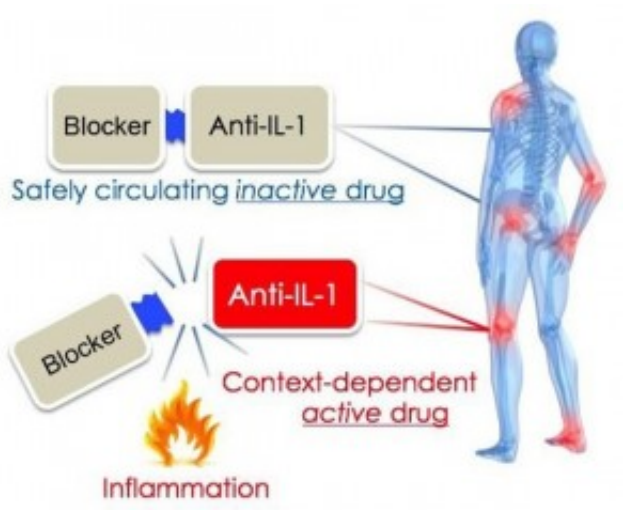
New smart drug targets and reduces site-specific inflammation

July 22 2015



Ben-Gurion University of the Negev (BGU) and University of Colorado researchers have developed a dynamic "smart" drug that targets inflammation in a site-specific manner and could enhance the body's natural ability to fight infection and reduce side effects.

The uniqueness of this novel anti-inflammatory molecule, reported in the current issue of *Journal of Immunology*, can be found in a singular property. When injected, it is as a non-active drug. However, a localized site with excessive inflammation will activate it. Most other anti-

inflammatory agents effectively inhibit inflammatory processes, though in a non-specific manner and in areas that include sites of necessary normal inflammatory homeostasis.

"This development is important because inhibition of inflammation in a non-specific manner reduces the natural ability to fight infections and is a common side effect of anti-inflammatory biologic therapeutics," says Dr. Peleg Rider of BGU's Department of Clinical Biochemistry and Pharmacology.

When a non-specific agent is used, any patient who suffers from local inflammation might then be exposed to opportunistic infections at distant sites, such as lungs, risking, for example, tuberculosis. This risk is mainly of concern to immunosuppressed patients, as well as older patients and patients undergoing chemotherapy as part of an anti-cancer treatment course.

"The beauty of this invention lies in the use of a known natural biological code," Dr. Rider explains. "We mimicked a natural process that occurs during inflammation."

The protein molecule is actually a chimera comprised of two domains, both originating from the potent inflammatory cytokine family of IL-1. The first part of the protein holds the functional part of the molecule inactive, as occurs in normal living cells, and is connected to a potent natural inhibitor of IL-1. When it encounters inflammatory enzymes, the molecule is cleaved and the functional part becomes active.

Dr. Rider, along with BGU's Dr. Eli Lewis and Prof. Charles Dinarello of the University of Colorado, demonstrated their findings in a mouse model of local inflammation. They showed that leukocytes, which infiltrate inflammatory sites, indeed activate the chimeric protein, which in turn reduces local inflammation. The activation of the protein

correlated with the amount of inflammatory stimuli.

"Thus, a point that is highly relevant to clinical practice arises. Upon resolution of inflammation, the activation of the protein is also reduced and side effects are avoided," Dr. Rider explains.

Provided by American Associates, Ben-Gurion University of the Negev