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ORIGINAL ARTICLE

Establishment of apoptotic regulatory network for genetic markers of colorectal cancer

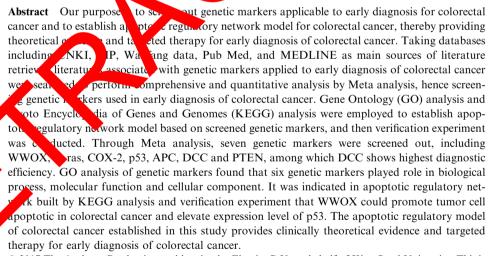


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KEYWORDS

Colorectal cancer; Genetic marker; Meta analysis; GO analysis; KEGG analysis



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1. Introduction

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 worldwide. In 2008, there were 1.2 million new cases of colorectal cancer globally, 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 low awareness,

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most patients have been in advanced stage when diagnosed, and metastasis has occurred in about 25% patients when first diagnosed. Therefore, elevation of early diagnostic rate for early treatment and improvement of prognosis for colorectal cancer are focuses in current and further colorectal cancer prevention and control.

Meta analysis refers to a quantitative literature review which takes multiple independent research results for the same topic as objects, and based on strict design, it employs proper statistical methods to perform systematic, objective, quantitative and comprehensive analysis, aiming to promote statistical test efficacy, evaluate inconsistency or contradiction of research results and discover disadvantages in individual research. In addition, it can process a large quantity of literatures without number limitation. Therefore, Meta analysis plays a significant role in clinical diagnosis, treatment, risk assessment, prevention and intervention, health service as well as decision-making (Zhou et al., 2010). Meta analysis not only promotes efficacy of statistical inference thus lessening inconsistency of single research and draw more comprehensive reliable conclusions (Zhang et al.. Chaiyakunapruk et al., 2014), but also puts forward some novel research subjects, guiding direction for further study.

Gene Ontology (GO) database (Hill et al., 2016) is a structured standard biological model established recently by GO organization, aiming to build a standard system of genes and their biological productions to analyze genes and their cellular component, molecular function and biological processes they are involved in.

Kyoto Encyclopedia of Genes and Genomes (KEG (Kanehisa and Goto, 2000) is a database that integrates geome, chemistry, and information of system function, which links gene catalogs obtained from genome that have an completely sequenced to system function of higher later of completely sequenced to system function of higher later of completely sequenced to system function of higher later of completely sequenced to system function of higher later of completely support of the completely structure of completely size understanding people to have an intuitive and completely size understanding of the metabolic participations. Taking databases including CN (VIP), Wanting data,

ng data, of literature retrie-Pub Med, and MEDLINE as ma sour val, literatures associated with enetic mark that are applied to early diagnosis of color cal cancer were striched to perform comprehensive and quantitative analysis by Meta analysis, hence screening gene marks which can be used in early Regarding the screened seven diagnosis of colorectal can WOY K-ras, COX-2, P53, genetic marker ding IIIL d PTE , their totic regulatory network APC, DCC model in crectal was established by GO analysis and KEGG a V is, and then verification experiment was conducted. The del defines programed death regulatory mechanism for color tal cancer cell, hence directing the individual diagnosis and targeted therapy of colorectal cancer.

2. Material and methods

2.1. Subjects

With CNKI, VIP and Wanfang databases were regarded as primary sources for Chinese literatures retrieval, literatures published between 1st January 1990 and 31 December 2013 were searched under key words of colorectal cancer, genetic

markers, and early diagnosis. Regarding English literatures, Pub Med and MEDLINE were considered as main sources, and literatures published between 1st January 1990 and 31 December 2013 were searched with key words "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 and 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 (2) the research markers in early diagnosis of colorect type is retrospective study; (3) the old standar in literature is histopathology or operative diagrams, and the harature takes patients with colorectal career as experiments group and healthy people or patients on benign mor ar ontrol group, and objects with no restriction of action, as well as sex; (4) literature should prove diagrase results of colorectal cancer separately diagnod by actic maters; (5) true positive (TP), false posite (FP), false negative (FN) and true negative (TN) of patients the colorecta concer that is separately diagnosed by genetic manyers can be obtained directly according to the literature employs cornethods and the study has normative process, and regardresearches multiply made by the same institution or on the in subject but ublished on different journals, the latest and sa the st compl report was adopted. All included literatures ere published full text in Chinese or in English in this all data were obtained from the original text.

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) subject is colon cancer or rectal cancer; (5) no control group is set in the study; (6) the literature studies application of genetic markers in postoperative recurrence diagnosis of colorectal cancer; (7) the literature shows no results of separate diagnosis but only combined diagnosis results of genetic markers for colorectal cancer.

2.2. Data extraction and quality assessment

Data extraction of included in literatures: (1) general data, including authors, published time, published journal, title, the numbers of cases in experimental group and in control group; (2) methodological characteristics: cutoff value; (3) characteristics of research results: diagnostic results of genetic markers for colorectal cancer, including TP, FP, FN and TN.

Quality assessment of included literatures: included literatures were separately and independently assessed and performed cross-check by two professional reviewers using quality assessment of diagnostic accuracy studies (QUADAS) developed by Whiting et al. (2003). QUADAS consists of 14 assessment indicators. Regarding each indicator, "Yes" indicates meeting the standard; "No" indicates not meeting the standard, "Not clear" indicates insufficient information can be got from the literature to determine whether the standard is met

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