

Investigative Treatment Division

The main goal of the research carried out at this Division is to develop new strategies for cancer prevention, diagnosis and treatment based on a better understanding of the biology of cancer tissue and the interaction between the cancer and the host. Improvement of preexistent modalities of cancer diagnosis and treatment is also within the scope of our research activity.

Drug Delivery Systems in Cancer Chemotherapy

One objective of DDS in cancer chemotherapy is to find methods by which anticancer agents can selectively target solid tumors. Two main concepts lie behind selective tumor targeting, active targeting and passive targeting. The former involves monoclonal antibodies or ligands to tumor-related receptors which can target the tumor by utilizing the specific binding ability between antibodies and antigens or between ligands and their receptors. The latter system can be achieved by the so-called EPR (enhanced permeability and retention) effect. The EPR effect in solid tumor tissue was named for its pathophysiological characteristics: (a) hypervascularity; (b) incomplete vascular architecture; (c) several vascular permeability factors stimulating extravasation within the cancer; (d) minimal drainage of macromolecules and particulates. Macromolecular anticancer agents such as liposomal or micellar drugs have long plasma half-lives because they are too large to pass through the normal vessel walls unless they are trapped by the reticuloendothelial system in various organs. Macromolecular agents such as these can diffuse out of tumor blood vessels, effectively reach the solid tumor tissue and be retained for a long period due to the EPR effect. It

has been revealed that the paclitaxel (PTX)-incorporated micelle nanoparticle, NK105, can extend in vivo antitumor activity and reduce the neurotoxicity of the parent drug. In addition, combining NK105 treatment with radiation appears to yield significantly superior antitumor activity than combining PTX treatment with radiation. The superior radiosensitising activity of NK105 is believed to be attributable to the sharper cell cycle arrest at the G2/M phase induced by NK105 than that induced by free PTX (90). SN-38, a biological active metabolite of CPT-11, has potent antitumor activity but has not been used clinically because it is a water-insoluble drug. For delivery by i.v. injection, we have successfully developed NK012, an SN-38-releasing micelle system. It was shown that NK012 markedly enhances the antitumor activity of SN-38, especially in highly VEGF-secreting tumors (91).

Noninvasive Diagnostic Test for Colorectal Cancer

Colon cancer is known to be almost 100% curable by operation if detected early. Thus, colorectal cancer is included in most early cancer screening plans, and many examination methods have been developed. More recently, a new method has been developed in which exfoliated colorectal cancer cells can be effectively isolated from naturally voided feces. The cell recovery method and apparatus we have developed simplifies the cell recovery process and allows cancer cells in stool to be recovered reliably and efficiently, providing a high level of determination accuracy.

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