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A new immune signature in people with Polycythemia vera: a modulator of disease progress?

Polycythemia Vera (PV) is a disease in which your body makes too many red blood cells (RBC), whose main function is to transport oxygen from the lungs to all parts of your body. The many circulating RBC makes your blood thicker and with the propensity to form blood clots, which can block blood flow through your arteries and veins and cause stroke or heart attack. In addition to RBC, people with PV can also make too many white blood cells and platelets, which may cause coagulation problems. The major cause of PV is a mutation in a gene called JAK2. This gene produces a protein that controls the formation of blood cells in the bone marrow and when mutated lose this control. It is important to note that the cause of the mutation in the JAK2 gene is unknown and not inherited. However, most investigators think that environmental factors (e.g., smoke, contaminants, diet, etc.) could be the cause of the JAK2 mutation. The disease develops slowly, is silent for many years and is often found during routine blood tests.

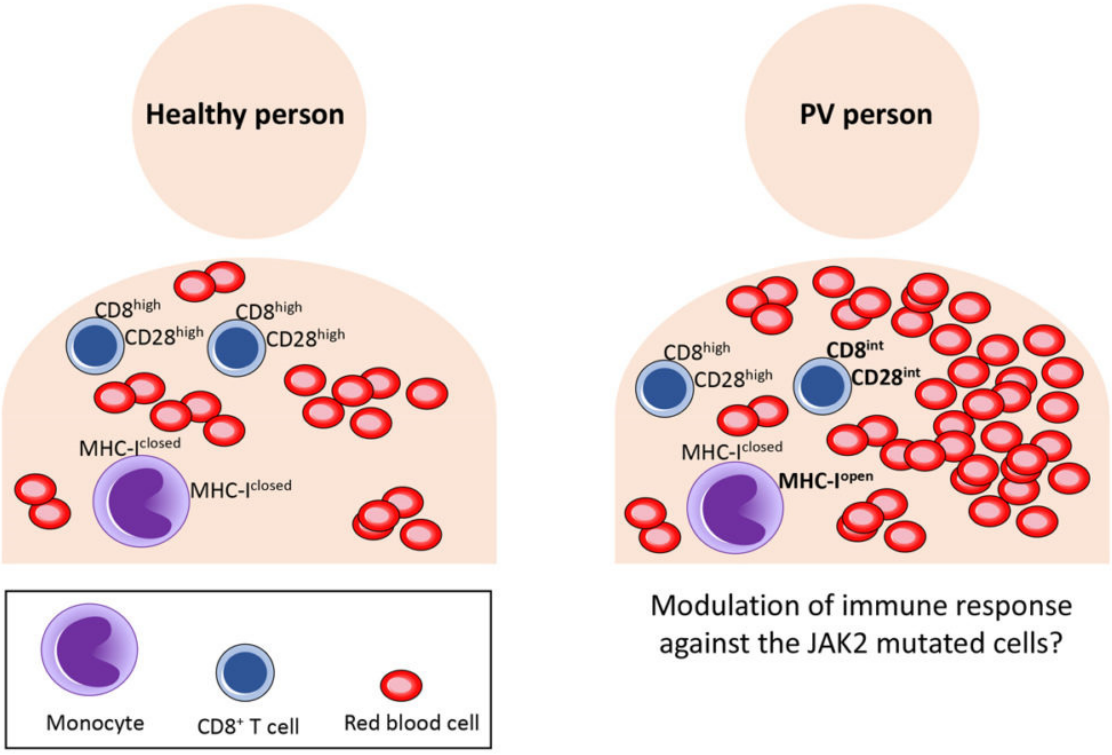

Fig. 1.

Currently, PV doesn't have a cure and the available treatments focus on the reduction of the risk of stroke and heart attack by reducing the number of RBC. These treatments include: 1) phlebotomy, a procedure that removes blood from your body in a process similar to blood donation; 2) administration of Hydroxyurea, a medication that reduces the number of RBC in your blood; and 3) administration of Interferon-alfa (IFNα), a

substance produced normally by your body in response to infections that helps your immune system to destroy the cells with the JAK2 mutation in your bone marrow. All these treatments help lower your RBC number in your blood, thus diminishing blood thickness and normalizing blood flow. A more recent treatment in people with PV that do not respond to the aforementioned classical treatments is Ruxolitinib, a medicine that inhibits the activity of the mutated JAK2. Interestingly, several studies addressing the characterization of immune cells suggest that people with PV have changes in the percentage of T and NK lymphocytes, two population of white blood cells present in the blood circulation and involved in the elimination of mutated and malignant cells, like the bone marrow cells with the JAK2 mutation. In this regard, our recent studies have revealed that most people with PV have a distinct immune signature in their blood (Fig. 1). First, a unique population of T lymphocytes with intermediate expression of the CD8 and CD28 receptors ($CD8^{int}CD28^{int}$). This population of T lymphocytes has alleged features of immune-regulatory cells. Second, the expression of high levels of an alternative form of major histocompatibility complex class I (MHC-I) molecules designated as "open MHC-I conformers" by blood monocytes and lymphocytes. Expression of open MHC-I conformers by lymphoid and myeloid cells has been associated with the regulation of cell function and the modulation of the immune response. The implications of this novel immune signature for the progress of the disease is presently unknown but warrants future investigations (Fig. 1).

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