

GHR106 and RP215 Monoclonal Antibodies for Potential Therapeutic Treatments of Different Types of Breast Cancer

Gregory Lee

UBC Center for Reproductive Health, Vancouver, Canada

Email: leecyg@gmail.com

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Abstract

GnRH receptor and CA215 widely expressed on many cancer surfaces can be suitably targeted, respectively by GHR106 and RP215 monoclonal antibodies for potential therapeutic applications of many human cancers. GHR106 was generated specifically against human GnRH receptor expressed mainly on anterior pituitary and most of cancer cells in humans. RP215 was shown to react with a carbohydrate associated epitope located in the variable regions of cancer cell-expressed immunoglobulin heavy chains designated, in general as CA215. Both antibodies at 1 - 10 µg/ml concentrations were shown to induce apoptosis of many human cancer cells in culture and cause dose-dependent reductions of several different implanted tumors in nude mouse experiments. By using ScFv fragments of either antibody in CAR (chimeric antigen receptor)-T cell constructs, cytotoxic cell killings and cytokine releases were observed upon incubations with targeted cancer cells in culture. Since pan cancer biomarkers are targeted, our effort has been focused more on the therapeutic applications in breast cancer (BCa), including hormone-positive and triple negative breast cancer (TNBC), which are among the most frequently occurring in women worldwide with high mortality rates. Although with less occurring incidence (10% - 20% of BCa), TNBCa with lack of receptor expressions of E2, progesterone and Her-2 has less effective treatment options and carries the worst prognosis due to high degree of metastasis. Therefore, TNBC treatments may become our primary concern. During our previous studies, we have been able to demonstrate high expressions of GnRH receptor among BCa tissue sections as well as TNBC cell lines. Apoptosis was consistently induced with all TNBC cells upon incubation with any of these two target-specific antibodies. Data of these preclinical studies were summarized to highlight the potential target-specific therapy with GHR106 and/or RP215 for the benefit of

patients with different types of breast cancers as well as other medically unmet human cancer.

Keywords

GHR106, RP215, GnRH Receptor, CA215, Cancerous Immunoglobulins, Target Therapy, Breast Cancer and Triple Negative Breast Cancer

1. Introduction

During the last two decades, two monoclonal antibodies, GHR106 and RP215 were generated and identified, respectively to react with distinct pan cancer biomarkers widely expressed on the surface of almost all cancer cells [1]-[3]. GHR106 was raised against extracellular domain peptide of human GnRH receptor [4], whereas RP215 was raised against OC3-VGH ovarian cancer cell extract. RP215 was found to react with a carbohydrate-associated epitope located mainly in the cancer cell-expressed heavy chain immunoglobulins (IgG's) designated in general as CA215, but not in normal IgG's [2]. Our binding/specificity studies revealed that GHR106 is highly specific to cancerous cells or tissues and rarely in normal tissues except in the anterior pituitary and minor reproduction-related tissues. Both GHR106 and RP215 at low concentrations were shown to induce apoptosis to culturing cancer cells of any tissue origins [2]-[5]. When constructed in CAR (chimeric antigen receptor)-T cells through the use of ScFv fragments of either antibody, cytotoxic killings and cytokine release were observed upon incubations with targeted cancer cells [6] [7]. Therefore, we believe that any of these two antibodies can be further developed for potential treatments of human cancer including those of the breast (BCa) (hormone-positive BCa and hormone-negative BCa or TNBCa) [8] [9].

Breast Cancer (BCa) is one of the highest incidence and mortality rates among women (33% and 15%, respectively) worldwide [10]-[12]. 10% - 20% of BCa cases are grouped into TNBCa due to the absence of receptor expressions in E2, progesterone and Her-2. The options for the effective treatments of TNBCa of high mortality rates are limited [10]-[12]. GnRH analogs of small molecular size have been proposed for treatments of TNBC [7]-[9]. However, limited data and progress are available in terms of expression studies of GnRH receptor as well as its implications in proliferation and metastasis of TNBC [12] [13].

Since GnRH receptor and CA215 are known to be important pan cancer biomarkers for proliferation and survival of most cancer cells, either antibody might be useful in targeting different types of BCa for immunotherapy. Therefore, comparative preclinical studies are summarized to assess if either antibody in good formulations is suitable for potential therapeutic treatments of medically unmet TNBCa as well as those of hormone-positive BCa [7] [9].

2. Roles of GnRH Receptor and CA215 as Pan Cancer Biomarkers

2.1. Widespread Expressions of GnRH Receptor and CA215 in Human Cancer Cells Including TNBCa and Hormone-Positive BCa

GHR106 and RP215 antibodies were used as the probes to study specific binding/affinity of human cancer cells derived from different tissue origins [13]. Three different methods were adopted for comparative binding studies, including: 1) Immunohistochemical staining (IHC), 2) Western blot assay, and 3) RT-PCR [1]-[4]. From previous studies with different cancerous tissue sections, it was established that the percentages of positive bindings of GnRH receptor to GHR106 were ranked as follows: Breast (52%), Prostate (86% - 100%), Endometrium (77% - 100%), Ovary (70% - 80%), Renal or Kidney (80%), and Pancreas (57% - 100%). Results of these comprehensive and comparative studies between the binding studies and RT/PCR are consistent with mRNA expressions of GnRH receptor of the cancer cells [7] [8]. IHC studies were performed with RP215 antibody probe, the percentages of positive staining to cancerous tissue sections are given as follows: Ovary (64%), Cervix (84%), Endometrium (78%), Stomach (50%), Colon (44%), Esophagus (76%), Lung (31%), Breast (32%), Liver (5%) and Prostate (9%) [2]-[4].

In this review, two established humanized monoclonal antibodies, GHR106 and RP2215 were selected for cancer therapeutic applications, mainly based on their nature of targeting surface pan cancer biomarkers. Both TNBCa and hormone-positive BCa could be treated with similar level of clinical efficacy. This conclusion was based on the results of our comparative binding studies with numerous cancerous tissue sections and the relative ability of these two antibodies to induce apoptosis to different types of BCa cell lines. For GHR106, it was revealed that hormone-positive BCa and TNBCa were positively stained at 50% - 60% and 74% with GnRH receptor, respectively. This observation may suggest that hormone expressions in BCa are not closely related to their respective hormone expressions. Therefore, we propose that the majority of BCa ($\geq 80\%$) cases which are hormone-positive, can also be targeted effectively by GHR106, similar to that of TNBCa. A similar situation was also applied to the RP215 targeting of all BCa (Table 1 and Table 2).

Table 1. TUNEL apoptosis assay to demonstrate induced apoptosis of cancer cells upon incubation with GHR106 antibody in cell culture.

Cancer cell lines (ATCD)	Antibody Concentration ($\mu\text{g/ml}$)	Incubation Time (hours)	A/N Ratio** (Induced/Spontaneous Apoptosis)
Antide (positive control)*	0.1	48	3.9
1. MDA-MB-435	10	24	4.4
	20	24	7.5
	10	48	2.8

Continued

	10	48	4.4
2. PC-3 (Prostate)*	10	48	4.4
3. T-47D (Breast-H+)**	10	24	4.5
	20	48	6
4. A549 (Lung)	10	24	3.1
	10	48	2.7
5. OC-3-VGH (Ovary)	10	24	3.6
	10	48	4.3

*Decapeptide GnRH antagonist, Antide was used as the positive control; **A/N Ratios are statistically significant at $P < 0.01$; ***Hormone-positive (H+) breast cancer cell line.

Table 2. TUNNEL apoptosis assay to demonstrate induced apoptosis upon incubation with RP215 antibody in cell culture.

Cancer cell line (ATCC)	Antibody Concentration ($\mu\text{g/ml}$)	Incubation Time (hours)	A/N Ratio** (Induced/Spontaneous Apoptosis)
1. MDA-MD-435	10	24	6.1
(Breast, TNBCa)	20	48	5.4
2. PC-3 (Prostate)	10	24	2.7
3. T-47D (Breast-H+)*	10	24	3.8
4. A549 (Lung)	10	24	4
5. C33A (cervix)	10	24	2.9
6. OC-3-VGH (Ovary)	10	24	2.8
	1	48	7.5

*Hormone-positive breast cancer cell line; **All A/N Ratios are statistically significant at $P < 0.01$.

As many as 30 established human cancer cell lines from ATCC were cultured and employed for similar binding staining or expression studies with either GHR106 or RP215 as the binding probe. Generally speaking, either GHR106 or RP215 revealed positive staining, binding or expressions to almost all the tested cell lines ($\geq 95\%$). These include those of Breast (including TNBCa), Ovary, Cervix, Colon, Glioblastoma, Hepatoma, Lung, Lymphoma, melanoma, Neuroblastoma, placenta and Prostate [5]. Consistent with those of IHC studies of cancerous tissue sections, it can be concluded, in general that GnRH receptor and CA215 can be targeted specifically by the corresponding antibody for potential therapeutic treatments of human cancer.

In the case of BCa, the positive staining rates are in the range of 52% and 32%, respectively with GHR106 and RP215 probe [2] [3]. However, all BCa cell lines were positively stained with either antibody probe including those of TNBCa cell lines (MDA-MB-231, MDA-MB-435 and MDA-MB-468), none of which express receptors for E2, progesterone and Her-2. Earlier studies also indicated high ex-

pression rates of 74% for GnRH receptor among TNBCa tissues or cell lines, which can be a good target for GHR106 in therapeutic treatments [8] [9]. IHC studies of a TNBCa cell (MDA-MB-435) with either antibody probe are presented in **Figure 1** as example, together with other human cancer.

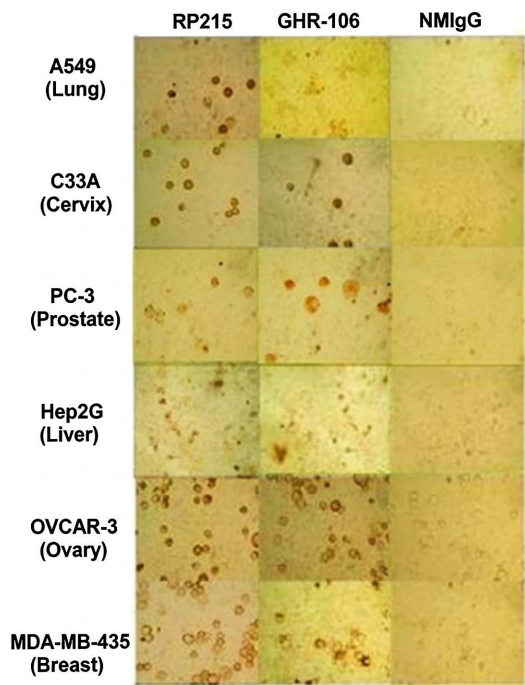


Figure 1. Comparative immunohistochemical staining of six different cancer cell lines using RP215, GHR106 and normal mouse IgG (NMIgG) as the respective binding probes (from left to right). The cancer cell lines from top to bottom are A549 (lung), C33A (cervix), PC-3 (prostate), HeP2G (liver), OVCAR-3 (ovary) and MDA-MB-435 (breast-TNBCa), respectively (Magnification, ×100).

In conclusion, both RP215 and GHR106 can target hormone-positive BCa and TNBCa with little difference in terms of the sensitivity and degrees of positive staining.

2.2. Induced Apoptosis of Cancer Cells upon Interactions with GHR106 or RP215 Antibodies

Through years of preclinical studies, it has been established that apoptosis of culturing cancer cells of many tissue origins was observed upon 24 - 48 hours of co-incubation with either GHR106 or RP215 [1] [3]. Typical examples with a TNBCa cell line, MDA-MB-435 as well as others including those of prostate, lung, cervix and ovary are presented in **Table 1** and **Table 2**. Both cancer cell lines of TNBCa and hormone-positive BCa origins (MDA-MB-435 and T-47D, respectively) were also compared. They were found to have no significant differences in degrees of induced apposes by GHR106 (**Table 1**) or by RP215 (**Table 2**), respectively under the same experimental conditions. Following incubations with 1 - 10 µg/ml of GHR106 or RP215, the degrees of induced apoptosis were determined and as-

sessed by TUNEL assay [3], A/N Ratios [percent of positive/spontaneous (negative)] ratio were included in the same table to facilitate comparisons. GHR106 either in murine or humanized isoforms gave the same degrees of induced cellular apoptosis under the same experimental conditions [3] [14] (Table 1). Antide, a decapeptide GnRH antagonist was used as the positive control and was found to be comparable to GHR106 or RP215 as GnRH antagonist. Similar results were obtained for the effect of RP215 on the apoptosis of TNBCa, hormone-positive BCa and many other cancer cell lines (Table 2). The apoptosis data were graphically presented in Figure 2(A) for comparisons of several cancer cell lines including those of ovary, lung and peptide antagonist, Antide. Antibody-dose dependent apoptosis and GHR106 in different antibody isoforms are also presented in Figure 2(B) for comparisons. Based on the results of these studies, it can be concluded that both antibodies are suitable in clinical treatments of patients with TNBCa or BCa, as well as several others which are medically unmet [12].

3. "Proof of Concept" Nude Mouse Experiments to Demonstrate Anti-Cancer Efficacy of GHR106 and RP215 Monoclonal Antibodies

Antitumor Activities of GHR106 and RP215 in several different human cancer cells were demonstrated with typical nude mouse experiments [5] [14], including that of ovary (OC-3-VGH), cervix (C33A), lung (SK-MES-1), and liver (Hep-2G). Results of these four nude mouse experiments to reveal dose-dependent reductions of implanted tumors upon injections of either RP215 or GHR106 monoclonal antibody were summarized in Table 3 for comparisons.

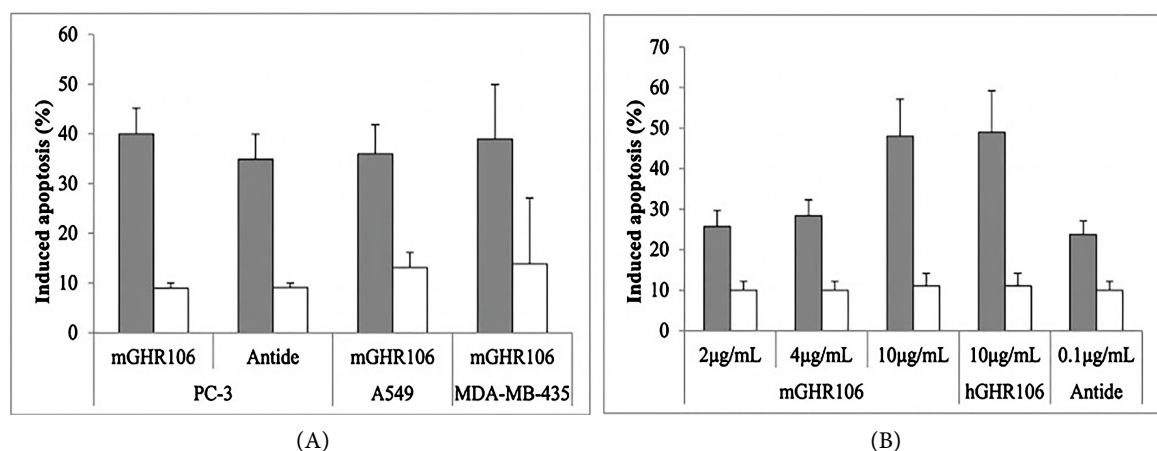


Figure 2. Effects of GHR106 and Antide (decapeptide GnRH analog) on induced apoptosis to OC-3-VGH ovarian cancer cells by TUNEL assay after 48 hours incubation. In (A), data are presented in histograms listed as follows: (■) in the x-axis indicates percent induced apoptosis upon 48 hours incubation of 10 µg/ml GHR106 or Antide (0.1 µg/ml) with culturing PC-3 (prostate), A549 (lung) or MDA-MB-435 (breast, TNBCa) cancer cells. (□) represents the negative control with 10 µg/ml of normal mouse IgG for the corresponding sets of experiments. (B): Dose-dependent induced apoptosis by GHR106 of murine origin and humanized form of GHR106 (2, 4 and 10 µg/ml). Decapeptide GnRH antagonist, Antide was used as the comparative positive control (All data in Figure 2(A) and Figure 2(B) are statistically significant at $P < 0.01$).

Table 3. Summarized results of nude mouse experiments to demonstrate the anti-cancer efficacy of RP215 or GHR106 Mab.

cell line model ^a (tissue)	Mab used (treatment scheme)	Tumor volume (mm ³) mean $\pm$ SD (n)			
		NC	PC	AH*	AL*
OC-3-VGH (ovary) ^a	RP215	160.8 $\pm$ 20.1 (4)	92.3 $\pm$ 8.3 (4)	85.5 $\pm$ 1.9 (4)	113.7 $\pm$ 29.4 (4)
	one dose (Day 0)			10 mg/kg	2 mg/kg
SK-MES-1 (lung) ^c	RP215	500.9 $\pm$ 66.0 (5)	99.3 $\pm$ 28.1 (5)	218.8 $\pm$ 24.0 (5)	276.8 $\pm$ 27.9 (5)
	two doses (4th and 5th week)			0.75 mg/mouse/dose	0.14 mg/mouse/dose
C33A (cervix) ^d	RP215	295 $\pm$ 105 (4)	75 $\pm$ 13 (4)	86 $\pm$ 34 (5)	283 $\pm$ 105 (5)
	two doses (Days 2 & 15)			10 mg/kg/dose	2 mg/kg/dose
Hep2G (liver) ^d	GHR106	1560 $\pm$ 192 (5)	763 $\pm$ 229 (4)	800 $\pm$ 177 (5)	1350 $\pm$ 260 (5)
	two doses (Day 1 & 15)			10 mg/kg/dose	2 mg/kg/dose

1. OC-3-VGH, NC vs. AH ($P < 0.05$), NC vs. AL (NS); 2. SK-MES-1, NC vs. AH ($P < 0.001$), NC vs. AL ($P < 0.001$); 3. C33A, NC vs. AH ($P < 0.01$), NC vs. AL (NS); and 4. Hep2G, NC vs. AH ($P < 0.05$), NC vs. AL (NS); AH vs. AL ($P < 0.05$). a. Protocols for OC-3-VGH, C33A and Hep2G models with RP215 Mab are described in the text. NC: Negative Control, PC: Positive Control, AH: Antibody High Dose (10 mg/kg), AL: Antibody Low Dose (2 mg/kg). b. Tumor volumes were determined on Day 15 following initial tumor implant and drug/antibody injections. 8 (n) is the number of mice in each treatment group. c. Tumor volumes were determined on the 6th week after tumor implant following treatment protocol outlined in the text for SK-MES-1 model. AH: Antibody High Dose (0.75 mg/mouse/dose), AL: Antibody Low Dose (0.14 mg/mouse/dose). d. Tumor volumes were determined on Day 22 following initial tumor implant and two antibody treatments on Days 1 and 15 with GHR106 Mab. *Statistical analysis of Tumor volumes measured in mice (NS: Non-significant).

The established hepatoma cell line, Hep-2G (ATCC-HB8065) was used as a tumor model to study the effects of injected GHR106 on tumor growth in nude mice according to the established protocols. Briefly, on Day 0, each mouse was inoculated with cultured Hep-2G cells of 1 mmE3 size, when viewing under a dissection microscope. The antibody drug treatments were given to mice by intraperitoneal injection on the same day within 2 hr as well as on Day 15. The mice in the negative control group were injected with no antibody, whereas those in the positive

control group were injected with 60 mg/Kg of cyclophosphamide on Day 0. The mice in the high-dose antibody group (AH) were injected with 10 mg/Kg of GHR106, whereas in the antibody low-dose group, were injected with 2 mg/Kg of the same antibody (AL). The tumor volume and body weight of each mouse were recorded on Day 4, 8, 12 and 16. Data obtained on day 16 are presented in **Table 3** for comparisons with others.

RP215 was also employed in three separate nude mouse experiments including those of OC-3-VGH ovarian cancer, SK-MES-1 lung cancer and C33A cervical cancer with similar protocols. Results of these three studies were also presented in **Table 3** for comparisons. Based on the results of these four nude mouse experiments, it can be concluded that both GHR106 and RP215 are effective in targeting many different human cancers, as long as GnRH receptor and/or CA215 (cancerous immunoglobulins) are highly expressed on the surface of these cancer cells. Therefore, we believe that TNBCa should be considered to be one of the preferred choices for being targeted by either of these specific cancer cell targeting antibodies [14].

4. Two Distinct Roles and Mechanisms of GnRH Receptor

Through decades of studies, it has been well established that GHR106 can serve as long-acting GnRH antagonist and react with pituitary GnRH receptor to cause reversible suppressions of reproductive hormones including estradiol, progesterone, testosterone and gonadotropins. This was clearly demonstrated by “Proof of Concept” experiments in rabbits. Therefore, we believe that the pharmacological action of GHR106 may be beneficial to therapeutic treatments of hormone-positive BCa which may consist of more than 80% of all BCa cases. On the other hand, GnRH receptor widely expressed on the cancer cell surface is subject to autocrine/paracrine regulations in the presence of GnRH and its analog such as GHR106. This will result in the inhibition of growth/proliferation of all cancer cells including all cases of BCa. In view of dual functional roles, GHR106 may be used to treat these two different types of BCa with similar effectiveness during therapeutic cancer treatments. This was demonstrated from the experiments of inducing apoptosis upon comparative incubations with TNBCa or with hormone-positive BCa cell lines in vitro. No practical differences were observed between these two types BCa cell lines (MDA-MB-435 vs. T-47-D) (**Table 1** and **Table 2**), as shown by induced apoptosis assays.

In GnRH receptor therapy of human cancer using GHR106 as GnRH antagonist, the anterior pituitary receptor may be damaged following the exposure of GHR106 therapeutic antibody. However, destructions of gonadotroph cells may even be beneficial to those suffering from hormone-dependent conditions or hormone replacement therapy, following successful therapy of BCa. The assisted reproductive technology ART may be a good option for restoring the fertility conditions to those women recovered from targeted GnRH receptor cancer therapy.

5. Cancer Immunotherapy by Using CAR-T Cell Constructs of GHR106 and RP215 for Potential Treatments of TNBCa as Well as Hormone-Positive BCa

The newly evolving CAR-T (Chimeric antigen receptor-transfected -T cells) technology has been a popular choice for therapeutic treatments of different human cancer of blood origins [6] [7]. Briefly, humanized isoform of GHR106 is packaged as ScFv fragment in the lentiviral vector for constructions of chimeric antigen receptors (CAR). Following transfection of patients' own T cells with ScFv-GHR106 CAR constructs, CAR-T cell cancer immunotherapy can be performed. These CAR-transfected T cells can be infused to cancer patients to induce cytotoxic killing of cancer cells together with cytokine releases to achieve objectives of cancer immunotherapy. This was demonstrated in model experiments by using C33A cervical cancer cell line [6] [7].

Similarly, when ScFv fragment of hRP215 was employed in a CAR-T cell construct, cytotoxic killing and cytokine release were also observed upon incubations with tumor cells such as C33A cervical cancer cells [6] [7]. Judging from these two model studies, we believe that TNBCa and other hormone-positive BCa with high binding activities to either antibody, can be effectively treated with similar CAR-T cells-based cancer immunotherapy [6] [7].

6. General Conclusion and Priority of Drug Development

Two monoclonal antibodies, GHR106 and RP215 were introduced to target pan cancer biomarkers, GnRH receptor and CA215 (cancerous immunoglobulins) which are broadly expressed on cancer cell surface [1]. These two antibodies were humanized and extensively characterized with respect to their binding specificity, affinity and induced apoptosis to a variety of human cancer of differently tissue origins including BCa of different types. Finally, "proof of concept" nude mouse experiments with any one of four implanted tumors (cell lines from ovarian cervical, liver and lung cancer) were performed to reveal antibody-dose dependent reductions in the volume of implanted tumors [5]. These studies strongly suggested that the corresponding cancer biomarkers are essential for survival of many types of cancer cells [15]-[17].

It has also been previously established that GHR106 act as antibody-based GnRH antagonist in the GnRH/GnRH receptor-related autocrine/paracrine regulatory system among almost all cancer cells. This result is similar to the actions by GnRH analogs of small molecules [12]. Similarly, RP215 can be used to target cancerous immunoglobulins (CA215) expressed by almost all cancer cells which were also shown to be essential for their proliferations or survival under our normal human serum environment [15]. In principle, these two monoclonal antibodies might be suitable in targeting many different human cancer, as long as these markers are highly expressed in a particular cancer of being targeted [1].

Among different human cancer, Breast cancer (BCa) is known to be one of the highest incidence of occurrence (33%). TNBCa is also associated with the highest

mortality rates among women worldwide. Among all cases of BCa, 10% - 20% were classified as TNBCa due to lack of receptor expressions in E2, progesterone and Her-2 [12] [13]. However, the options for effective treatments of TNBCa are relatively limited and medically unmet. A five-year survival of TNBCa is 8% - 16% lower than that of other types of BCa. According to the global forecast of market analysis, the CAGR from 2023 to 2032 is 9.9% for BCa (\$28.8B USD to \$73.68B USD), whereas that of TNBCa is 12.2% (\$11B USD to \$20B USD). Therefore, we believe that these two antibodies in treating TNBCa should stimulate us in promoting applications of cancer targeting/cancer immunotherapy [12] [13].

Based on our previous preclinical studies, GHR106 and RP215 revealed little differences in terms of binding specificity or induced apoptosis on the two types of BCa. Further studies during the last two decades also revealed that in TNBCa, mRNA expressions of GnRH receptor are significantly higher than other types of BCa (expression rate of 74% vs. 50% - 64%) [8] [9]. Therefore, by utilizing GnRH receptor/GnRH related autocrine/paracrine system among different cancer, we believe that GnRH receptor can be a promising pharmaceutical target by GHR106 in case of TNBCa and hormone-positive BCa for their potential therapeutic applications [10] [12].

Strategy and Priority of Drug Development

GHR106 and RP215 were finally selected as suitable candidates for further development as anticancer drugs for many types of human cancer. Due to the limited resources, the priority of this drug development project should be focused on the medically unmet situations. Among the two antibody candidates, GHR106 should be considered in a much higher priority than RP215 for FDA-IND enabling during initial applications. There are unique advantages of GHR106-based drugs over the RP215 case. Based on our preclinical studies, it was clearly concluded that GHR106 is a first in class long-acting antibody-based GnRH antagonist, similar to those of small molecular analogs.

Furthermore, GnRH receptor was widely expressed as a pan cancer biomarker on the surface of almost all cancer cells in humans for growth regulations through autocrine/paracrine regulations systems. Anti-proliferative and anti-metastatic actions of GnRH or GHR106 antagonist to cancer cell were universally observed and investigated previously. It can be concluded that GnRH receptor on the cancer cell surface can uniquely be targeted by GHR106 in cancer therapy. Following the preclinical studies, our FDA IND enabling effort should be focused on clinical treatments of Breast cancer (BCa), especially the medically unmet triple negative breast cancer (TNBCa). As mentioned, BCa was considered to be one of the highest incidence and mortality worldwide. Therefore, our initial applications will be aimed to achieve FDA IND enabling of GHR106 for effective clinical treatments of TNBCa. Similar treatment protocols will concurrently be used to treat hormone-positive BCa, during different stages of clinical trials for BCa.

Therefore, based on the available preclinical data, it is logical to place our pri-

ority on the therapeutic applications of these two antibodies in targeted therapy and immunotherapy. These two well characterized antibodies can be applied singly or in combinations as bispecific formats. Either one can also be adopted in CAR-T or CAR-NK constructs to carry out locally enhanced cancer therapy [6] [7] (Figure 3). Finally the various formulations of ADC (Antibody drug conjugates) [12] [13], for therapeutic treatment applications in TNBCa are in progress.

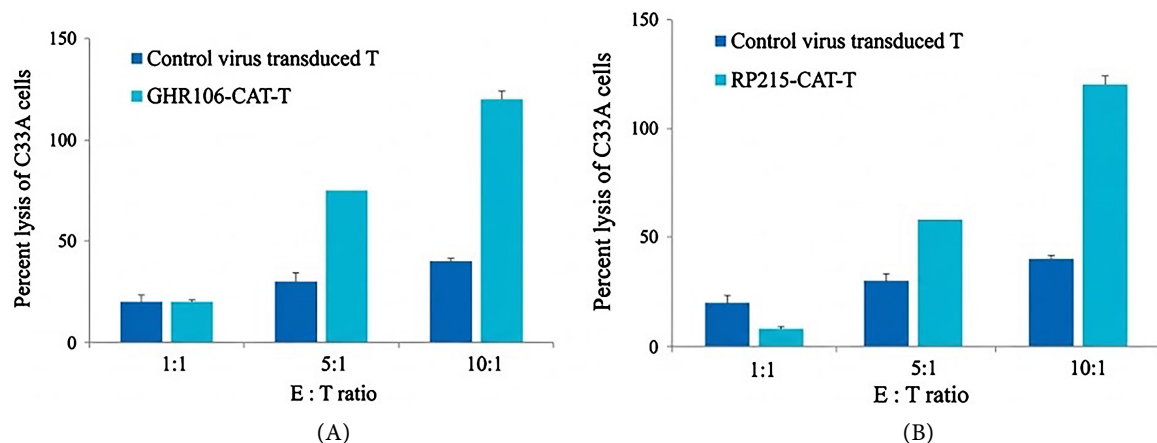


Figure 3. (A) *In vitro* Cytotoxicity of GHR106-CAR-T C33A cancer cells (T) were co-cultured with GHR106-CAR-T cells (E) or with control virus transduced T cells at three different E/T (Effect/Target) ratios for 6 hours. The percentage of tumor cells lysis was measured by lactate dehydrogenase (LDH) levels. In the E/T ratio of 5:1 and 10:1, GHR106-CAR-T could significantly increase the cell lysis, indicating that GHR106-CAR-T had the ability to kill tumor cells. (B) *In vitro* Cytotoxicity of RP215-CAR-T C33A cancer cells (T) were co-cultured with RP215-CAR-T cells (E) or with control virus transduced T cells at three different E/T (Effect/Target) ratios for 6 hours. The percentage of tumor cells lysis was measured by lactate dehydrogenase (LDH) levels. In the E/T ratio of 5:1 and 10:1, RP215-CAR-T could significantly increase the cell lysis, indicating that RP215-CAR-T had the ability to kill tumor cells.

Conflicts of Interest

The author declares no conflicts of interest regarding the publication of this paper.

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