

MEETING ABSTRACTS

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P506**A novel protein-binding RNA aptamer, Apta-1 - a new therapeutic tool to combat sepsis**

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Introduction:

Sepsis remains one of the major causes of morbidity with mortality rates as high as 50 % worldwide, representing significant clinical challenge to confront highly intangible therapeutic needs. RNA-based structures are emerging as versatile tools encompassing a variety of functions capable to bypass the current protein- and cell-based therapies. RNA aptamers act as disease-associated protein antagonists. Here, the effects of an aptamer, Apta-1, were evaluated in animal models that mimic systemic inflammation in humans.

Methods:

High dose of LPS endotoxin was used to induce systemic inflammation in mice and in non-human primate animal models. Apta-1 was administered intravenously in two doses post LPS infection. Animals were monitored and blood samples collected up to 72 hours after Apta-1 administration. Healthy- and LPS-only treated animals served as control groups. Complex analyses of clinical parameters, hematology, serum biochemistry, inflammation and tissue damage markers were performed.

Results:

Apta-1 increased survival of endotoxin challenged animals up to 80% in a dose-dependent manner and exerted profound effects on well-being and recovery of healthy eating habits. Administration of Apta-1 led to delayed coagulation and enhanced fibrinolysis; maintained the complement cascade activated while preventing it from further amplification. Expression of pro-inflammatory cytokines was reduced while anti-inflammatory increased. Endogenous pro-inflammatory molecules (DAMPs), secreted from injured cells, were preserved at healthy level in animals treated with Apta-1.

Conclusions:

Systemic inflammation and sepsis lead to severe dysregulation of several arms/axis of innate immune response. Our studies showed that Apta-1 affects various components of this system and restores the organism's control over its dysregulated immune response. Thus, Apta-1 might be a promising potential therapeutic candidate to treat life-threatening conditions such sepsis.