Novel Therapeutic System to Treat Osteoarthritis (Mor)

Dror Robinson, Department of Orthopedics, Rabin Medical Center, HaSharon Campus
Uzi Gafter , Department of Nephrology, Rabin Medical Center.
Zvi Nevo
Talia Weinstein, Hemodialysis Unit, Tel Aviv Sourasky Medical Center.

Background

GAGs (glycoaminoglycans) are the most abundant polysaccharides which play important roles in many body systems. GAGs are major constituents of the extracellular matrix (ECM) of cartilage, skin, blood vessels, synovial fluid, bone and others. Their deficiency is associated with a wide range of disorders.

Along with the high viscosity of GAGs comes low compressibility, which makes these molecules ideal for a lubricating fluid in the joints. When the GAGs found in articular cartilage are reduced or depleted, the body develops various forms of arthritis, including osteoarthritis, leading to a decrease in cartilage thickness and reduced cartilage stiffness.

Osteoarthritis is one of the most frequent causes of physical disability in adults. The disease involves progressive deterioration of articular cartilage with minimal inflammation. Osteoarthritis presently has no cure, and physicians have little hope that a cure will be available in the near future.

The current invention offers a novel therapy focused on increasing or replenishing the level of GAGs in the synovial fluid and cartilage, thereby relieving or even reversing symptoms of the disease.

This strategy may also be applied to aged wrinkled skin.

The Invention

One of the systems that balances GAG synthesis in the body is the renin-angiotensin system, an hormonal system that plays an important role in regulating blood volume, arterial pressure, and cardiac and vascular functions. Studies have shown that when renin-angiotensin levels increase, GAGs content decreases, thus a decrease of renin-angiotensin can be achieved by the administration of inhibitors.

This forms the basis of the Invention, which has been experimented with various kinds of renin-angiotensin inhibitors. These are drugs currently being prescribed for other disorders (e.g. high blood pressure, renal disorder).

The principal investigators have performed many in vitro as well as in vivo trials and established a strong support for their hypothesis. We demonstrated in vivo and in vitro that rennin-angiotensin

inhibitors can activate the de novo synthesis of GAGs and thus replenish the loss of GAGs in osteoarthritis cartilage.

According to this novel therapeutic system, osteoarthritis is treated by the administration of a therapeutically effective amount of renin-angiotensin inhibitor. Dosage amount and interval may be adjusted individually, and the agents are administered locally via injection directly into the synovial fluid of the joint.

To replenish the content of GAGs in the skin, a system delivery such as a topical cream could be utilized.

Market Opportunity

Osteoarthritis

Osteoarthritis is a highly prevalent disease, affecting approximately 12% of the elderly population with the common seven major pharmaceutical markets around the world. In 2003, the number of non-institutionalized adults with symptoms of the disease was 46 million in the United States, about 21% of that country population. In general, women are more susceptible than men.

Since osteoarthritis is associated with aging, the impact of this disease will continue to grow over the next decade as life span and the average age increases. With no cure available, physicians can only attempt to control the symptoms.

It is estimated that the osteoarthritis drug market sales topped $3.5 billion in 2002. The primary drug classes include primarily analgesics, traditional non-steroidal anti-inflammatory drugs (NSAIDs), selective cyclooxygenase (COX-II) inhibitors, and oral and injectable steroids. These treatments do not offer a cure for the disease.

Therefore, a drug that could up-regulate articular GAGs directly could be of therapeutic value, beyond symptomatic effects.

Aged Skin

Aging of the skin leads to the appearance of wrinkles, which are a major topic in dermocosmetology and a market of billions. By immunohistology staining techniques, it has been shown that there is a marked decrease of GAGs in the papillary dermis under wrinkles, combined with an asymmetrical

variation of GAGs on both edges of wrinkles.

These altered elements in skin physiology, makes the development of specific treatments possible in order to mitigate this unwelcome cutaneous deterioration.

Patent Status

The patent "Inhibition of the renin-angiotensin system for the treatment of renal, vascular and cartilage pathology" has entered recently its National Phase.

Contact for more information:

Sari Prutchi-Sagiv PhD, Director of Technology transfer Phamaceuticals, 052-8594444

38 Habarzel st.
Ramat Hahyal, Tel Aviv, 69710
Tel: 972-3-9233227
Fax: 972-3-6233228