PERSPECTIVE

The influence of BMI on adaptive immune cells in human bone marrow

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ABSTRACT

Obesity has been linked to oxidative stress and chronic inflammation. In the aetiology of age-related disorders like immunosenescence, both states are crucial. By secreting chemicals that affect the phenotypic of immune cells, adipose tissue can modify how the immune system responds to foreign invaders. It has been demonstrated in mice that the Bone Marrow (BM) is crucial for the upkeep of adaptive immune cells that have encountered antigens. Recently, various research teams have looked into how long effector/memory T cells can survive in the human BM. Despite this, it is unknown if having a high Body Mass Index (BMI) will have an impact on the generation of chemicals that support the maintenance of immune cells in the BM. In matched BM and PB samples taken from people with various BMIs, the frequency and phenotype of immune cell groups were assessed by flow cytometry. The expression of BM cytokines was also evaluated. Additionally, the effect of Cytomegalovirus (CMV) on T cell subsets was taken into account by separating the donors into CMV- and CMV+ groups. According to our research, a higher BMI may have an impact on the phenotypic and maintenance of adaptive immune cells in the BM. While levels of IL-15 and IL-6, which support the survival of highly differentiated T cells, and oxygen radicals rose in the blood of overweight individuals, $CD8^+$ T cell production of IFN and TNF decreased.

Key Words: *BMI, CMV, T lymphocytes, Bone marrow, Peripheral blood, human*

INTRODUCTION

Subcutaneous adipose tissue and visceral fat accumulate excessively in obesity, which compromises general health and encourages the emergence of a number of illnesses, including age-related disorders. In fact, type 2 diabetes, cancers, and cardiovascular disorders have all been linked to high Body Mass Index (BMI). Obesity has been linked to oxidative stress, chronic inflammation, and other factors that are important in the development of many diseases. In the Peripheral Blood (PB) of obese people, elevated levels of acute phase proteins and pro-inflammatory cytokines including IL-6 and TNF have been observed. Accumulation of fat may have an impact on the frequency and phenotype of lymphocyte populations due to the intimate relationship between adipose tissue and the immune system, which occurs either through the production of soluble mediators or through direct contact. In recent years, numerous studies have shown that the Bone Marrow (BM) is crucial for memory T cells and long-lived plasma cells to be maintained throughout time. Reactive Oxygen Species (ROS) and the pro-inflammatory cytokines IFN and TNF are expressed at high levels in the BM of aged people. In this instance, IL-15 and IL-6 expression is also elevated, supporting the survival of highly differentiated $CD8^+$ T cell subsets in the BM. Furthermore, compared to CMV seronegative individuals, latent Cytomegalovirus (CMV) infection increases IL-15 expression and the frequency of highly differentiated CD28-CCR7-CD45RA bright $CD8^+$ TEMRA cells in the BM. Hematopoietic and skeletal lineage cells surround Marrow Adipose Tissue (MAT), which is found in the bone marrow microenvironment. It is well known that subcutaneous White Adipose Tissue (WAT) regulates metabolism by storing extra energy in the form of triglycerides and supplying fatty acids during fasting. WAT also performs the function of an endocrine organ by creating and secreting adipokines. Our team recently reported that, in compared to White Adipose Tissue (WAT), MAT is characterised by greater ROS levels and produces larger amounts of IL-15, IL-6, and TNF. Furthermore, it has been demonstrated that BM adipocytes compromise plasma cell functionality. At least in mice, increased marrow adiposity has been linked to obesity, and it is reasonable to predict that MAT will have an impact on immune cells that are present in the BM. However, it is unclear if a person's body weight may have an impact on the number and phenotype of immune cells present in the marrow environment as well as the creation of chemicals that support the survival of adaptive immune cells in the Bone Marrow (BM). The effect of body weight on immune cell subset frequency in the BM and niches supporting the survival of adaptive immune cells was evaluated in the current investigation. Additionally,

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in both BM and PB, the phenotypic of T cell subsets in individuals with various BMIs was examined. The studies were carried out separately in CMV - and CMV+ persons since CMV has a significant impact on the frequency and phenotype of T cell subsets. Overweight people had higher levels of ROS and the BM cytokines IL-15 and IL-6, which are known to boost the survival of highly differentiated CD8 + T cells. BMI had an impact on the frequency of B cells, CD4+ T cells, and a number of T cell subsets. In the same scenarios, the BM alterations mirrored the circumstances in the periphery. So, for the first time, our research demonstrates that body weight may influence both the maintenance and phenotypic of adaptive immune cells in the BM.

CONCLUSION

The maintenance of memory T cell subsets in the BM may shift in response to BMI, as our study reports for the first time. In fact, when the markers CD28 and CD57 were taken into consideration, no relationships were found. So, in addition to age and CMV, BMI is another factor to take into account, especially when researching the phenotypic of effector/memory T cells. Planning metabolic therapies will help determine whether the scenario described in overweight people can be reversed, enhancing the ability of adaptive immune cells.