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ORIGINAL ARTICLE

Establishment of apoptotic regulatory network for genetic markers of colorectal cancer and optimal selection of traditional Chinese medicine target



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Abstract The paper aimed to screen out genetic markers applicable to early diagnosis for colorectal cancer and establish apoptotic regulatory network model for colorectal cancer, and to analyze the current situation of traditional Chinese medicine (TCM) target, thereby providing theoretical evidence for early diagnosis and targeted therapy of colorectal cancer. Taking databases including CNKI, VIP, Wanfang data, Pub Med, and MEDLINE as main sources of literature retrieval, literatures associated with genetic markers that are applied to early diagnosis of colorectal cancer were searched and performed comprehensive and quantitative analysis by Meta analysis, hence screening genetic markers used in early diagnosis of colorectal cancer. KEGG analysis was employed to establish apoptotic regulatory network model based on screened genetic markers, and optimization was conducted on TCM targets. Through Meta analysis, seven genetic markers were screened out, including WWOX, K-ras, COX-2, P53, APC, DCC and PTEN, among which DCC has the highest diagnostic efficiency. Apoptotic regulatory network was built by KEGG analysis. Currently, it was

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reported that TCM has regulatory function on gene locus in apoptotic regulatory network. The apoptotic regulatory model of colorectal cancer established in this study provides theoretical evidence for early diagnosis and TCM targeted therapy of colorectal cancer in clinic.

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1. Introduction

Worldwide, colorectal cancer, as a common malignant tumor in digestive system, ranks third among male common malignant tumors and ranks second among female common malignant tumors in terms of morbidity. In 2008, there were 1.2 million new cases of colorectal cancer in the world, among which 609 thousand died of the disease (Jemal et al., 2011). In China, colorectal cancer mainly attacks people aged 40–60 years old and due to its occult onset and people's low awareness of the disease, most patients have been in advanced stage when diagnosed, and metastasis has occurred in about 25% patients when first diagnosed. Therefore, the prevention and control of colorectal cancer for now and the future should be focused on increasing early diagnostic rate, early treatment and improving prognosis of colorectal cancer.

Meta analysis refers to a quantitative literature review which takes multiple independent research results on the same topic as objects, and based on strict design, it employs proper statistical methods to perform systematic, objective, quantitative and comprehensive analysis, playing a crucial role in clinical diagnosis, treatment, risk evaluation, prevention and intervention, health service and decision (Zhou et al., 2010). And this method not only promotes efficacy of statistical inference thus lessening inconsistency of single research and drawing more comprehensive and reliable conclusions (Zhang et al., 2013; Chaiyakunapruk et al., 2014), but also puts forward some novel research subjects and guides direction for further study.

Kyoto Encyclopedia of Genes and Genomes (KEGG) (Kanehisa and Goto, 2000) is a database that integrates genome, chemistry, and information of system function, which links gene catalogs obtained from genome that has been completely sequenced to system function of higher levels of cell, species and ecosystem. It is characterized by powerful image function, enabling people to have an intuitive and comprehensive understanding of the metabolic pathways they study.

With the development of traditional Chinese medicine (TCM), active components of Chinese herbs play an important part in the whole treatment of colorectal cancer; specifically, they work positively in inducing cell apoptosis, inhibiting cell proliferation, impacting invasiveness of tumor cells and drug-resistance reversion, which indicates unique advantages of TCM over colorectal cancer treatment.

Taking databases including CNKI, VIP, Wanfang, Pub Med, and MEDLINE as main sources of literature retrieval, literatures related to genetic markers that are applied to early diagnosis of colorectal cancer were searched and performed comprehensive and quantitative analysis by Meta analysis, hence screening genetic markers which can be used in early diagnosis of colorectal cancer. Regarding screened seven genetic markers, including WWOX, K-ras, COX-2, P53, APC, DCC and PTEN, their apoptotic regulatory network

model in colorectal cancer was established by KEGG analysis. The model defines regulatory mechanism of colorectal cancer cell's programmed death, and the current situation of TCM target in the established network was analyzed, hence directing individual diagnosis and targeted therapy of colorectal cancer.

2. Material and methods

2.1. Subjects

With CNKI, VIP and Wanfang databases as major sources for Chinese literatures retrieval, literatures published from 1st January, 1990 to 31st December, 2013 were searched under keywords of colorectal cancer, genetic marker, and (early diagnosis). Regarding English literatures, Pub Med and MEDLINE were considered as main sources, and literatures published from 1st January, 1990 to 31st December, 2013 were searched with keywords “colorectal cancer”, “genetic markers” and “diagnosis”.

All literatures meeting inclusion criteria were carefully read, including the whole text and references, and related literatures were searched as well. The full text of included literatures were either in Chinese or in English, and concerning researches made by the same institution or on the same subject but published on different journals, the latest or the most complete report was adopted.

Inclusion criteria for literatures: (1) the literature should be in English or in Chinese with content of application of genetic markers in early diagnosis of colorectal cancer; (2) the research type is retrospective study; (3) the gold standard in literature is histopathology or operative diagnosis, and the literature takes patients with colorectal cancer as experimental group and healthy people or patients with benign tumor as control group, and there is no restriction of nation, age and sex for all subjects; (4) literature should provide diagnostic results of colorectal cancer separately diagnosed by genetic markers; (5) true positive (TP), false positive (FP), false negative (FN) and true negative (TN) of patients with colorectal cancer that is separately diagnosed by genetic markers can be obtained directly according to the literature or by calculation; (6) the literature employs correct methods and the study has normative process, and regarding researches multiply made by the same institution or on the same subject but published on different journals, the latest or the most complete report was adopted. All included literatures in this study were published in full text in Chinese or in English, and all data were obtained from the original text.

Exclusion criteria for literatures: (1) the literature involves either an unoriginal or repetitive research, or serious design defect, or incomplete data; (2) the type of literature is review or abstract; (3) cases are not diagnosed by gold standard; (4) subjects are colon cancer or rectal cancer; (5) no control group

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