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Commentary

Actions of Antibody Drug Conjugates in Cancer Therapy

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DESCRIPTION

Antibody drug conjugates are the biopharmaceutical products used for the targeted therapy used in the treatment of cancer. Antibody Drug Conjugates (ADC) excludes the healthy cells and targets mainly on the tumor cells. ADC is the complex molecules which are made of an antibody combined with anticancer drug molecules, where these are combined with targeting properties of monoclonal antibody properties with cancer destroying property of cytotoxic drugs, designed to discriminate between healthy and diseased tissue. It is a three component system including a potent cytotoxic anticancer agent with antibody by using biodegradable link. Once the monoclonal antibodies exert their therapeutic effect by binding tumor specific cell surfaces on their surfaces, after binding starts destroying the tumor cells by following the process of destroying the cells leads to apoptosis where antibody drug conjugates binds to specific markers (receptors of antigens) at the cancer cell, then the whole cell body incorporates within the cancer cell by degrading the link present between the cytotoxic agent and the antibody, then the active drug is released. It is designed in such a way that the cytotoxic agent mainly concentrates on the delivery of the drug molecules maximize their anti-tumor activity of the ADC and makes normal to its tissue exposure which potentially leads to enhanced therapeutic index. ADC are generally administered intravenously which prevents the monoclonal antibodies from being destroyed by gastric acids and proteolytic enzymes, these monoclonal antibody component of the ADC enables to circulate in the bloodstream till it finds the tumor specific antigen receptor on the surface target cancer cells, the major benefit for this type of mechanism in the ADC is that it prevents the unwanted release of the cytotoxin and increase the drug delivery to cancer cells and ideal biodegradable link have the stability in the bloodstream which are also capable of releasing the active of the cytotoxic drug when required. After the internalization process done with formation of a clathrin-coated early endosome containing the ADC-antigen complex, influx of hydrogen ions takes place in the endosome which results in an acidic environment that facilitates the interaction between the monoclonal antibody component of a ADC's and human neonatal Fc receptors (FcRns). The bound ADC's are transported outside the cell, the physiological pH is 7.4 which enable to release the ADC from the FcRn. This will helps to prevent the healthy cell death. The excessive binding to tumor cells FcRns will also restrict the release the cytotoxic drug and prevent the ADC from receiving effect. The ADC which is remained in the endosome without binding the FcRn receptors forms the late endosome. These endosome subsequently undergoes the lysosomal degradation by allowing the release of the cytotoxic drug into the cytoplasm. It is important to ensure that a threshold concentration of the drug is present within the cancer cell for its destruction to be guaranteed, where the cell surface antigens are quite limited and the process of internalization, rather insufficient. The whole process involved in the mechanism has 50% efficiency only. All targeted therapies are used for the resistance. Developments in site specific conjugation modalities, optimization of linkers with balanced stability and identification of potent cytotoxic agents will enhance the greater safety and efficacy of the drugs which will help in the better treatment.

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