TUMOR NECROSIS FACTOR (TNF) IN INFLAMMATORY CONDITIONS

DEFINITION OF TUMOR NECROSIS FACTOR (TNF)

Tumor Necrosis Factor (TNF) is an intercellular chemical messenger, or cytokine, that is involved in the inflammatory process. Its primary role is the regulation of immune cells. TNF is produced by various blood cells, such as T lymphocytes, or white blood cells, known as macrophages and monocytes, which are responsible for the body's immune response.

ROLE OF TNF IN IMMUNE RESPONSE

TNF and its receptors play important roles in many immune reactions. During a normal immune response, TNF attaches to certain cells throughout the body, including those in the skin and joints, causing them to release chemicals that can lead to inflammation. Normal inflammatory responses act to defend the body against invading organisms that can cause infection.

TNF exerts its effects by binding with specific TNF receptors on cell surfaces. These transmembrane receptors extend from inside the cell through the cell membrane to the outside. The protruding part of the receptor acts as the lock into which the TNF key fits. These cells also can release their TNF receptors as free-floating molecules or soluble TNF receptors (sTNFR). Whether TNF receptors are still attached to a cell or are in soluble form, they can bind to TNF. TNF that binds to a cell surface receptor can activate the inflammatory response. Conversely, when TNF binds to sTNFR, it inhibits the inflammatory cascade. Ordinarily, the body tightly regulates and balances the amount of TNF produced and the quantity of both cell-surface and soluble forms of the TNF receptors.

AUTOIMMUNE INFLAMMATORY CONDITIONS AND TNF

Autoimmune disorders develop when the immune system destroys normal body tissues. Normally, the immune system is capable of differentiating "self" from "non-self" tissue. If some immune system cells (lymphocytes) become sensitized against "self" tissue cells, these cells are usually controlled by other lymphocytes. Autoimmune disorders occur when the control process is disrupted or when normal body tissue is altered so that it is no longer recognized as "self." There are more than 80 types of autoimmune diseases and a person may experience more than one autoimmune disorder at the same time. Examples of autoimmune (or autoimmune-related) disorders include: rheumatoid arthritis, ankylosing spondylitis, ulcerative colitis psoriasis and Crohn's disease, among others.

As part of the immune response, the body naturally produces the protein TNF-alpha to mobilize white blood cells to fight infections and other invaders. This response temporarily causes inflammation in the affected area. A person with an inflammatory condition is not able to remove TNF-alpha naturally, causing more and more white blood cells to travel to the affected area. As TNF-alpha continues to build up, it causes excessive inflammation, leading to pain and tissue damage.

HOW TNF INHIBITORS WORK

TNF-alpha inhibitors block the action of TNF-alpha in the body. By preventing the effects of TNF-alpha, these drugs reduce inflammation and other signs and symptoms. Autoimmune disorders affect nerves and muscles, as well as the endocrine and digestive systems. The National Institutes of Health (NIH) estimates up to 23.5 million Americans suffer from autoimmune disorders and that the prevalence is rising. These diseases are chronic and can be life-threatening.

TNF-alpha INHIBITOR	INDICATIONS	TYPE
infliximab (Remicade)	- Rheumatoid arthritis - Psoriatic arthritis - Ankylosing spondylitis - Ulcerative colitis - Moderate to severe Crohn's disease	monoclonal antibody
adalimumab (Humira)	- Rheumatoid arthritis - Psoriatic arthritis - Moderate to severe Crohn's disease	monoclonal antibody
etanercept (Enbrel)	- Rheumatoid arthritis - Juvenile rheumatoid arthritis - Psoriatic arthritis - Psoriasis - Ankylosing spondylitis	circulating receptor fusion protein
certolizumab pegol (Cimzia)	- Moderate-to-severe Crohn's disease	monoclonal antibody

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