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(54) Title: POLYMER CONJUGATES OF INTERFERON-*BETA* WITH ENHANCED BIOLOGICAL POTENCY

(57) Abstract: Methods are provided for the synthesis of polymer conjugates of cytokines and receptor-binding antagonists thereof, especially a non glycosylated interferon-*beta*, which conjugates retain unusually high biological potency. Preparation of polymer conjugates according to the methods of the present invention diminishes or avoids steric inhibition of receptor-ligand interactions that commonly results from the attachment of polymers to receptor-binding regions of cytokines, as well as to agonistic and antagonistic analogs thereof. The invention also provides conjugates and compositions produced by such methods. The conjugates of the present invention retain a high level of biological potency compared to those produced by traditional polymer coupling methods that are not targeted to avoid receptor-binding domains of cytokines. In assays *in vitro*, the biological potency of the conjugates of non-glycosylated interferon-*beta* of the present invention is substantially higher than that of unconjugated interferon-*beta* and is similar to that of interferon-*beta*-1a that is glycosylated. The conjugates of the present invention also exhibit an extended half-life *in vivo* compared to the corresponding unconjugated cytokine. The present invention also provides kits comprising such conjugates and/or compositions, and methods of use of such conjugates and compositions in a variety of diagnostic, prophylactic, therapeutic and bioprocessing applications, including treatment of multiple sclerosis.