TAILORING IMMUNOTOXIN AS ANTICANCER DRUG

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ABSTRACT

The conventional treatments for cancer have been considered unsatisfatory, with limited efficiency in terms of discriminative cancer cell adverse reaction against the normal compartments, a number of immunological approaches had been implemented. Since cancer cells could exhibit tumor specific antigen (s), a highly specific antibody could be used to direct any anticancer drug, biological agent or radioisotope selectively against the cancer cells and does not harm the normal cells. The specific antibody could be raised by immunization with purified tumor specific antigen (s). The biological agent could be obtained as toxin, either derived from bacteria e.g. diphtheria toxin or derived from plants e.g. castor ricin, which could destroy and kill cancer cells after contacts.

A hybrid molecule constructed between antibody and toxin has been known as "immunotoxin". The selectivity of the antibody against a given tumor specific antigen could be increased by using a monoclonal antibody, made by hybridoma technique and immunological engineering. Accordingly, the efficiency of the destructive or killing effect of the toxin could be eventually increased by purification technique, biochemical and genetic engineering.

In a preliminary study ricin from castor (Ricinus communis) have been purified and separated into two protein fractions (RCAI = 12.000 dalton and RCA II = 60.000 - 65.000 dalton). The latter showed toxin property, and was tested in vitro both against normal cells and against cancer cells. In the microcytotoxicity assay the ricin showed both the short term and the long term killing effect as measured after 1, 4, 16 and 24 hours. The killing effect against cancer cells was stronger as compared to that against normal cells. The acute or short term effect was observed at lower concentration of ricin (10^{-6} and 10^{-12} g/ml) after 1 and 4 hours contacts. The long term effect resulted in 90% and nearly 100% cytotoxicity in higher concentration of ricin. Further development of the immunotoxin are in progress. Various aspects dealing with technical problems and clinical aplications will be discussed.

QUESTIONS AND ANSWERS :

1. Question: Recent advance in genetic engineering allow us to synthesise functional protein(s) by using the expression system. If it can also be used to make immunotoxin and the result is more reproducible, cheaper for mass production and uses less toxic materials. What is your opinion ?

   Answer : Yes, but it is still a great problem to do so.
   In respect to the mechanisms of action one would let the conjugate clearable, so that the toxin will go into its pathway (penetrating the endosome) to work in the cytoplasm to inactivate either EF_2 or ribosome. We need higher toxicity of material to kill cancer cells.

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