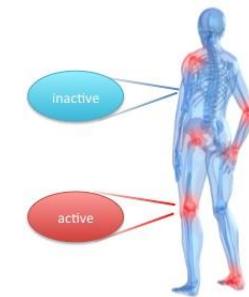


Inflammation-Induced Anti-IL-1 Therapy

Anti interleukin-1 therapy using recombinant IL-1 receptor antagonist (Anakinra) was introduced in 1993 for the treatment of Rheumatoid Arthritis. Since then, emerging evidence indicates beneficial effects of IL-1 receptor antagonist in many other diseases, including the auto-inflammatory diseases RA, CAPS and FMF, as well as myocardial infarction, Type-1 and Type-2 diabetes and multiple myeloma. Accordingly, Anakinra was approved in 2013 for treating NOMID, a neonatal onset multisystem inflammatory disease. The marketing company SOBI (Biovitrum), continues to invest in developing and marketing recombinant IL-1 receptor antagonist under the name Kineret. The major risks in decreasing or eliminating IL-1 include opportunistic infections and neutropenia, since IL-1 serves as a pivotal neutrophil chemoattractant and growth factor. Anakinra has a half-life of about 6 hours, which makes it on the one hand, safe (due to rapid termination of treatment), but on the other hand inferior in as far as patient compliance (multiple injections are required). While the development of anti-IL1 antibodies, which have a half-life of several weeks, solves the pharmacokinetic and patient compliance issue, excessive long term neutralization of IL-1 is also not desired. Thus, there is an unmet need for a drug with a longer half-life than Anakinra and with an optimized safety profile specifically tailored for IL-1 blockade. A drug that can be activated locally at the desired location, without systemic consequences. And lastly, a drug that can be neutralized upon demand, even after administration.



The Technology

Our solution is based on a compound with an IL-1 antagonist activity which is inactive upon injection, and is only induced at the specific site of inflammation. Moreover its activity is relative to the severity of the inflammation (chimeric-IL-1Ra). By this we prevent the decrease in IL-1 activity where not required. In addition, localized blockades of IL-1 activity will allow treating patients with an already compromised immunity (steroids or chemotherapy) for which Anakinra and anti-IL-1 antibodies are currently contraindicated.



Applications

Selected inflammatory conditions that contain a high risk for opportunistic infection and therefore represent attractive candidates for chimeric-IL-1Ra treatment are:

- Melanoma and Breast Cancer
- Lung metastases
- Rheumatoid arthritis
- Gout
- Liver pathologies
- Type 1 Diabetes
- Pancreatic islet transplantation

Probe cleavage was assayed *in vivo*. Left footpad was injected with LPS, and as a result inflammation was observed in the foot joint. Following the development of the inflammation the mice were injected systemically through the tail vein with the quenched probe and were scanned using an *in vivo* imager. **The results show that the probe was cleaved only at the inflammation site and only in the treated mice.**

Patent Status

Patent Pending

Research Team

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