Microreviews in Cell and Molecular Biology 2012

MicroRNA Cause of Cancer?

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Key Words:
MicroRNA, regulator, cancer, mutations, deletions, over expression, under expression

Cancer is one of the leading causes of death in the world today. While we know more about the development and treatment of cancer than we did twenty years ago there are still many unanswered questions. Questions such as, what are the primary causes of cancer? Where does it start? And why does cancer occur? Knowing the answers to these questions is important in learning what we can do to treat cancer or even to prevent cancerous cells from forming. One finding that may be important for answering these questions is the presence of microRNA (miRNA), discovered in 1993. Over-expression or reduced-expression of miRNA has been found in many cancerous cells. In this article we will examine miRNA in ovarian cancer. Over-expression and reduced-expression of miRNA occur in many types of cancer. Currently scientists are trying to find ways to manipulate miRNA by adding miRNA or anti-miRNA, in order to suppress and hopefully one day prevent cancer cells from forming.

Introduction

Small, non-coding RNA known as miRNA are regulators of various gene expressions. They bind to complimentary sequences of messenger RNA, repressing translation and even aiding in translation when needed. MiRNA organize and silence the expression of certain protein-coding genes, in other words, they regulate translation (2, 4). Cancer is believed to be caused by mutations and deletions in protein genes. These proteins include oncogenic and tumor-suppressor genes (1). Activated oncogenic genes can cause cells that should die (cancerous cells), to instead survive and proliferate. A tumor-suppressor gene is an anti-oncogenic gene that protects a cell from progressing to cancer. When miRNA does not work properly oncogenic genes may be allowed to multiply or tumor-suppressor genes may not work, causing cancer to develop in cells. It is MiRNA's job to turn off oncogenic genes and to turn on tumor suppressor genes. Over expression of certain types of miRNA and low expression of others correlates with the types of cancer cells present. Different forms of miRNA include, but are not limited to, *miR-155*, *let-7*, *MiR-200*, *and MiR200a*. In B-cell lymphoma, higher levels of *miR-155* are present and in most malignancies the expression of *let-7* is reduced, this shows that different types of miRNA cause different types of cancers (3). In ovarian cancer cells it has been found that miRNA helps to regulate oocyte maturation and follicular development. Although it is much needed in the ovaries, miRNA can also be harmful. MiR-200a, miR-141, miR-200c and miR-200b tend to be over expressed and miR-199a, miR140, miR145 and miR-125b1 tend to be under expressed in ovarian cancer cells as compared to normal cells (4). A short list of MiRNA expressions in other cancerous cells can be seen in Figure 1. Being able to recognize the differences in miRNA expression in cancerous cells versus normal cells can help in diagnosing cancer earlier and further experimental studies could lead to better treatment. MiRNA may be a leading cause of cancer, but it also has positive attributes.

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MiRNA contributes to cell proliferation control, hematopoietic B-cell lineage fate, B-cell survival, brain patterning, pancreatic cell insulin secretion and adipocyte development (1). MiRNA and anti-MiRNA can be used as drugs to induce apoptosis or cell cycle arrest which would both end the progression of a cancerous cell (3). Experiments with mice have been successful with the suppression of many tumors; this is achieved by inhibiting the dysregulation of MiRNA. Dysregulation can be caused by many factors, including deletions and mutations. The dysregulation in the following study is a result of reduced expression of miRNA in liver cancer cells.

Recent Progress

In June 2009, scientists at John Hopkins University discovered after inserting miRNA into mice with aggressive liver cancer, a cancer with reduced levels of miRNA, that the cancer had been suppressed. To do this experiment the scientists injected one group of mice with a micro-containing virus and another group of mice with a control virus that did not contain miRNA using a viral delivery system which delivers genes to the tissues. Both groups of mice had aggressive liver cancer. After just three weeks most of the control group experienced progression of the cancer and most of the experimental group had smaller tumors and some even had an absence of tumors. What was even more amazing was that although the cancer cells were dying rapidly the normal liver cells were not affected. This year, Manjeet Rao, Ph.D., an assistant professor of cellular and structural biology in the School of Medicine and a principal investigator at the Greehey Children's Cancer Research Institute of The University of Texas Health Science Center San Antonio and his research team discovered a type of miRNA that is able to sensitize drug-resistant triple-negative breast cancer to chemotherapy drugs. Triple-negative breast cancer does not respond to hormone drugs and over time becomes resistant to chemotherapy. This makes this type of cancer hard, if not impossible, to treat. The additions of miRNAs caused the cancer to be more sensitive to treatment (6). This could end up being a big step for finding a treatment for this type of cancer and maybe even other forms of cancer.

Discussion

The experiments at John Hopkins University and the Greehey Children's Cancer Research Institute have been great steps for cancer research. The addition of miRNA to tumors with reduced miRNA for treatment was previously just a theory. A little over a decade ago miRNA was only just being discovered. Although the question still remains whether or not these types of treatments will work with humans, these experiments give us hope that we are on the right path to not only treating cancer, but to preventing cells from ever progressing into cancer. Knowing how different types of miRNA expression are linked to cancer may be the key to beating cancer. Individuals may someday be able to have their cells evaluated to see if the cell has a dangerous expression of miRNA. If the expressions are related to those found in cancerous cells, addition of miRNA and anti-miRNA could possibly be used to prevent these cells from progressing into cancer cells.

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Types of Cancer	MiRNA over expression	MiRNA reduced
Breast	MiR-29 MiR-17-92 MiR-21 MiR-222	MiR-34 MiR-145 MiR-29 Let-7 family
Lung	MiR-155 MiR-17-92 MiR-21	Let 7 family MiR-29
Ovarian	MiR-200a MiR-141 MiR-200c MiR-200b	MiR-145 Let-7 family MiR-199a MiR-140 MiR-125b1

Figure 1: Brief summary of MiRNA in cancerous cells compared to normal cells (There are many more types of MiRNA and many other forms of cancer that show differences between MiRNA in cancer cells versus normal cells, this figure simply gives an idea to how many can affect a cell.)

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