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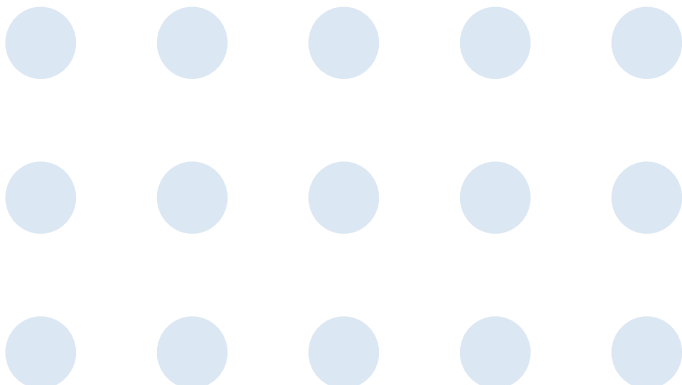
Capstone Project



**SAMPLE**

# Examining the Role of Cancer Care in Reducing Mortality Among Patients

**Abstract**



Over the course of medical history, perceptions of cancer and treatments have changed dramatically. From a view gained in the context of spiritual practice and rooted in religion to the exploration of DNA sequence and epigenetic marks, humankind continues to seek new frontiers and explanations to describe the onset of this malignant disease. One of the most challenging facets of cancer research is due to the inherent intricacies of the disease that affects a plethora of different tissue types, whose claim to survival involves stochastic and cumulative subtle changes in the cell phenotype starting from the common progenitor indistinguishable from the building blocks that we are comprised of.

Due to this, the development of cancer bears many similarities to the progression of several types of infectious disease. Indeed, many similar mechanisms involved in viral surveillance and infection quarantine are employed by the immune system in response to both pathogenic infections as well as tumors. The basis of immunotherapy aims to utilize the paradigm of immune recognition and resolution of disease with the challenges of cancer treatment, which faces many of the same hurdles experienced by immuno-pathologists at the dawn of infectious disease research.

Approaching cancer as a pathogenic disease involves understanding multiple aspects of disease progression, development, and resolution. Much work has already been undertaken in all of these fields, leading to a wellspring of clinical and research observations, which has proved invaluable in formulating new hypotheses and driving potential lifesaving clinical trials. As researchers gain a deeper understanding of the tumor microenvironment as well as the macromolecular interactions involved in growth dysregulation, the role of the immune system becomes more important.

Long viewed as the study of harnessing an organisms' hard-wired defense system against other invasive organisms, immunology is now playing an increasing role in identifying the mechanisms in defending against alterations in itself as well. However, the application of immunology to oncology necessitates more than simply potent immunity activators. Although these drugs are highly popular in clinical trials and pharmaceutical manufacturing, the underlying mechanisms behind the resulting immune response are also exceedingly valuable to expanding the efficacy of these drugs for multiple tumor types and

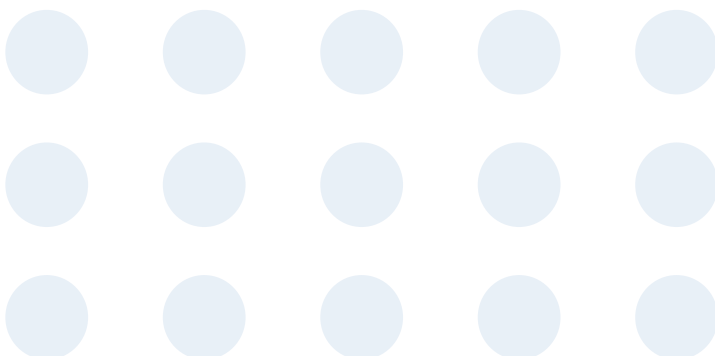
stages. Ultimately, the goal of immunology in cancer research must not only involve the study of immune activation but also explore facets of the tumor phenotype as well as the interactions with the surrounding stroma (Criscitiello, Esposito, & Curigliano, 2014).

As a tumor grows, it can accumulate mutations resulting in subsequent generations of tumor cells appearing almost completely different and autonomous from the original clone. Although it is necessary to eliminate the original tumor cells, it is also worth understanding that tumor cells can also outcompete each other for nutrients and that selection is a powerful tool for tumorigenesis to give rise to more aggressive and more highly dysregulated cells. In order to combat tumors that have passed the stage of immune equilibrium and have started to overcome immune defenses, common strategies for treatment include the surgical removal of the lesion as well as radiation and chemotherapies, which seek to damage rapidly proliferating cells. Although these chemical and physical therapies have proven more effective than remaining treated, it is also worth exploring the risks these methods pose to lymphocytes and other immune cells, which are also highly proliferative and highly sensitive to the effects of radiation and chemo damage from therapeutic agents. However, due to the integrative effects of the cellular damage response, the emergence of neoantigens due to damage and necrosis (James, Chen, & Green, 2016), and surviving lymphocytes, many of the patients receiving this therapy experienced complete remission several years after treatment. In recent years, there has been a move to unite localized radiation therapy with agents to increase immune activation in order to augment the efficacy of either treatment alone. Many ongoing clinical trials are not only exploring new compounds for checkpoint blockade and cytokines but also combining previous treatment regimens to explore synergistic effects between uniting immune-modulating drugs with tumor-modulating agents.

For many years, the mutations acquired in the DNA sequence of tumors have been of great interest to researchers. With the completion of the human genome project, it was hoped that cancer treatment would become more personalized and much more effective. To be sure, the availability of human sequence data has been an integral part of cancer immunology research, but it also has become clear that the DNA sequence itself is not the only factor at play in the field of tumorigenesis.

When clustering common mutations in several types of cancer, there are some particular mutations that are more highly represented in a tumor population, but there are always tumors that do not possess a specific mutation type. Although DNA sequence can provide information about the possible malignancy of a cell based on the type of gene mutated (Ring, Grafstrom, Thorn, Wiman, & Ringborg, 1993), there is also the matter of gene expression – the mutated gene that does not get transcribed is, for all intents and purposes, silent. For this reason, epigenetics is also a highly interesting aspect of tumor immunology that is becoming more significant in many cancer studies. Additionally, protein screens and the quantification of mRNA may serve as better indicators of what functional changes occur in a cell during its transition from a normal cell to a tumor cell. DNMTIs, such as 5-azacytidine and decitabine, have been used to treat diseases such as seizures and lymphomas for over five decades (Gaynon & Baum, 2009). Recently, HDACis have also come to the forefront of cancer therapy, as they seem to augment immune responses to the tumor as well as possibly make the tumor less aggressive. It is possible that epigenetic drugs can force the expression of certain target molecules on the surface of the tumor that can serve as a target for immune cells or at least abrogate the tumor's ability to circumvent the immune response. These drugs can also serve to reprogram lymphocytes themselves, possibly affecting exhaustion, trafficking, and the way antigen is seen.

Many changes in T cells upon activation, including the transition to an effector phenotype and the secretion of IFN- $\gamma$ , are regulated on the epigenetic scale. It is important, therefore, to remember that all therapeutic agents elicit an effect on multiple aspects of the body, including the tumor itself as well as the immune system, which clears the tumor following treatment.



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