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RECOMBINANT B7-H1 FUSION PROTEIN AS A THERAPY CONCEPT FOR MULTIPLE ORGAN FAILURE IN SEPSIS

Technology Offer

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Branch
drug development, drug therapy, sepsis

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Offer
license or co-development

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Introduction

Sepsis and septic shock in response to infection are life threatening complications and among the leading causes of death in industrial society. Death is often the result of multiple organ failure (MOF) resulting from attack on organs by immunocytotoxic mechanisms, including cytotoxic (Tc) T cells. Current approaches to sepsis treatment focus on inhibition of inflammatory and cytotoxic mechanisms in order to suppress disease progression. However, despite recent major advances, the incidence of and mortality due to sepsis continue to increase. There is, therefore, a need for new methods for the prevention and treatment of sepsis.

Invention

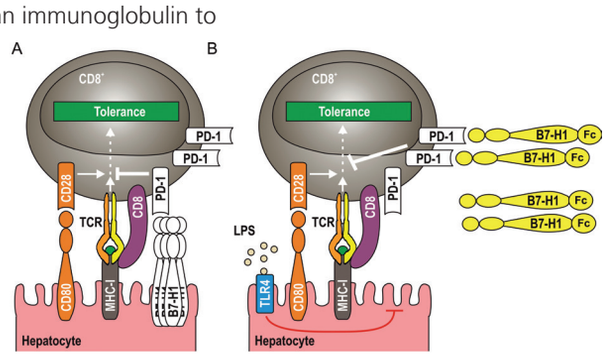
The invention relates to a fusion protein of the extracelluar part of an immunoinhibitory receptor and human immunoglobulin to be used for therapy of sepsis. The inhibitory receptor binds to a ligand on Tc cells and the specificity of the fusion protein can be enhanced by incorporating a binding peptide selective for Tc cells. The major advantage of this fusion protein is that it replaces inhibitory B7-H1 molecules on organs lost during sepsis and induces prolonged tolerance rather than just inhibition of Tc cells. The therapeutic protein thus offers more than just acute inhibition of inflammation. Similar proteins are used for other indications, but their use for sepsis has not been reported previously.

Market Potential

The fusion protein is intended for the acute treatment of sepsis and septic shock.

Development Status

The validity of the invention has been tested in animal experiments.



Activa of cytotoxic T lymphocytes (CTL) towards body´s own tissue during sepsis contributes to liver-(organ-) failure. In the control situation (A) B7-H1, a co-inhibitory protein which is expressed on hepatocytes, blocks CTL-dependent auto-immune activation. Preliminary results showed that addition of a recombinant B7-H1/Fc hybrid protein signifi cantly reduces CTL-dependent cytotoxicity in vitro (B). Using the cecal ligation and perforation (CLP) sepsis mouse model, intravenous application of B7-H1/Fc directly following the operation significantly improves serum markers of liver damage (AST/ALT).