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Gazing at The PubMed Reports on CRISPR Tools in Medical Research: A Text-Mining Study

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Abstract

CRISPR (Clustered Regularly Interspaced Short Palindromic Repeat) system is one of the promising methods for targeted genome editing without interfering with intracellular mechanisms. This system is useful for treatment of various diseases and identification of genes responsible for those diseases. In the current study, we performed scientometric analysis along with text-mining of PubMed reports on CRISPR based research in medicine. The upshot of the study revealed cancer, tumour and inherited hereditary diseases as the most prominently studied diseases using the CRISPR tool. Here, we present the outcome of the analysis in the form of a brief systematic review on application of CRISPR tools in the field of medical research using network analysis emphasizing the mostly studied diseases. The review will definitely help the researchers working in the field of medical research to get an overall idea as well as shape their objectives.

Keywords: CRISPR; Cancer; Tumour; Hereditary disease; PubMed; MeSH; Text-mining

Introduction

CRISPR tool has the ability to manipulate the nucleotides at precisely desired location. Therefore, CRISPR is becoming an important tool in medical research as well as in agriculture. Various ground-breaking developments have been done in medical research employing CRISPR tool for studying diseases such as cancer, tumour and inherited genetic diseases including hereditary retinal degeneration, HIV infection, inborn genetic disorders, and recessive genetic diseases [1-5]. To study any disease, availability of disease models is the crucial stage for understanding the disease and its associated pathology. CRISPR mediated approach is the easiest, versatile and mostly employed method in medical research for developing such disease models. Here, we present a meta-analysis to identify the mostly studied diseases in medical research using CRISPR tool from the available reports on PubMed.

Literature Review

Text mining search on PubMed for "CRISPR & Medicine" in the "Title and Abstract" section retrieved a total of 306 records of diseases (MeSH terms) associated with the help of R scripts and PubTator tool [6]. PubTator is an automated, web-based text mining tool for assisting biocuration. PubTator is publicly available tool. The text-mining search resulted in 137 MeSH terms and 196 PubMed IDs which were then analysed using Cytoscape to map the association between PubMed IDs and MeSH terms (Figure 1) [7]. Cytoscape is a publicly available software for integrated biomolecular interaction networks that visually integrate the network with expression profiles, phenotypes to databases of functional annotations. Based on the interaction networks degree distribution, the node, D009369 was found to be the most studied disease (degree=37) which corresponds to cancer and tumor research (Supplementary Table 1).

The study revealed cancer and tumor research (D009369) as the most prominently studied area using CRISPR tool. Numerous important approaches were developed using CRISPR tool to understand the complex cancer genome in the field of cancer research including precision cancer mouse models such as germline models, somatic genome editing models, lymphoma models and mouse models for drug treatment [1]. In addition, inactivation of mutations created by cancer was possible utilizing CRISPR tool [2]. Furthermore, new approaches such as patient-derived stem cell organoids are effective cancer and infectious diseases models for the development of novel targeted therapies [3]. Apart from mouse models, study of cancer in other animal models using direct *in vivo* CRISPR screens will be more beneficial to identify the cause of the disease [4]. Models of cancer research were also developed using human cell lines. Human scarless isogenic cell models of cancer variants were developed with CRISPR/Cas9 gene editing along with high-throughput Kompetitive Allele-Specific PCR genotyping technology [5]. Another report on cancer research using CRISPR tool revealed that inhibition of *STAG1* and *STAG2* in several cancer cell lines reduces cell proliferation [8]. These are the promising therapeutic targets in cancer research. Moreover, identification of biomarkers and therapeutic targets is a critical goal in cancer research. Potential biomarker such as N-glycoproteins and O-6-methylguanine-DNA methyltransferase gene were developed for cancer research using CRISPR-Cas9–mediated vulnerability screen [9,10]. Presence of an altered form of tumor suppressor gene, *p53* is considered as a common characteristic of many cancer cells. Utilizing the CRISPR tool, the normal *p53* phenotype in tumour cells were restored by replacing the mutant *p53* gene with a functional copy [11]. Along with cancer research, tumor research (D009369) is also mostly studied area as revealed by text-mining approach. A strategy has been developed to study the tumour mutations employing CRISPR/Cas9 to

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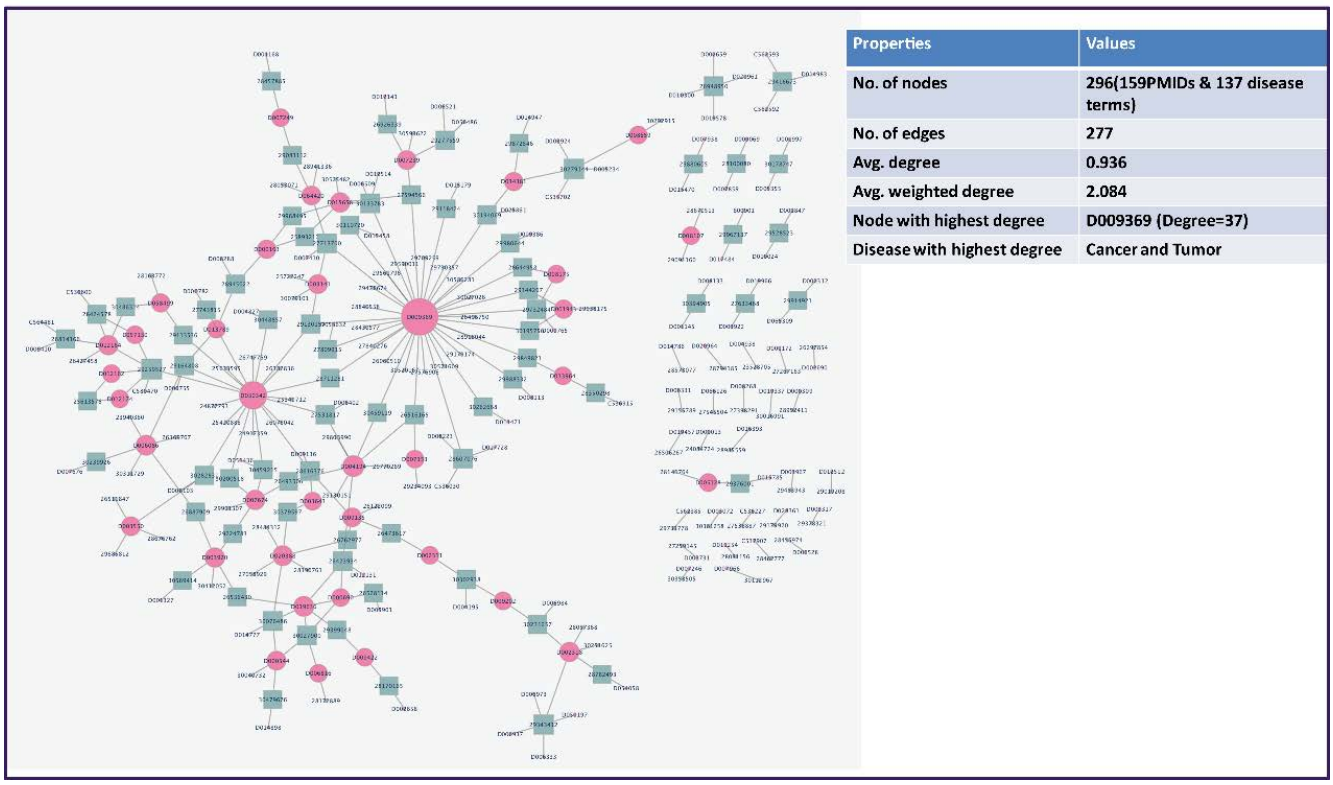

Properties	Values
No. of nodes	296(159PMIDs & 137 disease terms)
No. of edges	277
Avg. degree	0.936
Avg. weighted degree	2.084
Node with highest degree	D009369 (Degree=37)
Disease with highest degree	Cancer and Tumor

Figure 1: A conceptual framework on interaction network analysis between diseases and its research using CRISPR tool available in PubMed. The disease information for the respective code is provided in the Supplementary Table 1. The important properties of the network analysis are presented in the tabular form.

develop personalized medicine [2]. On the gene level, the altered form of tumour suppressor gene *p53*, present in most of the cancer cells were restored using CRISPR approach [11].

Discussion

Other emerging tumour suppressor genes are the *STAG1* and *STAG2*, a core component of cohesion. Through a vector-free CRISPR system, double gene knockout of *STAG1*/*STAG2* significantly reduces tumour cell proliferation [8]. Among the potential strategies developed, specific targeting of viral cancer drivers and oncogenes were one of them [12]. The tumor sphere formation was reduced in breast cancer cells using the CRISPR gene targeting [13]. Moreover, a gene target therapeutic platform was developed by taking the datasets of cancer and tumour using CRISPR tool on epidermal growth factor that effectively reduced the oncogenicity in thyroid cancer [14]. Similarly, using CRISPR mediated loss of dihydrotestosterone-inactivation activity promotes prostate cancer castration resistance [15]. Thus, CRISPR approach has many potential applications in medical research for studying cancer and tumour diseases.

Conclusion

With the availability of huge literature on public domains, it has become very difficult to review them manually. However, approaches such as scientometrics and text-mining have become very powerful data mining tools which grabbed the attention of researchers from any field, especially due to increasing number of inter-disciplinary researches. The current study analysed the reports related to use of CRISPR tools in medical research thereby revealing cancer and tumour diseases (D009369) as the most prominently studied area. Also, this approach for identifying the mostly studied area using text mining can be useful to other important areas within very short duration. Overall, the review work revealed that CRISPR plays important role in medical research for disease diagnosis, treatment as well as disease study.

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