

Targeting A Novel Choline Kinase For Rheumatoid Arthritis

Tech ID: 23728 / UC Case 2013-279-0

BACKGROUND

Rheumatoid arthritis (RA) is a systemic autoimmune disease that mainly affects the synovial joints leading to chronic inflammation, joint destruction and loss of function. Pathogenesis of the disease involves a complex interaction between the innate and the adaptive arm of the immune system in concert with the resident synovial fibroblasts. These fibroblasts-like synoviocytes (FLS), which display an aggressive/transformed phenotype, contribute to synovial inflammation and cartilage damage by producing inflammatory mediators, recruiting and activating immune cells, and invading articular cartilage. Although treatment of RA has improved, a significant proportion of patients are partial responders with continued disease activity. Furthermore, the currently available disease modifying drugs do not directly target FLS. Thus, new rationally designed disease modifying agents are needed to replace or complement current therapies.

TECHNOLOGY DESCRIPTION

Choline kinase (ChoK α) is an essential enzyme for phosphatidylcholine biosynthesis and is required for cell proliferation. The enzyme has also been implicated in cancer disease progression, metastasis, and invasiveness. The unique tumor-like behavior of rheumatoid arthritis (RA) fibroblast-like synoviocytes (FLS) led researchers to evaluate whether this pathway could play a role in inflammation and joint damage due to synovitis. Therefore, they examined the expression and function of ChoK α in RA FLS and performed a targeted metabolomics assessment of this pathway. These studies suggest that ChoK α contributes to the rheumatoid aggressive phenotype and that ChoK α inhibition could be an effective strategy for arthritis.

APPLICATIONS

ChoK α inhibitors, already thought to be useful as cancer therapeutics, could also be used to treat rheumatoid arthritis. A small molecule inhibitor that inhibits key signaling molecules in RA has been identified. Though not a NCE, this molecule has the potential to improve efficacy and to overcome limitations of other approaches to treating RA.

ADVANTAGES

Inhibiting this kinase is a novel approach to RA therapy.

RELATED MATERIALS

- [Choline kinase inhibition in rheumatoid arthritis](#). Guma M, Sanchez-Lopez E, Lodi A, Garcia-Carbonell R, Tiziani S, Karin M, Lacal JC, Firestein GS. Ann Rheum Dis. 2014 Oct 1. pii: annrheumdis-2014-205696. doi: 0.1136/annrheumdis-2014-205696. [Epub ahead of print] PMID: 25274633 [PubMed - as supplied by publisher] - 10/01/2014
- [American College of Rheumatology 2013 meeting](#) - 10/28/2013

PATENT STATUS

Patent Pending

CONTACT

University of California, San Diego
Office of Innovation and Commercialization
innovation@ucsd.edu
tel: 858.534.5815.



OTHER INFORMATION

CATEGORIZED AS

- [Medical](#)
- [Disease: Autoimmune and Inflammation](#)

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University of California, San Diego
Office of Innovation and Commercialization
9500 Gilman Drive, MC 0910, ,
La Jolla,CA 92093-0910

Tel: 858.534.5815
innovation@ucsd.edu
<https://innovation.ucsd.edu>
Fax: 858.534.7345

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