

## Cancer its Immune System Influence

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### Historical Background

Cancer disease has been recognized and proven, as far in history, as 5000 years with the Egyptians. Even Hippocrates during his study of body fluids, believed that the presence of black bile in the body, was responsible for cancer. He also used the terms carcinos and carcinoma are words, which relate today in terms commonly referred to as cancer [1,12].

However today, with our greater understanding and detailed knowledge of the immune system, we can appreciate the delicate balance, between our immune system, and the various immune cells, throughout our body. We see how important that balance is, particularly when trying to understand, the metabolic pathways, mechanisms, and complexity that can be involved, when reflecting how cancer occurs, and can interact within our body. This delicate balance can be demonstrated, with the simple interplay that can occur between T regs and Teff's.

These CD4 effector cells or Teff's (special white blood cells) may become overreactive, and instead of fighting infective cells, can at some time attack normal tissue cells. This can lead to an inflammatory response, that may get out of hand. It is T regs responsibility to keep the activity of Teff's in check. However, if for some reason the level of T-regs has diminished, this can allow Teff's to become overactive, and could result in excessive inflammation, and even possibly autoimmune disease. T-regs act by dampening the immune activity of Teff's, by the production of two cytokines, namely interleukin 10 (IL10), and translational growth factor beta (TGFβ). T-regs by these two cytokines, can "disrupt" mTORC1 signaling, in activated Teff cells". In a sense, T-regs ultimately control the translation of messenger RNA in Teff cells [2]. Current research supports the idea, that the "inhibitor rocaglamide A or RocA, may be used therapeutically, since it also has the ability to suppress protein synthesis, thru the "control of RNA translation" [2].

### Other T-cell functions

T-cells as generally recognized in order to become mature cells, must undergo their educational treatment while maturing in the thymus. Part of their T-cell training, involves the distinguishing between host cells, and nonhost tissue cells. Their responsibilities include protecting the body from pathogenic bacteria, viruses, and other disease causing organisms. In addition, they play an important role in recognizing self versus non-self antigens, as well as "regulate inflammation," and may help to "dampen an over reactive immune response. Other immune cells that are similar to T cells, have been described as mimic cells, which can take on the appearance of different tissue types. They are able to do this, by "co-oping various transcription factors, proteins that drive the expression of genes unique to specific tissues". However, these "mimetic cells, may be important in certain autoimmune diseases, and further research is needed [3].

### Recent ideal immunotherapy

Recent research by the University of California- Los Angeles Health Science has explored the idea of utilizing T-cells from cancer patients, and isolating their t-cell receptors. These receptors could be isolated, and reintroduced into a number of patients, “redirecting” the specificity of immune cells against tumor cells, and thus providing “antitumor activity”. It seems possible according to the author, to use T-cell receptors, in order to modify other cells, to attack cancer [4]. Another recently published approach of immunotherapy for treating metastatic breast cancer, centers around the molecule called p38MAPK. By treating p38MAPK with a p38MAPK inhibitor, in addition with immune therapy by an OX40 agonist, test mice had tumor remission for 80 days. Currently different OX40 agonist are being investigated in phase 2 clinical trails, and p38MAPK is being studied in the case of inflammatory diseases, rheumatoid arthritis, and chronic obstructive pulmonary disease [5].

### The blood brain barrier

The brain owes its protection in part to membranes that line the brain. These protective layers are called the meninges, and are composed of both nerve and immune cells. However, microorganisms that try to invade though this layer, when they are able to “exploit nerve cells, and suppress an immune response. Microorganisms when they are able to breach the blood brain barrier; they may enter the brain. This ability to activate pain receptors, and disable immune cells, allows them to be are able to overcome the natural brain barrier defenses, and thus enter the brain [5]. Current research has also demonstrated that certain toxins that activate brain neurons, in the meninges, can signal these neurons to release a signaling compound called CGRP. Its release can attach to an immune-cell receptor called RAMP1. Once the chemical CGRP is released and RAMP1 “engages” the receptor, the immune cell in essence is inoperative. According to the author, blocking either CGRP or RAMP1, should allow immune cells to function properly, and improve the brain barrier protection [5,6].

### Other immune related diseases and treatments

There is now more evidence that neurological diseases such as Alzheimer, may have in part an immunological basis. In an article by Washington University School of Medicine, their research has demonstrated that microglia cells, can “partner” with T cells, and possibly be responsible for “neurodegenerative disease”. Microglia have been found to release compounds, that draw T cells into the brain, which activate T-cells. Treatments may be possibly, by simply preventing the influx of T cells into the brain. This study therefore demonstrates, how T cells can play a “key role,” in tau-related diseases [7]. In a related study, in the treatment of Alzheimer’s disease, PLOS believes that by reducing the methylation of a key messenger RNA, should help to prevent the migration of myeloid cells into the brain, and the maturation of myeloid cells in the brain into macrophages with “resident” microglia, which can help to “consume amyloid-beta” [8].

With ongoing research on Parkinson’s disease, the molecule lissodendoric acid may be important in “counteracting other compounds that can damage DNA, RNA, whole cells and even proteins” [9]. Other research on Parkinson’s disease, has indicated a role in which a protein ring can occur, following exposure to large amounts of copper ions [10].

### Cancer future and predictions

The World Health Organization (WHO) has estimated 10 million deaths have occurred in 2020, due to various forms of cancer. Where the most common cancers are breast, lung, colon, rectum and prostate cancers. A third of cancer deaths are due to tobacco use, high body mass index, alcohol use, poor diet, and lack of physical activity. Nearly 30 - 50% of cancers can be avoided or prevented, by many of the common habits mentioned above. With good standards for early recognition, diagnosis, screening, and proper treatments, these methodologies can help the identification and treatment of cancer [11].

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