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CD95-L dual role in the regulation of experimental autoimmune encephalomyelitis

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Keywords

CD95-L, DNA vaccine, EAE

Context

CD95-L (Fas-L) is a TNF family protein that plays an essential role in both cytotoxicity mediated by cytotoxic T lymphocyte and homeostasis of the immune system. The implication of CD95-ligand-mediated apoptosis in autoimmune diseases is well documented. In some autoimmune diseases, such as systemic lupus erythematosus, CD95-L-mediated apoptosis can prevent disease development whereas in other autoimmune diseases, such as experimental autoimmune encephalomyelitis (EAE) or diabetes, CD95-L-mediated apoptosis can induce disease development. These results have been obtained by using CD95 or CD95-L deficient mice or CD95-L transgenic mice. In this paper, the authors used a DNA vaccine encoding CD95-L to induce CD95-L-specific auto-antibodies. They evaluated the role of this molecule in the regulation of EAE at various stages of disease development.

Significant findings

Naked DNA vaccine encoding CD95-L induces a breakdown of tolerance to membrane bound CD95-L and generates production of anti-CD95-L antibodies. These antibodies can inhibit the development of EAE before or even after the onset of the disease by inhibiting TNF-a production by macrophages and thereafter by inhibiting CD95-L-mediated apoptosis in the central nervous system. By contrast, anti-CD95-L antibodies inhibit the natural recovery from the acute phase of EAE by blocking apoptosis of activated T cells directed against the central nervous system. These results demonstrate the dual role of CD95-L, which can both induce disease development by inducing cell death in the central nervous system, or prevent disease development by killing autoimmune activated T cells.

Comments

Given our current level of understanding, it is as yet impossible to establish a model that explains the controversial role of CD95-L-mediated apoptosis in autoimmune diseases. In this paper, using a DNA vaccine encoding CD95-L during EAE development, the authors showed that the problem is even more difficult because CD95-L can play opposite roles during disease progression. These results suggest that the CD95-CD95-L interaction may play more than one role in the regulation of self-specific autoimmunity. Unfortunately, these results also show that CD95-L is not a good candidate for the development of therapeutic vaccines in autoimmune diseases such as EAE.

Methods

Naked DNA vaccine/EAE induction in lewis rats

References

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