



Technology Offer

Ref.-No. M0912

Methods and compounds for preventing, treating and diagnosing an inflammatory condition

Introduction

Uncontrolled inflammatory activation of the innate immune system plays an important role in infections, sepsis, septic shock, allergies, autoimmunity, as well as in cardiovascular diseases. Recently, so called danger-associated molecular pattern proteins (DAMPs) or alarmins attracted attention. They represent endogenous danger signals inducing inflammatory responses after being released from activated or necrotic cells. S100A8 and S100A9 belong to the group of DAMPs and promote inflammatory processes via activation of Toll-like receptor 4 (TLR4). They are expressed and released at local sites of inflammation in all disorders mentioned above. A hallmark of this invention is the identification of the binding sites of S100A8 and S100A9 for TLR4.

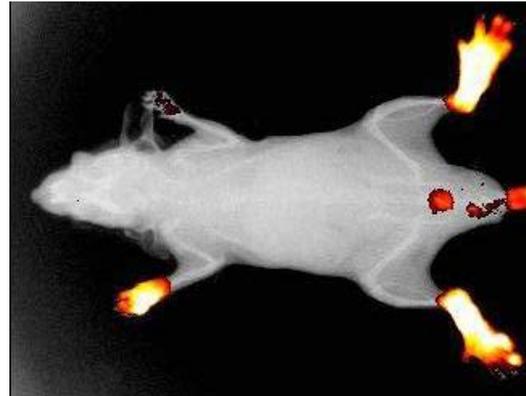
Invention

The invention comprises an antibody with specificity to an epitope of the human protein S100A9 or to an epitope of the human protein S100A8 involved in binding of TLR4.

Provided is further the use of such antibodies in the treatment or diagnosis of an inflammatory disorder.

Also provided is an *in vitro* method of identifying a compound capable of inhibiting the formation of a complex between a peptide corresponding to one of the epitopes of S100A9 or the epitope of S100A8 and a TLR4 receptor.

The invention also describes an *in vitro* method of identifying a compound capable of increasing the stability of a complex between a S100A8 protein and a S100A9 protein, where the two proteins are contacted in the presence of a compound suspected to affect the complex formation.



Local expression of S100A9 in inflamed joints during experimental arthritis shown by fluorescence reflectance imaging (FRI) using Cy5.5 coupled anti-S100A9 antibodies.

Advantages of the invention

Current therapies aimed at blocking TLR4 encompass an increased risk of infections, since such a therapy inevitably likewise blocks the response to bacterial products. Specifically blocking the endogenous TLR4 ligands S100A8 and S100A9 has the advantage to inhibit inflammatory reactions by an approach that avoids these adverse effects. The specific release of these proteins at local sites of inflammation implicates a very selective molecular approach.

New aspects of the invention

The method described in this invention is the first approach to block a member of the DAMP family. Targeting S100A8 and S100A9 in mice has shown major anti-inflammatory effects in many inflammatory conditions.

Patent situation

Patent applications filed in Australia, Canada, China, Europe, Japan and USA.

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