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Perspective
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GHR106 Monoclonal Antibody is Bioequivalent to GnRH Peptide Analogs

Gregory Lee*

UBC Center for Reproductive Health, Vancouver, Canada

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***Corresponding author:** Gregory Lee, UBC Center for Reproductive Health, Vancouver, Canada, Tel: (604) 325-4602; Fax: (604) 325-4677; Email: cyglee@yahoo.com

Perspective

GnRH (gonadotropin releasing hormone) is a decapeptide hormone and was discovered initially to react with GnRH receptor in the anterior pituitary. This hormone serves to stimulate the release of luteinizing hormone (LH) and follicle stimulating hormone (FSH) for the differentiation and maturations of reproductive functions. Due to the relative short half-life of GnRH (in min) in circulations, numerous peptide analogs were made available to increase the half-life of these GnRH analogs to hours. Due to structural modifications, they were classified into either agonists or antagonists, depending on their respective biological actions [1-3].

GHR106 is one of numerous monoclonal antibodies which were generated against N1-29 peptide in the extracellular domains of human GnRH receptor. It was demonstrated to be bioequivalent to GnRH analogs in many biological actions to GnRH receptor, except that the former has a much longer half-life in circulations (5-21 days) GnRH receptor was also identified in many extra-pituitary normal and malignant cells or tissues, but may play quite different biological roles from that in the anterior pituitary. For example, an antiperiferative effect of GnRH or its analogs on cancer cells have been known for decades and has been the molecular basis of cancer therapy since 1980's. Similarly, a specific monoclonal antibody to GnRH receptor such as GHR106 has been demonstrated to exhibit similar biological actions to cancer cells. Since GHR106 was shown bioequivalent to GnRH peptide analogs, both antibody and peptide analogs should be equally feasible for the treatments of many types of hormone-sensitive cancers, such as those of breast, prostate and ovary, or even pancreases. Although the efficacy of cancer treatment with GnRH peptide analogs is limited and variable, significant therapeutic improvements have been made compared to those of non-targeted chemotherapy.

Research on Development of GHR106 for Anti-Cancer Treatment

Since 2010, extensive biological and immunological studies have been conducted to demonstrate that GHR106 is a bioequivalent analog of GnRH peptide analogs. The induction of apoptosis to cancer cells of different tissue origins was observed for GHR106 (1-10ug/m) and GnRH antagonist, Antide (0.1ug/ml) following 24 to 48 hours' co-incubation with cultured cancer cells. Among the cell lines tested was OC3-VGH (ovary), PC-3(prostate), A549 (lung) and MDA-MB435 (breast). Furthermore, complement-dependent cytotoxicity (CDC) reactions were observed upon incubation of GHR106, but not with GnRH peptide analogs. Humanized forms of GHR106 (hGHR106) were also constructed and found to have identical biological/immunological properties to those of murine GHR106 [4-6].

During the subsequent development of GHR106 as anti-cancer drugs or for anti-cancer treatments, our recent efforts have been focused on the CAR (Chimeric Antigen Receptor) technology in combination with T cell therapy for personalized cancer treatments. Briefly, applications of GHR106 -related CAR-T Cell Therapy can be best achieved by modifying cancer patient's T cells to express chimeric antigen receptors (CAR) to recognize targets (GnRH receptor) on the cancer cell surface. The modified T cells can then be used in vivo to kill cancer cells. The process involves extracting a cancer patient's T cells which can then be transfected with a gene (scFV of hGHR106) specifically against GnRH receptor which is highly expressed on cancer cell surface. Following transfection, the modified T cells can then be expanded in vitro and transfused back to the same patients. The resulting efficacy of immunotherapy can be judged or demonstrated by cytotoxic killings of tumor cells. In view of the long half-life of GHR106 CAR-T cell therapy to cancer patients should be more effective than GnRH peptide analogs for cancer treatments or simply more feasible than the infusion of high quantity of hGHR106 as anti-cancer drugs to cancer patients through passive immunizations.

In addition to the applications for anti-cancer treatments, hGHR106 can also be used to replace GnRH peptide analogs for treatments of numerous indications in women health or fertility regulations. In view of the long half-life of hGHR106 as compared

to that of the peptide GnRH analogs, there might be certain unique benefit in using antibody drugs for clinical treatments in fertility regulations, especially in areas related to women health, such as endometriosis, cystic ovarian syndrome or ovulation inductions involved in vitro fertilization.

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