Treatment for Inflammatory Diseases and Cancer

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Overview

The development of kinase inhibitors to treat inflammatory diseases was proved beneficial, however, designing specific inhibitors with minimal side effects and prolonged efficacy is challenging as drug resistance often develops. The current technology includes inhibitors that specifically target the nuclear translocation of p38 kinase, thus inhibiting only its proâ€‘inflammatory activities without developing drug resistance. Two types of inhibitors were developed â€“ a uniquely designed peptide and small molecules. The inhibitors were tested in mice models and proved to effectively treat inflammatory bowel disease and prevent chronic inflammation-driven tumor development.

Background and Unmet Need

Inflammatory diseases include a wide variety of conditions that involve chronic inflammation and may contribute to tumor development in various tissues. Targeting the signaling pathways that promote inflammation by kinase inhibitors proved clinically beneficial in treating various inflammatory diseases1. The kinase p38, a central mediator of the inflammatory response, was the subject of many clinical development efforts, however many of them failed due to the very fast development of drug resistance, making the inhibitors ineffective. Therefore, there is a considerable unmet medical need to develop new treatments for inflammatory diseases.

The Solution

Prof. Rony Seger and his team developed new p38 inhibitors that effectively treat inflammatory bowel disease and prevent tumor development.

Technology Essence

Prof. Rony Seger and his team discovered that translocation of p38 to the nucleus, which results in inflammation activation, is dependent on interaction with Î²-like importins2. They further identified the site of interaction and designed accordingly a peptide that was found to prevent nuclear translocation. Small molecules that specifically inhibit p38 translocation to the nucleus were also developed. Since these agents only inhibit the nuclear activities of p38 (such as inflammatory activities) without modulating their cytoplasmic activities, they may serve as a therapeutic agent for inflammatory related diseases without potential side effects.

Applications and Advantages

- An effective treatment for inflammatory diseases and inflammatory induced cancer
- The inhibitors are either a specifically designed peptide or small molecules
- Specific inhibition of the kinase inflammation-related activity to reduce side effects

Development Status

The team developed a peptide and small molecules that specifically inhibit p38 translocation to the nucleus. The peptideâ€™s efficacy was successfully demonstrated in two in vivo model systems: Breast cancer xenograft model and DSS-induced colitis model. Small molecule inhibitors are currently being tested for efficacy, toxicity and safety in the preclinical mouse models.

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References:

Kinase inhibition in autoimmunity and inflammation | Nature Reviews Drug Discovery. Accessed April 29, 2021. https://www.nature.com/articles/s41573-020-0082-8 [1]

The nuclear translocation of the kinases p38 and JNK promotes inflammation-induced cancer | Science Signaling. Accessed April 30, 2021. https://stke.sciencemag.org/content/11/525/eaao3428 [2]

Patent Status

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