New therapeutic agents for treating inflammatory disorders

A new generation of inhibitors of tumour necrosis factor-alpha (TNF-α) production that are useful for the prevention and / or treatment of inflammatory diseases.

Description and essential characteristics

A new generation of inhibitors of TNF-α production that are useful for the prevention and/or treatment of inflammatory diseases such as rheumatoid arthritis, osteoarthritis, Crohn's disease, ulcerative colitis, asthma, bronchitis, chronic obstructive airways disease, psoriasis, allergic rhinitis, ankylosing spondylitis, hidradenitis supurativa, dermatitis and any other inflammatory condition which evolves with high levels of TNF-α.

These compounds are able to inhibit the expression of TNF-α at the transcriptional level in human primary monocytes, which suggests that the mechanism could be related to the activity of a transcription factor and might also regulate the expression of additional cytokines. The effect seems to be independent of p38 MAPK or c-jun activation. Preliminary data suggest that NFκB activity could be affected.

In addition to TNF-α, these compounds also down-regulate the production of IL-1β and IL-6 in THP-1 cells stimulated with LPS. The response to additional inflammatory stimuli such as poly I:C (an analogue of ssRNA) has been explored, and the results indicate that these compounds also inhibit the production of TNF-α and IL-12 in response to poly I:C stimulation by *in vitro* differentiated human dendritic cells.

Because metabolic diseases are related to low-grade inflammation, the action of the compounds on human mature adipocytes generated *in vitro* from human mesenchimal stem cells has also been explored. The results show a dose-dependent downregulation of IL-6 and leptin production by human adipocytes stimulated with LPS.

In vivo studies in animal models previously treated with low doses of these compounds show significantly less TNF-α production when challenged with a potent proinflammatory stimulus such as LPS. This result indicates that the compounds have anti-inflammatory efficacy when administered *in vivo*.

Regarding safety, long-term treatment of mice with low doses of these compounds shows no toxicity over kidney, lung or liver.

Competitive advantages

These new compounds, in addition to showing marked efficacy in inhibiting proinflammatory cytokine production or signalling (a strategy that has proved to be the most effective in treating inflammation) also allow oral administration, unlike recent anti-inflammatory protein-based biological therapies.

Furthermore, this new generation of inhibitors of TNF-α production have very few side effects, in contrast to the majority of drugs currently available on the market for the treatment of inflammatory disorders, such as steroidal anti-inflammatory agents (hormones), nonsteroidal anti-inflammatory agents (NSAIDs) and humanized anti-TNF-alpha antibodies.

Type of collaboration sought

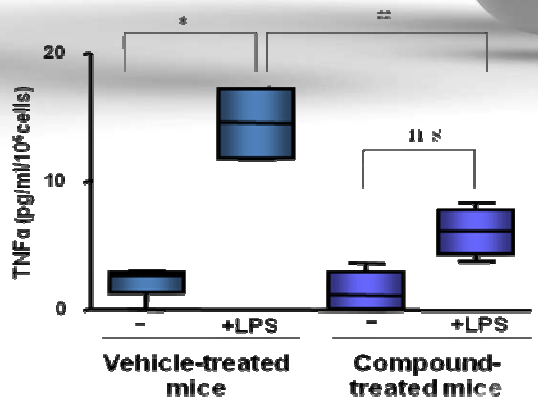
Cooperation is sought with any Party interested in partnering, licensing or investing in the technology, whether it be an investor to fund the project, a partner interested in getting involved in any of the various phases until its placement on the market, a patent licensee, etc. Organisations potentially interested in this technology are those devoted to the manufacture, commercialisation and/or distribution of pharmaceutical drug products; as well as research centres and all types of institutions engaged in inflammatory diseases diagnosis and treatment research.

Current stage of development

In vivo studies on animal models.

Current state of intellectual property

Spanish patents P201331143 and P201430411, granted in December and October 2015, respectively.
International patent application PCT/ES2014/070603.



Effect of *in vivo* administration of one of these new inhibitors.

For further information, please contact

Innovation Unit
Foundation for Biomedical Research of La Paz University Hospital (FIBHULP)-IdiPAZ
Telephone number: +34 91 207 12 34
e-mail: innovacion@idipaz.es
Web: www.idipaz.es

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