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First-in-class GnRH analog for cancer therapy

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A monoclonal antibody (Mab) designated as GHR106 was generated against the extracellular domain (N1-29 synthetic peptide) of human gonadotropin releasing hormone (GnRH) receptor. It is a first-in-class GnRH analog and can serve as a drug candidate for potential applications in the treatment of human cancers and/or fertility regulations. Both Mabs in murine (mGHR106) or humanized (hGHR106) forms were shown to have comparable specificity and affinity to intact GnRH receptor on cancer cells or to N1-29 synthetic peptides from humans and monkeys. Similar to decapeptide GnRH analogs, both Mabs were shown to induce apoptosis to cultured cancer cells of various tissue origins, including those from the ovary, breast, prostate, and lung. However, both Mabs were also found to induce complement-dependent cytotoxicity (CDC) reaction for lysis of cancer cells, an immune property which is not shared by peptide analogs of GnRH. By using semi-quantitative reverse transcriptase polymerase chain reaction (RT-PCR), both GHR106 Mabs and the GnRH decapeptide antagonist, Antide, were shown to be bioequivalent in terms of their respective effects on genes involved in the proliferation and apoptosis of cancer cells. In addition, GHR106 Mabs have a much longer circulating half-life than GnRH peptide analogs (days versus hours). Based on the results of these studies, it can be concluded that both mGHR106 and hGHR106 are bioequivalent to the GnRH decapeptide antagonist, Antide, in many biological and functional properties. Therefore, hGHR106 can serve as a long-acting alternative to the current decapeptide GnRH antagonists for therapeutic treatments in the immunotherapy of human cancers, including those of gynecologic origin.

Biography

Gregory Lee received his Ph. D from the California Institute of Technology and completed his postdoctoral studies at the University of California, San Diego. He became a full Professor at the University of British Columbia in 1989, and retired in 2012 with the title of Professor Emeritus. He is the co-founder of Vancouver Biotech Ltd. He has published more than 200 papers, including 30 papers in cancer research. He has been serving as an editorial board member of the Journal of Carcinogenesis and Mutagenesis, and the Journal of Cancer Science and Therapy since 2012.

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