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Multiple Myeloma Cancer and An Overview of the Disease

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Abstract:- Multiple Myeloma, a rare and complex form of blood cancer, presents significant challenges in both diagnosis and treatment. This malignancy arises from malfunctioning plasma cells and is characterized by excessive monoclonal immunoglobulin production, leading to damage to vital organs. Despite advances in cancer research and substantial funding, the disease remains difficult to detect in its early stages. Current treatment options, including chemotherapy, steroids, and stem cell transplantation, are associated with notable side effects. However, the emergence of CRISPR-based genome editing technology offers promising avenues for personalized treatment and novel research approaches, though concerns about off-target effects have slowed clinical adoption. As the battle against Multiple Myeloma continues, CRISPR represents a beacon of hope for more effective and precise interventions in the future. This study aims to explore the disease, the effect of the current treatments, and the possible impact CRISPR may have on finding a cure for the disease and changing the course of treatment.

I. INTRODUCTION

Our body contains trillions of cells, which regularly divide to create new cells. However, when these aging, damaged cells are not destroyed due to errors in cell division, they continue to divide and grow into lumps of tissue known as tumors that may or may not be malignant. Cancer, a disease that has swept the globe since 3000 BC, is another name for these malignant tumors. Despite receiving $5,370.1 million in funding from the National Cancer Institute, the cancer epidemic is still widespread today. In the United States, there will likely be 1,806,590 new instances of cancer in 2020, of which 606,520 individuals will probably pass away[1].

Consequently, cancer got the dreaded moniker "Incurable illness." Cancer spreads throughout the human body, from the bone marrow to the cells of the pancreas. However, if such malignancies are addressed in their early stages, some treatments may still be able to cure them. Multiple Myeloma is one form of blood cancer that does not react to such therapies, a growing issue in cancer research.

[1] "2021 NCI Budget Fact Book - Research Funding - NCI," cgvArticle, May 10, 2022, nciglobal,ncienterprise, https://www.cancer.gov/about-nci/budget/fact-book/data/research-funding.

II. AN OVERVIEW OF MULTIPLE MYELOMA

Plasma cell cancer is known as multiple Myeloma or, more commonly, Kahler's disease. When lymphocyte B cells combat an infection, they develop into plasma cells due to maturation. The antibodies in these plasma cells assist the immune system in assaulting and engulfing pathogens. When Multiple Myeloma is identified, the plasma cells multiply improperly and release excessive monoclonal immunoglobulin (a protein) into the bones and tissues, which can seriously harm internal organs. However, Multiple Myeloma is a very uncommon malignancy that makes up no more than 10% of blood cancers and no more than 2% of all cancers.

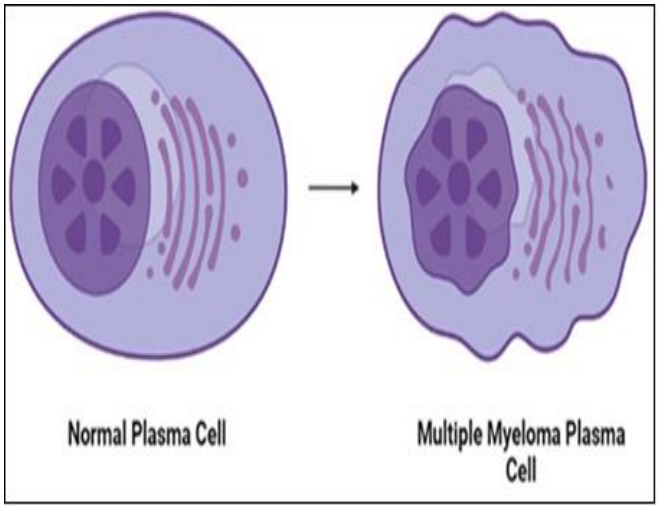

Fig 1 Illustrating the Normal and Diseased Myeloma Cell

These malignant plasma cells can release chemicals that stimulate other cells in the body to eat away at the bone, resulting in weak spots known as lytic lesions. This cancer frequently causes symptoms, including weakness in the arms and legs and recurring infections that cause bone pain, fatigue, dilemmas, and constipation. However, multiple Myeloma often does not manifest these symptoms until later stages. As a result, it is often quite challenging to detect multiple myelomas in their early stages. Blood tests that reveal abnormally high levels of protein in the blood, however, can aid in the early detection of multiple Myeloma. Vague symptoms may occasionally be present. Nevertheless, Myeloma is frequently misinterpreted as another illness.

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III. THE CAUSE OF MULTIPLE MYELOMA

The precise cause of multiple Myeloma is unknown. People with various Myeloma have somatic mutations, which are genetic changes that do not run in families and develop in a person's cells over time. Translocations, or abnormal exchanges of genetic material between chromosomes, are common in the somatic events of multiple Myeloma. (See Fig 2) Most of these translocations involve the exchange of chromosome 14 with another chromosome. These translocations most likely affect the genes that control cell growth and division. Multiple Myeloma is characterized by an increased plasma cell proliferation caused by mutations in genes that control cell division, which may interfere with proper cell growth and division control.

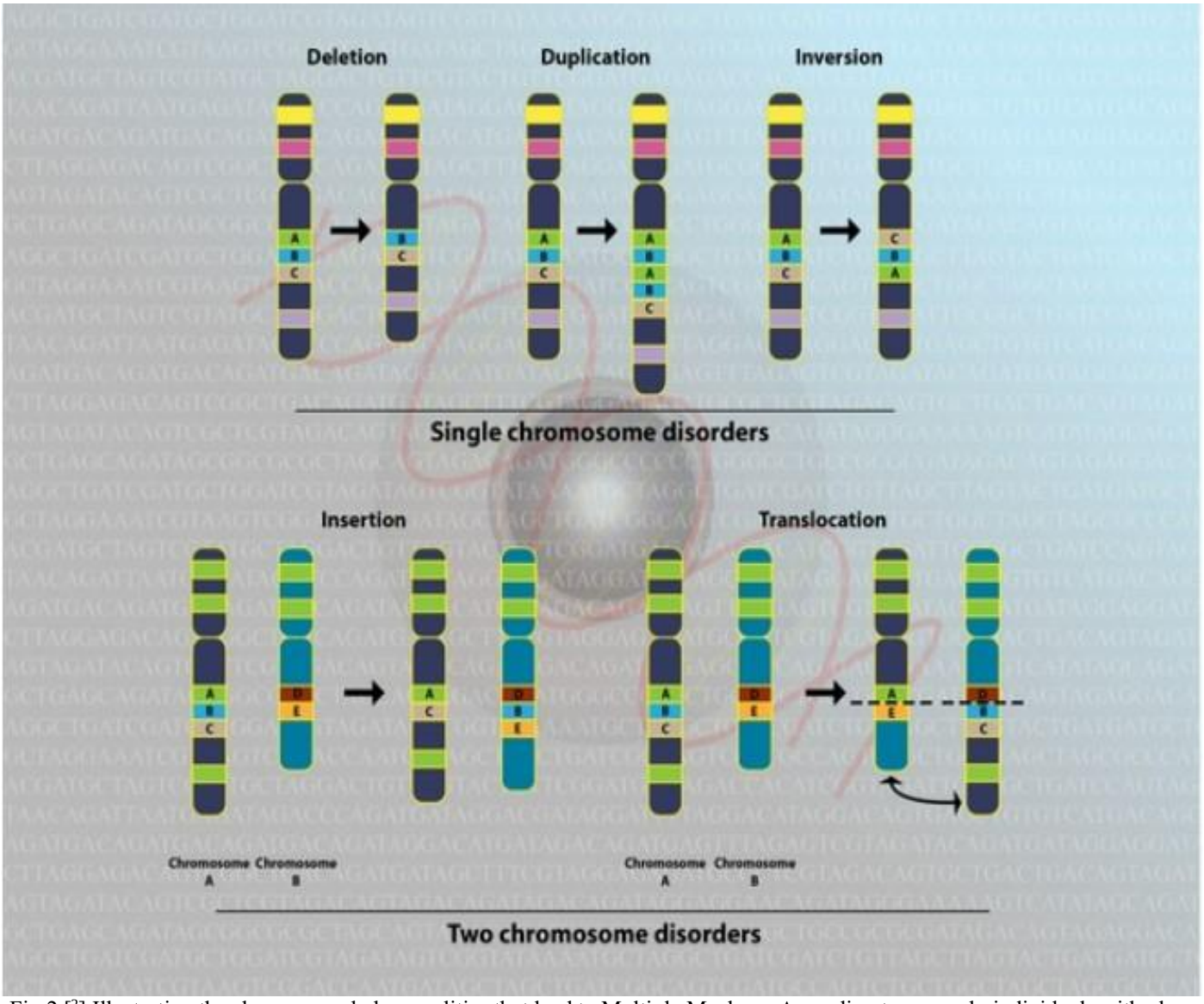

Fig 2 [2] Illustrating the chromosomal abnormalities that lead to Multiple Myeloma According to research, individuals with close family members with multiple Myeloma are more likely to contract the disease themselves. According to this, the development of the condition in certain people may be influenced by inherited differences in specific genes. Like the above, some inherited genetic changes also seem to lower the chance of multiple myeloma development.

[2] "Chromosomal Abnormalities Stock Illustration 248376691," Shutterstock, accessed August 19, 2022, https://www.shutterstock.com/image-illustration/chromosomal-abnormalities-248376691.

IV. TREATMENTS OF MULTIPLE MYELOMA

Not everyone with a Multiple Myeloma diagnosis has cancer's deadly symptoms. The diagnosis of a person with what is known as asymptomatic or smoldering Myeloma is not uncommon. In such circumstances, no therapy is given; instead, the patient is solely watched for any indications that the malignancy may start to cause issues. However, in instances where the patient faces symptoms, the following treatments are used [3]:

- *Chemotherapy:*

The first type of treatment for multiple Myeloma was chemotherapy. Chemotherapy drugs kill myeloma cells by preventing the cancer cells from proliferating, dividing, and creating new cells. Several medications are frequently combined to treat multiple Myeloma in the form of a tablet. These medications include carmustine (BCNU), bendamustine, doxorubicin (a generic drug), etoposide (a generic drug), melphalan (Alkeran, Evomela), cyclophosphamide (a generic drug), and etoposide (Benedek)[3]. However, they have drawbacks, including a higher risk of infections, sickness, hair loss, and nerve damage.

- *Steroids:*

Anti-inflammatory drugs called corticosteroids are used to treat multiple Myeloma because they help chemotherapy work better by helping to kill myeloma cells. The most common steroids used to treat Myeloma are dexamethasone and prednisolone. However, they, too, have side effects such as heartburn, indigestion, increased appetite, mood changes, and insomnia.

- *Immunomodulatory Drugs:*

The two drugs, thalidomide, and lenalidomide have been approved to treat newly diagnosed patients as they inhibit the formation of new blood vessels and feed myeloma cells.

- *Thalidomide*

Thalidomide, frequently advised to be taken every day in the evening, can aid in the death of myeloma cells. Nevertheless, these pills often have more severe side effects, including drowsiness, constipation, dizziness, and numbness or tingling in the hands and feet. The tablet also elevates the risk of blood clots developing; thus, more medications are given to prevent this, but this still results in more adverse impacts. Pregnant women are specifically warned against taking this medication because research has shown that it can lead to birth abnormalities in children [4].

- *Targeted Therapy:*

By focusing on cancer-specific genes, proteins, or the tissue environment that favors cancer survival and growth, targeted treatment, also known as novel therapy, has shown success in recent years in reducing Myeloma and improving prognosis. It stops the growth and spread of cancer cells and significantly reduces harm to healthy cells. To achieve better results than a single drug, targeted therapies are frequently combined with chemotherapy, immunomodulatory drugs, or steroids.

- *Proteasome Inhibitor:*

Inhibitors have shapes like the active site of specific enzymes called proteasomes that digest proteins in the cells. So, these inhibitors bind to the enzyme in place of the substrate, blocking the formation of substrate-enzyme complexes, thus, reducing the number of proteins digested in cells. Because Multiple Myeloma cells produce much protein, they are particularly vulnerable to this type of drug as it will result in a protein buildup. One example of a proteasome inhibitor is Bortezomib.

- *Bortezomib*

A protein buildup inside the multiple myeloma cells is brought on by the injection of Bortezomib, which kills the cancer cells. However, just like every drug on the above list, Bortezomib can also cause side effects, some of which are more detrimental than others, such as weakness, tingling, numbness in the arms and legs, burning pain in the muscles, swelling of the lower legs, and shortness of breath. Less severe side effects include fatigue, nausea, and appetite loss.

- *Stem Cell Transplant:*

When higher doses of chemotherapy are used for intensive treatment, it can harm healthy bone marrow. As a result, a stem cell transplant, also known as an autologous transplant, is performed to allow complete bone marrow recovery. During the transplant, the cancerous bone marrow is replaced with highly specialized cells known as hematopoietic stem cells, which can develop into healthy white blood cells, red blood cells, and platelets.

Hematopoietic stem cell transplantation is classified into two types based on the source of the replacement blood stem cells: allogeneic and autologous. Autologous therapy is commonly used in treating Multiple Myeloma, while allogeneic treatment is being studied in clinical trials. Irrespective, they both serve the same purpose of allowing bone marrow recovery.

V. CRISPR IN RESEARCH AND TREATMENT OF MULTIPLE MYELOMA

- *What is CRISPR?*

In recent years, there has been a remarkable advancement in genome editing research and clinical implementation. The Clustered, Regularly Interspaced Short Palindromic Repeats (CRISPR) discovery of the bacterial adaptive immune system and its rapid transformation into a robust and broadly applicable technology that completely revolutionized basic and applied biomedical research is the

[3] "Multiple Myeloma - Types of Treatment," Cancer.Net, July 29, 2015, https://www.cancer.net/cancer-types/multiple-myeloma/types-treatment.

[4] James H. Kim and Anthony R. Scialli, "Thalidomide: The Tragedy of Birth Defects and the Effective Treatment of Disease," *Toxicological Sciences: An Official Journal of the Society of Toxicology* 122, no. 1 (July 2011): 1–6, https://doi.org/10.1093/toxsci/kfr088.

most remarkable. CRISPR implementation makes genome modification easier, faster, and significantly less expensive than any currently available technology. As a result, CRISPR can provide clinicians with new diagnostic and prognostic tools, allowing for more accurate patient stratification and more efficient personalized treatment. It also has enormous potential for developing novel research approaches and future treatment options for various genetic diseases such as multiple myeloma [5].

➢ *CRISPR and Multiple Myeloma*

T cells are extracted from patients and expanded in the laboratory before being genetically engineered to fight Myeloma in the patient's body (See Figure 3). However, researchers are also looking for ways to kill

Multiple Myeloma and make it last longer for longer-lasting responses. Despite the numerous advances made in various parts of the world, such as China, scientists are still unsure what happens when a genome is edited. Because of the concern, many companies want to use CRISPR directly, but they do not know the off-target effects. As a result, there is a delay and hesitation in starting clinical trials.

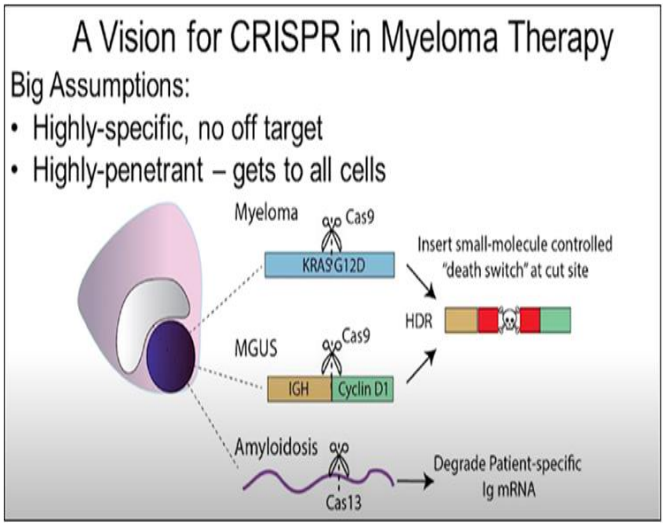

Fig 3 [6][7][8] Illustrating the Mechanism CRISPR Technology will follow to Genetically Engineer Myeloma Cells.

VI. CONCLUSION

Multiple myeloma research has advanced over the past generations, reaching significant milestones; however, researchers have been unable to conduct in-depth research due to a lack of appropriate equipment and infrastructure. "Our knowledge of myeloma genetics remained limited and lagged behind many other hematologic malignancies because of the inherent difficulties in generating metaphases within the malignant plasma cell clone [9]." All the treatment methods provided to patients now seem to have significant side effects, ranging from weakness and appetite loss to heartburn; nonetheless, with CRISPR trials on multiple myeloma cancer, I hope to see oncology taking small steps toward completely curing Multiple Myeloma in the coming years.

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