

Grant Proposal

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April 25,2018

Frontiers in Bio Sciences

A. Title: Rise in Recent Diagnosis of Colorectal Cancer in Young Individuals Can Be Linked to Mutations in the APC gene

B. Abstract

Recently, Colorectal Cancer in young individuals has been on the rise. There is no clear reason for this abrupt change. Medical doctors and scientists are still divided on the reasons behind this trend. There is limited knowledge on how to prevent, fight and treat this condition in young individuals. There is a confusion on whether this condition in the younger individuals is similar as that in old individuals.

This research aims at answering the question: Why are younger adults recently developing Colorectal Cancer? Are external factors involved? In answering this question the research aims at achieving several objectives including: comparing mutations in the colorectal cancer tumor cells between the older and younger individuals to understand reasons for the recent increase in the rate of the younger people contracting CRC determining whether Colorectal cancer in older people is similar to that of the younger individuals to understand whether environmental, genetics, diabetes or obesity can be considered risk factors for early development of colorectal cancer. This research will focus on which factors can affect the APC gene which is a tumor suppressor gene. Mutations in the APC gene causes genetic instability and selective advantage in the clonal expansion which are two factors required for the development of CRC in individuals. Using next generation sequencing, the mutations in the CRC tumor cells specifically in the APC gene from older vs. younger individual will be compared looking for differences. Once the differences are identified CRISPR will be used to change the mutation in the APC gene and see if it changes tumor growth.

The impacts that this research will have in the field include bringing a more understanding of the APC gene mutation in CRC and how to treat it, identify the risk factors and setting for more scientific research on CRC and determine the right medication for each group. The significance of this research includes developing new methods of treating and preventing CRC in the younger population which is currently unknown. Basically, this research will add more knowledge to this field and provide additional support for already existing concepts.

C. Research Plan

Introduction

Colorectal cancer (CRC) for long has been a common phenomenon among people of old age. However, this trend is changing drastically. Recently, the rates for young individuals contracting this phenomenon has been on the rise. Colorectal cancer is the second leading cause of cancer morbidity and mortality worldwide with a total number of deaths reaching 600,000 globally annually. About 8% of all cancer deaths is caused by colorectal cancer (CRC).

This research will focus on why are younger adults recently developing Colorectal Cancer and if external factors are involved causing a mutation in the APC gene. The first mutation commonly occurs in the APC gene which acts as a central gatekeeper protein in colorectal tumorigenesis. This gene is

classified as tumor suppressor gene which prevents the uncontrolled growth of the cells. APC protein helps to suppress tumor and a failure in this gene causes cells to grow and multiply leading to tumor.

Despite this condition being common and a major cause for cancer there is limited knowledge about the etiology and pathogenesis of CRC in the young individuals. Scientists are divided and unsure whether colorectal cancer (CRC) in older individuals and the younger individuals are similar or different and thus can be treated similarly or differently. The risk factors for Colorectal Cancer can include environmental, genetics, diabetes and obesity. This is just an assumption and there is no scientific evidence to prove or rather confirm this.

Research aims

To understand this problem, we will be analyzing young and adult mice, both with CRC tumor cells, by using next generation sequencing. This technology will focus on looking for insertions, substitutions or deletions that will give us accurate genome information. The analysis between the young and older individuals will majorly involve comparing the mutations in CRC tumor cells for older people and for the younger people. The comparison will display differences or similarities between the mutations in the two categories. The last part of the methodology will involve using CRISPR to change the mutation in the APC gene of adults and young individuals and look if it affects tumor growth. This technology will focus on the genome editing by undergoing precise deletion, insertion or replacement in the APC gene. By looking at this gene specifically, we will be able to determine the different reasons of why this gene undergoes alterations.

The first aim of this research is to compare mutations in the colorectal cancer (CRC) tumor cells between older individuals and younger individuals by analyzing and looking for differences between them using next generation sequencing. This will help understand reasons for the recent increase in the rate of the younger people contracting CRC.

The second aim of this research is to determine whether Colorectal cancer in older people is similar to that of the younger people and whether they can be treated similarly. Mutations in the APC gene in mice that were compared in aim one will be changed using Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR). This will also help understand whether environmental, diabetes, genetic or obesity are affecting the tumor growth and can be considered risk factors.

The expected outcomes of this research are a clear understanding of the cause for increased rates for this condition in the young individuals. It will also bring the difference or similarity of this condition between the older individuals and younger individuals. The findings of this research will have a great impact in the field. It will bring an understanding on how to treat CRC in the young individuals and why rates have increased. It will also make clear the risk factors of this condition which will be useful in putting precautionary or preventive measures. The outcomes of the research in a large extent will set a background to do more research on APC mutations that are causing CRC and determine the right medication for each group.

D. Background and Significance

Cancer has been the major cause for deaths in the world. It is estimated that about 600,000 people die annually from cancer. Colorectal cancer is considered the second major cause for cancer contraction and death. It is estimated that about 8% of all cancer deaths is caused by colorectal cancer (CRC). This is an extremely large number. For long, Colorectal Cancer has been mainly associated with old individuals but this trend is changing as the number of younger people are increasing. There is limited knowledge by scientists about CRC condition in young people and do not clearly understand the difference for this condition in the older and younger individuals. They are in dilemma whether the medication for the older individuals should be the same for the younger people. According to McDowell, S. (2017), the death rate as a result of colorectal cancer in the young individuals has been increasing since 2004. It gives three reasons as to why this has been increased. He explains that for long CRC has been thought to be a condition of people who are old resulting to delay in screening in the young people at early stage. He also explains that younger people who had a relative with this condition have high risk of contracting CRC.

There are many conditions related to genetic changes and Colorectal Cancer is one of them. The APC protein helps to suppress tumor and how a failure in this protein causes cells to grow and multiply leading to tumor. For Colon Cancer to develop two things must occur: genetic instability, that helps in the tumor progression, and enabling of selective advantage which is caused by the APC gene when mutated. This affects the Wnt pathways which are in charge of tissue generation, in this case in the intestine. When APC gene is mutated it creates genetic instability and selective advantage in the clonal expansion which generates more mutant cells that will expand. Clonal expansion can be defined as the meaning of natural selection in cancer. Therefore, when the APC gene is mutated clonal expansion occurs generating more mutant cells affecting the tissue generation of the intestine which leads to the development of colorectal cancer.

This research problem is significant in that it will bring an understanding of APC gene mutations in CRC in younger individuals and help develop new methods, preventive measures and treatment. This will prevent more deaths caused by cancer that is brought by this condition. According to Campos, F. (2017), colorectal cancer in younger adults is difficult to understand. This has made its treatment and prevention difficult. He explains why colorectal cancer in younger individuals is a complicated condition that calls serious and detailed research in the medical field. The difficulties when dealing with CRC in younger individuals is complicated by issues such as stage of diagnosis, biological aggressiveness and treatment outcomes.

The project also brings solution to the challenge that has befallen scientists on how to treat this condition in the younger individuals. Basically, this research will add more knowledge to this field specifically about the APC gene and its behavior regarding Colorectal Cancer development in young individuals.

E. References

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