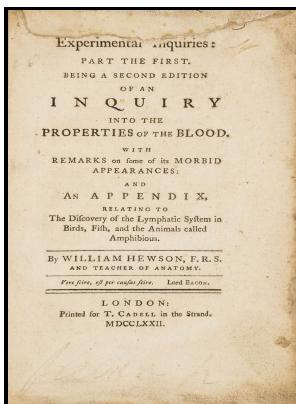


Experimental inquiry into the properties of the blood...

Readex Microprint - TGN1412: From Discovery to Disaster



Description:-

-experimental inquiry into the properties of the blood...

-Landmarks of scienceexperimental inquiry into the properties of the blood...

Notes: Microprint copy of the London edition of 1771.

This edition was published in 1970



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Tags: #TGN1412: #From #Discovery #to #Disaster

TGN1412: From Discovery to Disaster

A mouse antibody used in humans may have toxicity problems related to immunogenicity and problems related to effective functioning of antibody.

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Despite of this observation, sixth volunteer was still infused with the drug. Levels of IL-2, IL-6, and IL-5 were moderately increased in serum in animals treated with TGN1412.

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Thus, depending upon the condition of the immune system TGN1412 was thought to be useful for disease related to low numbers of activated T such as B-cell lymphoma or for treatment of autoimmune diseases such as rheumatoid arthritis. In 2006, a phase I clinical study was conducted for a CD28 superagonist antibody TGN1412 in six human volunteers.

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These results showed that TGN1412 had superagonistic activity for T cells obtained from healthy donars and that they could specifically react with CD28 receptor having sequence homology with human CD28 receptor. In addition, there was no signal from any of the animals treated with any dose of superagonist indicating symptoms of anaphylactic shock or development of autoimmune disease, or systemic immune suppression. In addition, healthy subjects would not only exclude effects of other medications administered to diseased patients, but also exclude the effects of functional activation or dysfunctionalization of T cells as a result of prior diseased condition.

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After these studies, toxicological studies using rhesus and cynomolgus monkeys were conducted. After a drug is confirmed as safe and efficacious in preclinical studies, it is tested in healthy human volunteers for first in man trials. Despite four increasing repeated doses of TGN1412 resulting in four plasma peaks concentrations of TGN1412, only one peak for increase in T-cell number was observed.

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