Editorial

Endoscopic innovation through animal experiments: a new in-vitro platform

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The development in endoscopy has been tremendous since the conceptof inspecting inside human's gastrointestinal tractfirst introduced in 1806. Flexible video endoscope became available with the advances in fiberoptics, image processing and technologies in CCD. In 1970s, the performance of sphincterotomy upon ERCP marked the start of the era of therapeutic endoscopy (1). The concept of en-bloc resection for early gastrointestinal cancers withendoscopic submucosal dissection (ESD) adopted the principles of surgery and applied through endoscopy using innovative instruments (2,3). Natural Orifices Transluminal Endoscopic Surgery (N.O.T.E.S.) became the next logical step for the development of endoscopic surgery (4). The concept of N.O.T.E.S. is to achieve surgical procedures through the natural orifices of human body without skin incisions. This revolutionary idea, however, cannot be applied to human immediately as the feasibility, safety and effectiveness of these procedures were not completely understand. Animal model became a very important means to establish the achievability of new endoscopic diagnostic and therapeutic procedures (5). These in-vitro experiments, however, were limited by the use of large scale animals toaccommodate large diameter of an ordinary endoscope which is at least 9mm. Establishment of a tumor model in these large scale animal is extremely difficult when compared to nude mice models.

Endoscopic diagnosis for gastrointestinal cancers had evolved tremendously over the past decade. With the development of novel technologies including narrow band imaging and autofluorescence imaging, the detection of early gastrointestinal neoplasm is greatly enhanced (6). Endoscopic diagnosis is evolving towards optical histopathology, molecular and immunological imaging (7,8). One of the important issues to enhance the advances in these technologies is the effectiveness of visualizing neoplastic or cellular changes. Animal model becomes an essential tool forpreclinical investigations of these technologies before its application in human patients. Kiesslich et al observed the presence of epithelial gaps between intestinal cells in a living mouse model and correlated this finding to confocal observation of similar gaps in human ileum (9). Though these gaps were identified in living mouse small intestinal epithelium initially, these were not observed in fixed and sectioned human small intestine. This means that a living animal model is essential, otherwise important features may not be detected even using human cadaveric model.

In the current article, Anders et al reported the success of using a new experimental model to allow the use of ordinary clinical endoscopes to examine a small animal tumor model (10). The tumor model was developed through injection of cancer cell lines to 4 sites of cecal wall of rat through laparotomy. A second laparotomy was then performed 23 days after the injection, and the growth of tumor was confirmed upon opening of the cecum. Endoscopic examination of the tumor was then performed while the cecum was still perfused, hence confocal endomicroscopy could be performed after intravenous administration of 5% fluorescein. In previous mentioned animal model examining gaps between small bowel mucosal cells, topical spray of Acriflavine was used for staining. The current model confirmed that intravenous contrast using fluoresein is feasible and safe in animal.

The current model, however, cannot completely simulate the clinical use of endoscopy to recognize

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gastrointestinal cancers. Normal endoscopy is performed to differentiate neoplastic lesions from inside the lumen of the gastrointestinal tract, while the current model allows the endoscopic technologies to observe tumors when the gastrointestinal tract is surgically unbolted. Therefore, the effectiveness of screening and recognition for early gastrointestinal neoplasia using novel endoscopic technologies could not be fully simulated. Moreover, the tumor utilized for this model is derived fromrhabdomyosarcoma cell line. The feasibility of using other gastrointestinal tract related cancer cell lines necessitate further experiments.

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