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Drug delivery to cancer based on nanomedicine utilizing EPR effect

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History of anticancer agents can be traced back 70 years and that of photodynamic therapy (PDT) or boron/thermal neutron capture therapy (BNCT) to more than 100 years or 50 years, respectively. However, WHO or NCI of USA admit that most of cancer drugs developed were failure of >90%. A major reason for these failure is attributed to that, there is no general principle to deliver the drugs to cancer tissue until the EPR (enhanced permeability and retention) effect was discovered in 1986 by us. I will present the advantages of macromolecular drug or nanomedicine for cancer drug-targeting to tumor based on the EPR effect in solid tumor. Also, I will talk about the history and controversial issues of the EPR effect, including various factors involved, such as heterogeneity, genetic mutational diversity, obstacles to the tumor blood flow or thrombi formation and counter measures to overcome these problems in the EPR based drug delivery. Also gaps between experimental models of mice, in contrast to practical human clinical setting, will be discussed. Issues of cell internalization, which is greatly affected by the nature of active pharmaceutical ingredient was demonstrated using HPMA-polymer(P)-conjugated-pirarubicin (THP) and P-doxorubicin (P-DOX), where P-THP was more than 30-fold better than P-DOX. Critical importance of the enhancers of the EPR effect such as nitroglycerin are also discussed and brief results of clinical pilot study of P-THP will be presented.

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