New Approaches combating Cancer & Aging 2015; Vol 2:110-112
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Nanjing Municipal Hospital of Chinese Medicine (www. Njszyy.cn) and Nanjing Public Health Bureau (www.nanjing.gov.cn)

Mini-review

Molecular markers for cancer risk assessment and detection

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New Approaches combating Cancer & Aging 2015; 2: 110-112

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Received: 2015.09-18; Accepted: 2015.09-25; Published: 2015.10-08

Abstract

A wide range of cancer-related biomarkers have been extensively studied at various levels including the genome, epigenome, proteome, and glycome, while a very few have been approved by the FDA for cancer risk assessment and early detection. This mini-review attempted to briefly summarize the progresses achieved during the past and also to introduce the new funding opportunities from the American National Cancer Institute (NCI) for cancer risk assessment and early detection.

Mini-review

Cancer is a difficult-to-treat disease that is a major threat to human health, causing the death of more than 7.5million people every year in the world. Reducing the mortality caused by cancer requires better treatment and effective prevention that involves risk assessment for targeted screening and chemoprevention, proper nutrient intakes and physical activity for overall health, and elimination of harmful environmental exposures.

Molecular markers are biological signatures in the human body, also called biomarkers that have great potential for being utilized for cancer risk assessment, early detection, diagnosis, and precision medicine and treatment as well as for studying gene and environmental interaction on cancer initiation for prevention. Biomarkers are very broad while having been widely studied at

小综述

癌症风险预测和检测的分子标记

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新法抗癌抗衰 2015 年第 2 期第 110 至 112 页

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收稿：2015,09-18；接受：2015,09-25; 发表：2015,10-08

摘要

种类繁多的癌症相关的生物标志物，已在不同层面或水平(如基因组学、表形基因组学、蛋白质组学和糖组学）被广泛深入地剖析。然而，仅有为数极少的这些标记物获食品和药物药物管理局的批准而用于癌症风险的预测和早期检测。此小综述旨在简要总结既往取得的进展，同时介绍美国癌症研究所目前资助的癌症风险预测和早期检测的项目。

小综述

癌症是一种极其难治的疾病，严重危害人类健康，每年在全球造成七百五十多万人死亡。减少癌症死亡率不仅需更好的治疗方法和药品，而且需要有效的预防措施, 如对癌症的风险评估，有针对性地的筛查和化学预防、 适当的营养摄入和身体运动以提高整体健康水平，清除有害的环境因素。

分子标靶是人体内重要的生物标签，也称生物标记。生物标记有极大的潜能用于癌症风险预测，早期检测，诊断和精准医学治疗，以及研究基固和环境的相互作用，进而进行有针对性的预防。生物标记定义甚广。既往实验已 在 不同水平（如基 因组学、表型基因组学、

various levels including the genome, epigenome, proteome, and glycome. Here, examples of clinical applications of molecular markers and new research opportunities are demonstrated.

Genomic markers largely include genetic variations, such as single nucleotide polymorphisms (SNPS), and mutations of oncogene, tumor suppressors, and DNA repair genes. One of the most significant discoveries has been the identification of BRCA1 and BRCA2 genes, encoding BRCA proteins for the repair of DNA double strand breaks. Women who inherit mutations in these two major genes could have up to an 85%increased risk to develop breast cancer. In addition, modifying genes have been discovered and validated in large populations, such as the RAD51 gene, which binds to BRCA2 to form a DNA repair complex. The SNP, G135→C in the 5' untranslated region (UTR) of RAD51 has been identified and validated to increase risk by 2-3 times of breast cancer among BRCA2 mutation carriers.

Furthermore, DNA sequencing of breast cancer genes, BRCA1 and BRCA2 and several other genes are commercially available from clinical diagnosis companies for hereditary breast cancer and risk assessment that provides the information for establishing prevention strategies. Epigenetic markers include methylation, histone acetylation and deacetylation, and noncoding RNAs (ncRNAs), a novel class of biomarkers, which do not encode proteins, but are functional transcripts, regulating gene expression, RNA stability, translation, cell development, and cancer initiation as well as serving as markers for early detection and screening. The prostate cancer antigen 3 (PCA3) gene encodes a long ncRNA (lncRNA). The US Food and Drug Administration (FDA) has approved an assay to test the ratio of PCA3 RNA to prostate specific antigen (PSA) RNA in urine for prostate cancer. For protein markers, examples are thelectin-bound Alpha-fetoprotein (AFP-L3) and des-carboxyprothrombin (DCP), which have been approved by the US FDA for predicting the risk of hepatocellular carcinoma (HCC).

The National Cancer Institute, National Institutes of Health (NCI/NIH) supports the Early Detection Research Network (EDRN) that is leading the biomarker research field in the areas of early detection, risk assessment, and prevention through national and international collaborations as well as supporting biomarkers and imaging, pancreatic cancer research, innovative research on adductomics , cancer risk assessment, and prevention. Some Funding Opportunity Announcements(FOAs)

蛋白组学、糖组学等方面）进行了深入研究。在此，我们列举一些已用在临床方面的生物标记，以及一些新的科学研究机遇。

基因组学标志主要包括遗传变异，如单核苷酸多态性 (SNPS); 原癌基因、肿瘤抑制基因、和 DNA 修复基因的突变。最重要的发现之一是已鉴定 BRCA1 和 BRCA2 基因。这两种基因编码 BRCA 蛋白质，修复 DNA 双链断裂。携带 BRCA 突变的妇女，其乳癌的发病率较非携带者高 85％。此外，既往在大样本人口实验中，已发现一些与 BRCA 相关的修饰基因(如 RAD51，其和 BRCA2 联接，形成 DNA 修复复合体)。在 BRCA2 突变携带者中，RAD51 5' 非翻译区 (UTR) G135→C 的单核苷酸多态性，已被确定并验证有高出 2-3 倍患乳腺癌风险。

此外，对 BRCA1，BRCA2，以及其他几个基因的 DNA 测序已成商业化运作。这些基因的测序结果，可用作对遗传性乳腺癌的预测，以及预防措施的选择。表形遗传标记包括甲基化、 组蛋白乙酰化、去乙酰化、与非编码 RNA (ncRNAs)。ncRNAs 是一类新型的生物标志物; 它们不是编码蛋白质，但属功能性转录物，参与调节基因表达，RNA 稳定、 翻译、 细胞的发育，和癌症萌生，以及作为癌症早期检测和筛选标记。前列腺癌抗原 3（PCA3）基因编码一个长的非编码 RNA（lncRNA）。美国食品和药物管理局（FDA）已经批准一个用用前列腺癌诊断的检测方法： 测试尿液的 PCA3 RNA 对前列腺特异性抗原（PSA）RNA 的比率。对于蛋白标志物，实例是凝集素结合甲胎蛋白（AFP-L3）和 DES 羧基凝血酶原（DCP）。这些蛋白已获得美国 FDA 的批准作为预测肝细胞癌（HCC）的风险的生物标记。

美国国家癌症研究所，美国国家卫生科学院（NCI / NIH）支持早期检测研究网络（EDRN）。EDRN 通过国内和国际的广泛合作，引导癌症风险预测，早斯检测，和预防领域中生物标记的研发。EDRN 同时支持临床影象技术，胰腺癌研究、以及在基因修饰学、癌症风险预测和预防方面的开创性研究。部分具体资助项

are listed here:

PAR-15-307: Translational Research on Adducts in Cancer Risk Identification and Prevention (U01).
http://grants.nih.gov/grants/guide/pa-files/PAR-15-307.html

PAR-15-308: Innovative Basic Research on Adducts in Cancer Risk Identification and Prevention (R01).
http://grants.nih.gov/grants/guide/pa-files/PAR-15-308.html

PAR-15-309: Innovative Basic Research on Adducts in Cancer Risk Identification and Prevention (R21).
http://grants.nih.gov/grants/guide/pa-files/PAR-15-309.html.

目列举如下：

AR-15-307：Adducts 在癌症风险识别与防范的转化研究（U01）
http://grants.nih.gov/grants/guide/pa-files/PAR-15-307.html

PAR-15-308：Adducts 在癌症风险识别与防范的开创性基础研究 R01)
http://grants.nih.gov/grants/guide/pa-files/PAR-15-308.html

PAR-15-309：Adducts 在癌症风险识别与防范的开创性基础研究 （R21）
http://grants.nih.gov/grants/guide/pa-files/PAR-15-309.html