**The Relapse of Cancer Stem Cells and the Importance of Their Biomarkers in Cancer Research**

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**Abstract** Biomarkers have become a point of interest to scientific researchers in cancer stem cells when it comes to tumor relapse. Experiments and research have provided data of the probability of relapse by evaluating cancer stem cells in the tumor’s environment. Cancer stem cells are known to have a higher chance to relapse when being compared to regular cancer cells due to their resistance of radiation/chemotherapy. The biomarkers on cancers that are known for high mortality rates have been conducted in numerous studies in the relativeness of treatment in cancer patients. It has been concluded in studies that cancer therapy may differ to each patient and perhaps may require a second type or alternative of treatment based on the tumor’s characteristics.

**Key Words:**

Cancer stem cells, tumor growth, biomarkers, cancer treatment, radiation therapy, radiation resistance, chemotherapy, cancer treatment resistance, CD44, CD123, CD33, cancer studies, tumors, cancer research, cancer biomarkers

**Introduction**

For many years, biomarkers have been utilized in the early detection and prevention of cancer. In recognition of modern technology and scientific research, the study of biomarkers has advanced profoundly. This has given scientific researchers the opportunity to evaluate cancer patients extensively when it comes to treatment and prevention. Researchers have studied abnormal biomarkers before and after patients have undergone cancer treatment. More specifically, the interest that has sparked these scientific researchers are the biomarkers that are located on cancer stem cells. Cancer stem cells differ from the regular cancer cells because they are considered more malicious, since they tend to relapse and prohibit tumor cell growth. Just in the last two years, researchers have undergone numerous experiments on these unique biomarkers that are located on cancer stem cells. Many scientists hypothesize that cancer stem cells undergo significant changes while a cancer patient receives radiation treatment, these changes being exasperated. These undesired effects can eventually lead to relapse and even metastasis. Because of this, it has been researchers’ goals to identify the biomarkers on cancer stem cells and to remove these radiation-resistant cells, including the cancer stem cells themselves when it comes to therapeutic strategies in cancer patients.

 Regarding new treatments, researchers have started to introduce the possibility of using a strategy that utilizes lab created receptors that bind to the cancer stem cells. The primary goal for these artificial receptors is to ultimately remove the cancer stem cells. Scientific researchers that are involved in this undergoing study are aiming for this method to be given to cancer patients who are affected by the cancers with the highest death rates, such as lung, colorectal, and gastric cancers. However, this can be considered a very difficult task to achieve because these cancers have all different stem cell characteristics. Therefore, tailored treatments would be required for each different cancer to eliminate it entirely in the cancer patient.

Tumor cells that are the biggest in size become the center of interest when it comes to depletion. Although, upon the success, cancer stem cells may still survive. Furthermore, regular tumor cells alter into a state of growth arrest due to the chemo or radiation therapy. This may cause changes to the tumor’s environment and because of this environmental change, cancer stem cells can be newly constructed. In these types of circumstances, these cells can derive from non-cancerous stem cells or from any cell that has been exposed to chemo or radiation therapy. For this reason, it is vital to understand these cells’ mechanisms in the beginning of their tumor formation and their relapse as well. To gain an understanding of these unique cells, scientists must first examine their biomarkers to get an early recognition of these cancer stem cells that are resistant to chemo and radiation therapy.

**Recent Progress**

A few specific biomarkers that are known to be associated with cancers are CD44, EpCAM, CD123, and CD33. One biomarker in particular that is certainly appealed to scientific researchers when it comes cancer is CD44. This biomarker is known to be very common in many types of cancers and has the reputation to be resistant to chemo and radiation therapy. However, only a few studies have been executed to the biomarker CD44. A strategy that has been executed include a re-conjugate antibody approach against CD44. At first, the effects of this method were beneficial, but the long-term effects were not. However, on a positive outlook, there has been promising results that showed anti-cancer reactions with sarcoma cancers when cytokine killer cells were introduced to the biomarker CD44.

Researchers have also examined the biomarker EpCAM as a consideration when it interacts with certain natural killer cells, this study was performed on colorectal cells. The results showed that it did have an effect against the tumor by blocking its growth and secreting cytokines, this study also resulted in a slower growth of the tumors.

 Studies with the biomarkers CD123 and CD33 have shown some tolerableness. However, the progression of the cancer was still there. Additionally, the trials that were executed resulted in unfavorable effects. The mixture of artificial T Cells and kinase inhibitors have proven to decrease the tumor’s environment, but not tumors that were known to be bigger in size, more specifically in gastric cancers.

Cancer researchers have also directed the center of their attention to targeting a single biomarker, a mixture of therapies into one, and even targeting more than just one biomarker as well. The analyzation of combining more than one biomarker has shown to be the best fit and more appropriate due to the data that has been evaluated in these trials. Although, in specificity, biomarkers CD33 and CD123 was found not to be fit.

Current treatments for tumor removals are surgery and chemo and radiation therapy. These strategies however, prompt damage of DNA and can somewhat be considered as a domino effect, since the DNA damage causes an attraction of immune cell variety. Over time, these anti-tumor effects eventually disappear, causing relapse of the tumor. Factors that promote DNA damage, such as chemo and radiation therapy, have also been a central focus to these cancer researchers because it is such an impacted factor for long-term effects in cancer patients. These treatments have been thought as a mixed blessing because of the immune cell attraction and the results have ending in a good treatment outcome. However, this can act as a promotion for cancer stem cell growth as well.

In conclusion, numerous studies have shown how vital it is to determine the tumor’s environment before and after cancer treatment. Since every individual has unique biomarkers, cancer patients’ treatment would need to be customizable due to that tumor’s makeup. Once a patient’s treatment strategy has been placed, the efficiency of their treatment will improve and the side effects will decrease as well.

**Discussion**

The overall look on these biomarker studies have validated the importance of evaluating the tumor’s environment before and after treatments have started to be introduced to cancer patients. This is relative to the customizable treatment of each individual cancer patient because their treatment should be influenced by the tumor’s characteristics. The detection of tumor cells post cancer treatment is a key part in these cancer studies because it will determine if a second type of therapy is necessary. Treatments that include the interaction of the artificial T Cells as discussed above, are currently being utilized. These specific treatments so far convey to be comprehensive and low in side effects, no long-term side effects have been noted.

The entire objective of these cancer studies is to meet cancer patients’ treatment requirements that are most appropriate and that will have less side effects. The importance of evaluating the tumor after treatment is to measure its risk of relapse that are influenced on the unique biomarkers. Before determining any type of cancer treatment that is most suitable in a cancer patient, it is important to understand the tumor’s environment beforehand because this allows a direct treatment and therefore, a second type of therapy may not be needed. It is also important to monitor the post treatment phase closely because blood tests are currently unable to detect any changes in the tumor’s environment. This post evaluation also provides data to foresee a second type of treatment in a reasonable time frame and this is important because a relapse may be possible, therefore the potential tumor cells could be eliminated before causing any detrimental damage that is irreversible.

To summarize, the data that has been provided through these studies by scientific researchers have provided an outstanding outline of the biomarkers that are most influential on cancer stem cells and that are also located in the tumor’s environment. It is vital to emphasize the correct diagnostics of these biomarkers pre and post cancer treatment to eliminate the chances of tumor relapse.

When considering therapy in cancer patients, the ideal therapy that is aimed to be created will assist in saving patients from unpleasant side effects and possible tumor relapse.

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