IMMUNOMODULATOR POLYPEPTIDES DERIVED FROM IL-2 AND THEIR USE THEREOF IN THE THERAPEUTIC OF CANCER AND CHRONIC INFECTIONS.

SCOPE OF THE INVENTION.

The present invention is related to the field of biotechnology and particularly immunology. The invention is related to technical solutions with therapeutic applications for human health. It particularly relates to the therapeutic modulation of the immune system using analogs of natural molecules.

PRIOR STATE OF THE ART:

Interleukin 2 (IL-2) was the first growth factor described for T cells. Since its discovery it showed a strong capacity to promote proliferation and survival of T cells *in vitro* (Smith, KA (1988) Science. 240, 1169-76) and to enhance T cells immune response in vivo, in the context of viral infections (Blattman, JN, et al. (2003) Nat Med 9, 540-7) or vaccines (Fishman, M., et al. (2008) J Immunother. 31, 72-80, Kudo-Saito, C ., et al. (2007) Cancer Immunol Immunother. 56, 1897-910; Lin, CT, et al. (2007) Immunol Lett. 114, 86-93). However, this classical role of IL-2 as a promoter of T immune response has been questioned recently by numerous experimental data (Almeida, A.R., *et al.* (2002) J Immunol. 169, 4850-60; de la Rosa, M., *et al.* (2004) Eur J Immunol. 34, 2480-8; Malek, T.R., *et al.* (2004) Nat Rev Immunol. 4, 665-74) showing that this cytokine is a homeostatic growth factor for natural regulatory T cells T CD4 + CD25 + FoxP3 + (Tregs).

Interleukin-2 is a major player in the mechanism by which regulatory T cells suppress the activity and expansion of other effector cells such as CD4 helpers T cells, CD8 cytotoxic T cells and NK cells. Specifically,it has been recently proposed that regulatory T cells suppress other T cells, inducing the local decrease in the levels of IL-2 (Pandiyan, P., *et al.* (2007) Nat Immunol. 8, 1353-62). This suppressive effect is based in: a) their ability to inhibit directly the production of IL-2 by the effector T cells that they suppresses: (Almeida, A.R., *et al.* (2002) J Immunol. 169, 485060; Takahashi, T., *et al.* (1998) Int Immunol. 10, 1969-80; Thornton, A.M., *et al.* (1998) J Exp Med. 188, 287-96; Wolf, M., *et al.* (2001) Eur J Immunol. 31, 1637-45); b) The ability to consume fast and efficiently the IL-2 in their microenvironment (Pandiyan, P., *et al.* (2007) Nat Immunol. 8, 1353-62); and c) its capacity to over-express IL-2 alpha chain receptor (Kuniyasu, Y., *et al.* (2000) Int Immunol. 12, 1145-55), which enables them to use the IL-2 more efficiently when its concentrations are low.

Summarizing, IL-2 is a highly pleiotropic cytokine which is very significant for the biological activity of different cell populations. This property makes IL-2 an important

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