Universidad de Alcalá

NEW THERAPEUTIC AGENTS FOR THE TREATMENT OF INFLAMMATORY DISORDERS

TECHNOLOGY OFFER

Code

BIO_UAH_17

Application areas

- Biological Sciences

Type of collaboration

- Technical cooperation
- License agreement

Main researches

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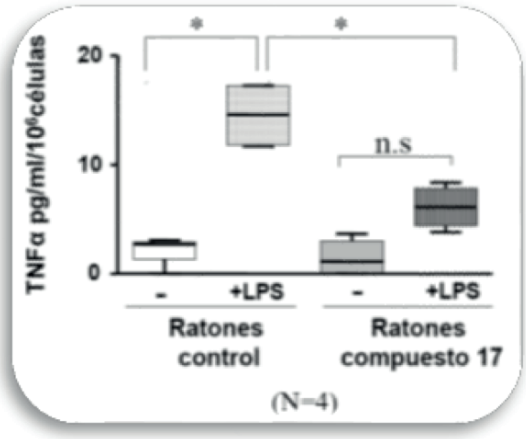

ABSTRACT

New inhibitors of TNF-α production are useful to prevent and/ or treat inflammatory diseases such as rheumatoid arthritis, osteoarthritis, Crohn disease, ulcerative colitis, asthma,bronchitis, chronic obstructive pulmonary disease, psoriasis, allergic rhinitis, ankylosing spondylitis, Hidradenitis suppurative, dermatitis and any other state with TNF-α high levels.

This compounds are capable to inhibit TNF- alpha expression at transcriptional level in primary human monocytes, what suggests that the mechanism could be related with some transcription factor and could regulate also the expression of additional citokinins. The effect seems to be apart independent from p38 MAPK or c-jun activation. The preliminary data suggest that NF-κB activity could be affected.

Besides TNF-α, these compounds also regulate the low production of of IL-1β y de IL-6 in THP-1 cells stimulated with LPS. The response to additional inflammatory stimulus has been explored such as poly I:C (ssRNA analogous) and the results show that this compounds also inhibit the TNF-α production and IL-12 response to stimulation with poly I:C in dendritic human cells differentiated in vitro.

Since metabolic diseases are related to low degree s inflammation, the action of those new inhibitors has been explored in mature human adipocytes produced in vitro from mesenchymal stem cells. The results show a lower regulation that depends on IL-6 production and leptin in human adipocytes stimulated with LPS.

In vivo studies in animal models, previous treated with low doses of this compounds, exhibit significantly lower TNF- alpha production when are subjected to powerful pro-inflammatory stimuli such us LPS. This result indicates that the compounds present anti-inflammatory effectivity when are administrated in vivo.

In relation to safety, long term treatment in mice with low doses of this compounds present absence of kidney, lung or liver toxicity.

ADVANTAGES AND INNOVATIONS

- Less secondary effects than steroidal anti- inflammatory drugs (hormones) and non steroidal anti- inflammatory drugs (NSAIDs) used nowadays.
- Oral administration.