Colorectal cancer, which is one of the major causes of mortality and morbidity, is usually treated by surgical resection. Just like any other cancers, early detection of colorectal cancer is critical for successful treatment. Colonoscopy has been effectively used for screening colorectal cancer with its ability to provide a definitive diagnosis. The cancer present in the mucous membrane is often treated by resection. Alternatively, the cancer can be treated by minimally invasive operation, known as endoscopic mucosal resection. While the colonoscopy procedure is critically important, it has a major limitation. It can only detect tumor tissues that are larger than 1 cm in size, which has a relatively high possibility of metastasis. Although magnifying endoscopy has contributed to the detection of small-sized colorectal cancer, accurate differentiation of neoplastic mucosal changes in real-time remains a significant challenge. Thus, there is a great need for developing an endoscopic imaging agent that can provide early detection of small-sized colorectal cancer which has low risk of metastasis.

In an article in this issue [1], Sakuma et al. developed lectin-immobilized fluorescent nanospheres for detecting human colorectal cancer cells. Colorectal cancer first develops in the mucous membrane of the large intestine. They noted this mechanism to design an imaging agent that could recognize tumor-derived changes on the mucosal side of the cells in the large intestine. The agent is composed of submicron-sized fluorescent polystyrene nanospheres with two functional groups, peanut agglutinin (PNA) and poly(N-vinylacetamide) (PNVA), on their surfaces. The Thomsen–Friedenreich (TF) antigen is specifically expressed on the mucosal side of colorectal cancer cells. In normal cells, the terminal sugar of the TF antigen is masked by oligosaccharide side chain extension or by sialylation. PNA was immobilized on the nanosphere surface as a targeting moiety that binds to the TF antigen with high affinity and specificity through recognition of the terminal sugar, \( \beta-D\text{-galactosyl-(1-3)}-N\text{-acetyl-D-galactosamine} \). The tumor-derived change in the large intestinal mucosa, however, is very small throughout the whole large intestine. To detect such a small change accurately, the imaging agent should have strong affinity for target cancer tissues with minimum nonspecific interactions with normal tissues. PNVA, which is highly hydrophilic and nonionic, was also immobilized on the nanosphere surface to enhance the specificity of PNA by reducing the nonspecific interactions between the imaging agent and normal tissues. In vitro studies demonstrated that the imaging agent bound to the TF antigen-expressing cancer cells with high affinity and specificity. In vivo studies further indicated that the imaging agent recognized the mucosal invasion of human colorectal tumors implanted orthotopically in the large intestinal serosa of nude mice.

It is anticipated that intracolonic (enema) administration of an imaging agent leads to specific accumulation on the surface of tumor tissues in the large intestine. Real-time accurate diagnosis of small-sized colorectal cancer can be achieved through observation of a clear fluorescence contrast between the normal and tumor tissues under the standard fluorescent endoscope. The study by Sakuma et al. has clearly shown that grafting of a lectin on nanospheres results in specific binding of an imaging agent to tumor cells. This particular study can be easily extended to the targeted delivery of an anticancer agent, increasing the possibility of developing the next generation medicine that achieves therapeutics and diagnosis (theragnosis) by the same delivery vehicle.

Reference


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