Song-Nan Chow et al., Gynecol Obstet 2018, Volume 8
DOI: 10.4172/2161-0932-C4-034

Anti-GnRH receptor monoclonal antibodies are long acting biosimilar GnRH antagonists

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Monoclonal antibodies were generated against a synthetic peptide corresponding to N1-29 sequence located in the extracellular domain of human GnRH receptor. Among the fourteen established monoclonal antibodies GHR103 and GHR106 were shown to have the highest affinity (Kd≈2x10-9 M) to the synthetic peptide as well as to the native GnRH receptor in cancer cell extract as well as those from the anterior pituitary in humans. Through immunoglobulin gene analysis, both GHR103 and GHR106 were shown to have identical DNA sequences in both heavy and light chains of IgG1 subclass. GHR106 was shown to be highly specific to N1-29 peptides derived from GnRH receptor of human and money, but not to that from mouse. Immunohistochemical studies were performed with as many as 30 different cancer cell lines and were found to positively stain more than 80% of cases, irrespective of their tissue origins. Consistent results were obtained with other assays such as Western Blot, indirect immunofluorescence and RT-PCR. Similar to GnRH decapeptide antagonist, Antide, GHR106 was shown to induce apoptosis and inhibit cell proliferation to culturing cancer cells by TUNEL and MTT assays, respectively. Furthermore, GHR106 was shown to induce lysis of cancer cells in culture through complement-dependent cytotoxicity reactions (CDC) which are absent with GnRH peptide analogs. Humanized forms of GHR106 (hGHR106) were generated and found to be bioequivalent to murine GHR106 (mGHR106) as well as to GnRH antagonist, Antide in terms of their respective binding affinity and biological properties. Due to widespread expressions of GnRH receptor among various human cancer, hGHR106 can be bioequivalent alternative to GnRH decapeptide analogs and can serve as the antibody-based anti-cancer drugs of much longer half-life as compared to that of GnRH decapeptide analogs (days vs. hrs.). Furthermore, humanized GHR106 can be long-acting substitute to GnRH decapeptide analog for numerous gynecological indications in fertility regulations and women health.

Biography

Song-Nan Chow has completed his Graduation in the College of Medicine at National Taiwan University (NTU) in 1968 and, PhD in Graduate Institute of Clinical Medicine at National Taiwan University in 1983. He has completed an internship at Maimonides Medical Center, New York City, USA during 1972-1973. He was a Senior Investigator at University of British Columbia, Vancouver, Canada and Eastern Virginia Medical School, Norfolk, USA during March 1984 to August 1984. He served as Professor and Head in Department of Obstetrics & Gynecology, College of Medicine and the Hospital of NTU from 1999 to 2005. He was the Principal Investigator of International HPV-008 Cervical Cancer Vaccine Trial (PATRICIA) during 2004-2010 at National Taiwan University Hospital, Taipei, Taiwan. He got a patent of ovarian cancer biomarker from USA and Taiwan in early 21st century.

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