individual proteins in the cell, aptamers are considered to be promising molecular tools. Thus, researchers are using appropriate peptides to find out whether it is possible to inhibit the division activity of cancer cells by blocking growth-promoting proteins. By selectively switching off proteins whose role in cancer development is not yet explored, potential new targets for cancer treatment may be identified.

Evangelia Tomai, Karin Butz, Claudia Lohrey, Fritz von Weizsäcker, Hanswalter Zentgraf and Felix Hoppe-Seyler: Peptide-aptamer mediated inhibition of target proteins by sequestration into aggresomes. Journal of Biological Chemistry, 22 May 2006

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