## Newsletter - Fighting bladder pain with immunomodulation

Why do we get sick from infections? Where do the symptoms come from? Are the bacteria and viruses toxic for the tissues? Why does our immune system fail to remove bad bacteria or viruses?

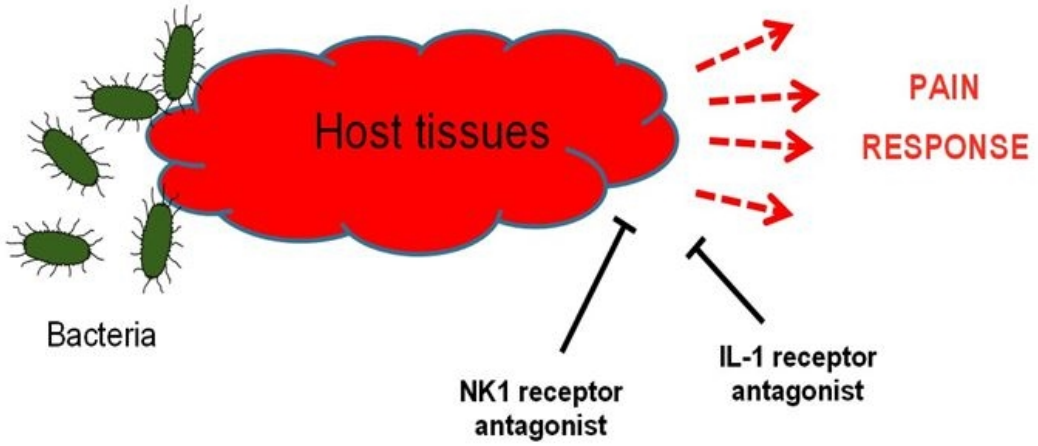
The immune system actually plays a dual role as both protector and cause of disease. It has become increasingly evident that the immune response, which should be our main defense, also is the cause of symptoms during infection, including pain, especially in certain patients where the immune response is poorly controlled and too strong.

SelectImmune Pharma is currently developing a range of different molecules to help the immune system respond more efficiently to infections and reduce the symptoms and disease that they cause.

This newsletter focuses on the pain response to infection and describes the positive results of immunomodulation to achieve pain relief in patients suffering from Bladder Pain Syndrome.

Infections cause pain, in part, by direct bacterial interactions with nerve cells. Pain is sensed by a loop from the infected tissues to the central nervous system, which leads to the sensation of pain. Infection triggers the production of neuropeptides, which are messengers and activate nerve cells by binding to their receptors. Pain is further fueled by inflammation, also triggered by the bacteria, but in other cells that communicate with the nerve cells.

Is there then a way to target the specific process that causes bladder pain, in a way that can help patients?



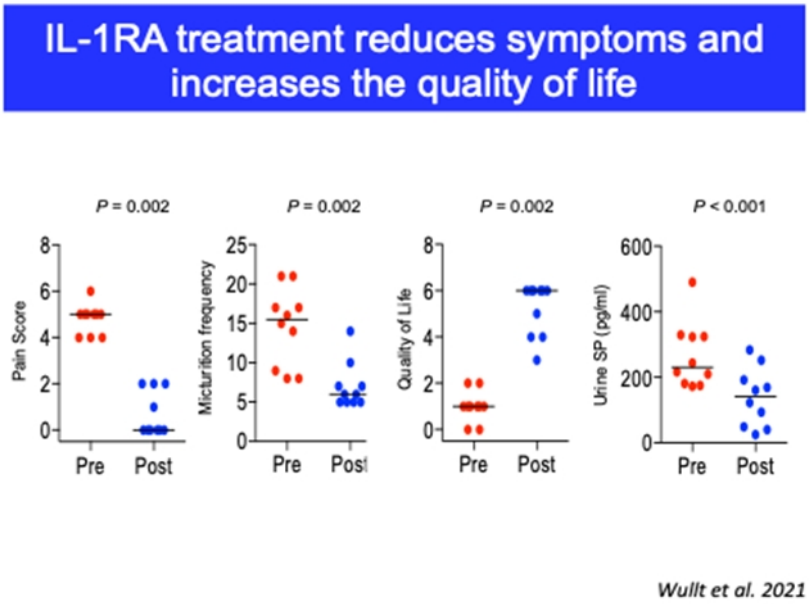

*By analyzing the molecules involved in the pain response, we can find ways of interrupting this process with different substances and reduce the pain. One way is to block the pain receptors in the nerve cells (NK1 receptor antagonist), which is efficient in animal models, but has not yet been tested clinically. A second way is to block the IL-1 receptor in the tissue (IL1 receptor antagonist), which reduces inflammation and pain. This approach has given positive results in patients with bladder pain and is being tested in patients with recurrent cystitis.*

**Immunomodulation – a molecular solution to treating patients with severe bladder pain syndrome?**

Patients with bladder pain syndrome experience debilitating pain at bladder filling, extreme frequency of urination and urgency of micturition, which altogether destroys careers, social life and sexual health. Current therapeutic options are all insufficient, as a number of clinical trials unfortunately have been disappointing. Numerous therapeutic approaches have been tested, but there are currently no specific therapies available. Regular painkillers, or even morphine fails to provide adequate symptom relief and even after surgical removal of damaged parts of the bladder, the pain often returns.

Reducing pain is obviously a key goal in patients with Bladder Pain Syndrome. We have explored immunomodulation as a way to target the specific process that causes bladder pain. In animal models, a receptor antagonist (IL-1RA) was shown to not only reduce inflammation and pain, but also the bacteria.

Based on these results, patients suffering from severe Bladder Pain Syndrome were offered off-label treatment with IL-1RA, which is an already existing drug, approved for use in other diseases.




*Graphs showing patient data before and after treatment with IL-1RA, and the effects on pain and nerve cells. A short treatment reduced pain, micturition frequency and nerve cell activation (SP) and increased the quality of life.*

The results are very promising: the treatment reduced bladder pain and frequency of urination in most of the participating patients, who could return to a more normal lifestyle. Participating patients were able to sleep through the night again. Patients that had needed morphine to cope with the pain, no longer needed it after the treatment. After the initial treatment, a majority of the patients chose to continue IL-1RA treatment long-term.

The encouraging results we have gained so far suggest that IL-1RA therapy might be useful and effective in patients with Bladder Pain Syndrome, but controlled clinical trials should be performed to validate these effects. We are currently making preparations for placebo-controlled trials.

Read more about our work at www.selectimmune.com

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*SelectImmune Pharma is a pharmaceutical company whose shares are traded on the Spotlight Stock Market. The company goal is to develop new immunotherapies, which act as immune enhancers and offer alternatives to antibiotics.*

*Bacterial infections affect large parts of the population and are becoming increasingly difficult to treat due to increasing antibiotic resistance. SelectImmune Pharma develops immunotherapies that can supplement or replace antibiotics. Urinary tract infections (UVI) are one of the world's most common infectious diseases, affecting about 150 million people each year. The need for alternative treatments for bacterial infections is currently very large as are potential markets.*