

GCPGC - Pegylated G-CSF

Compound: Pegylated GCSF (granulocyte colony stimulating factor)

Indication: Neutropenia caused by cancer

Development Stage: Phase II/III clinical studies in KR

Intellectual Property: KR0230579, PCT/KR2006/002841 (KR0735784)

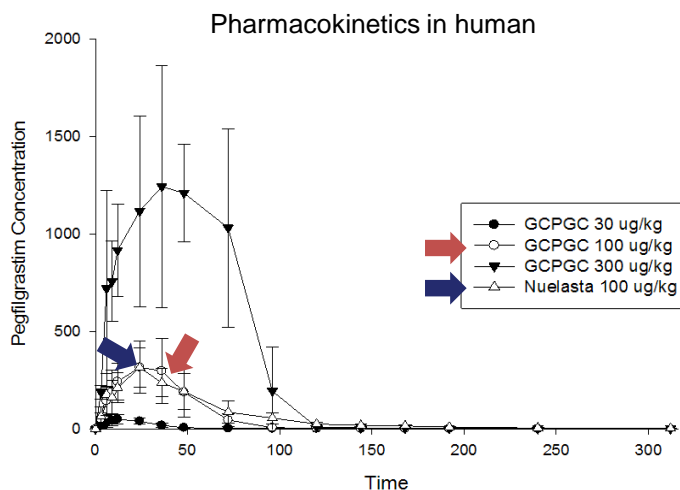
Introduction

GCSF is a glycoprotein that induces the survival, proliferation and differentiation of neutrophilic granulocyte precursor cells and activates mature blood neutrophils.

Pegylated GCSF is a long acting form of GCSF used to treat neutropenia caused by chemotherapy or bone marrow transplantation and is given only once after each chemotherapy unlike GCSF that requires daily dosing for the period between chemotherapies. GCPGC is a new pegylated GCSF made using a site-specific pegylation technology.

Development Summary

- Site specific pegylation is achieved by two step modifications
 - Step 1. Free cysteine amino acid is introduced to GCSF at a specific site using a site specific mutagenesis
 - Step 2. The sequence modified GCSF is pegylated at the introduced free cysteine residue using a cysteine-specific pegylation process
- The sequence modified GCSF is purified from an inclusion body in *E. coli* and prepared *via* an efficient refolding process.
- The sequence modified GCSF is stable and shows biological activity equivalent to that of the natural form.
- The introduced cysteine is pegylated with high specificity without any side reaction and iso-form generation.
- GCPGC exhibited *in vitro* activity equivalent to Filgrastim in promoting M-NFS 60 cell proliferation.
- The half-life of GCPGC was about 18 hrs in rat, which is 4-fold longer than that of Filgrastim and similar to Neulasta® (see figures below)



Competitive advantages

- A site specific, novel pegylation technology is used
- *In vivo* PK/PD data and *in vitro* biological activity and are comparable to Neulasta®

Partnering Interests:

Co-Development and Licensing Out

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MG1102 - rhLK8

Compound:	Recombinant human kringle domain V of apolipoprotein(a)
Indication:	Hormone refractory prostate cancer, anti-tumor/metastasis
Development Stage:	Phase I clinical studies in KR and the US
Intellectual Property:	KR523734, KR523737, PCT/KR99/00554 (KR481206), PCT/KR04/00357 (KR595364), PCT/KR05/00214 (KR595864), PCT/KR05/00075 (KR681762)

Introduction

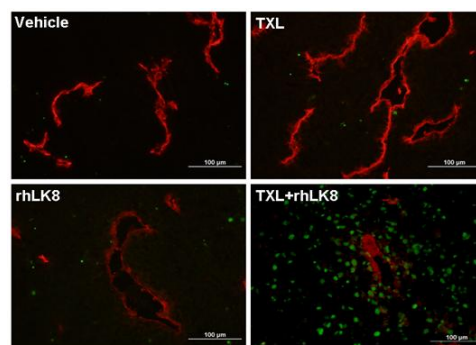
Lipoprotein(a) (Lp(a)) consists of an LDL-like particle and the specific apolipoprotein(a) (apo(a)), which is covalently bound to the apoB of the LDL-like particle. Apo(a) is mainly synthesized in the liver and is characterized by its repetitive kringle domains. Kringle domain is a 106~114 amino acid long protein motif arranged in a triple loop structure. Of the kringle domains in apo(a), the kringle domain V shows a significant sequence homology with the kringle domain V of plasminogen, which is reported to have a strong anti-angiogenic effect.

MG1102 is a 86 amino-acid long recombinant human kringle domain V of apolipoprotein(a) (rhLK8) and it is produced in yeast *Saccharomyces cerevisiae*. Anti-angiogenic effect of MG1102 has been shown previously using *in vitro* and *in vivo* assays such as CAM assay (a neovascularization assay in chicken embryo) and the Matrigel plug assay and anti-cancer effect has been proven using *in vivo* cancer models.

Development Summary

- MG1102 inhibits endothelial cell migration *in vitro*, by inhibiting the activation of focal adhesion kinase and consequently the formation of actin stress fibers/focal adhesions.
- MG1102 inhibits neovascularization in CAM assay and Matrigel plug assay.
- Alone or in combination with chemotherapeutic agent, MG1102 induced a significant apoptosis of tumor-associated endothelial cells and tumor cells in the orthotopic animal models of human prostate, colon, pancreas, kidney, and skin cancers.
- MG1102 inhibits experimental pulmonary metastasis of murine melanoma cells and bone metastasis of human prostate cancer cells.
- MG1102 inhibits experimental liver metastasis of human colorectal cancer cells in nude mice and significantly improves survival of the hosts.
- MG1102 improves host survival in animals bearing orthotopic human colorectal tumors in nude mice
- Expression system *Saccharomyces cerevisiae* is established.
- 350L production and purification process is established

CD31 / TUNEL



Double immunofluorescence staining for CD31 (red) and TUNEL (green). Mouse prostate cancer tissues in a mouse orthotopic model of human prostate cancer.

Competitive advantages

- Promising candidate molecule for treatment of cancers and their metastases.
- No significant toxicity observed in preliminary toxicology studies.
- MG1102 may have potential benefits for other diseases where angiogenesis plays critical roles in the disease development and/or progression (e.g. diabetic retinopathy).

Partnering Interests:

Co-development and (clinical trials)

Licensing Out

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MG1109 - Avian Influenza Vaccine

Compound: Inactivated whole cell avian influenza vaccine

Indication: Avian influenza infection

Development Stage: Phase I/II clinical studies in KR

Introduction

MG1109 is a sterile, aqueous suspension of a strain of influenza virus, type A grown in fertilised hen's eggs and inactivated in such a manner that their antigenic properties are retained. The amount of haemagglutinin antigen for single strain present in the vaccine is 15µg per dose(0.5mL). MG1109 contains the strain H5N1 (NIBRG-14) derived by reverse genetics from the avian influenza virus A/VietNam/1194/2004. The vaccine contains a mixture of aluminium hydroxide as adjuvant. Thiomersal is added as a preservative.

Development Summary

- MG1109 is built on the knowledge, experience, equipment and manufacturing infrastructure gained with the development of the approved inactivated split seasonal vaccine, GCFLU®.
- Antibody response after 2nd vaccination in ferrets measured by hemagglutination inhibition (HAI) assay and neutralization analysis indicated the vaccine is efficacious against A/VN and A/Indo strains. (Fig. 1~2).
- MG1109 treated ferrets were able to effectively combat avian flu challenges by two types of influenza, A/VN and A/Indo (Fig.3).

Fig. 1. Antibody Response by Neutralization assay (A/VN/1203/04)

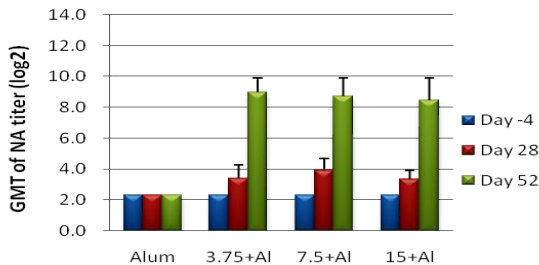


Fig. 2. Antibody Response by Neutralization assay (A/Indo/5/05)

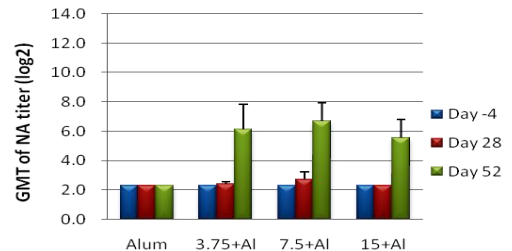
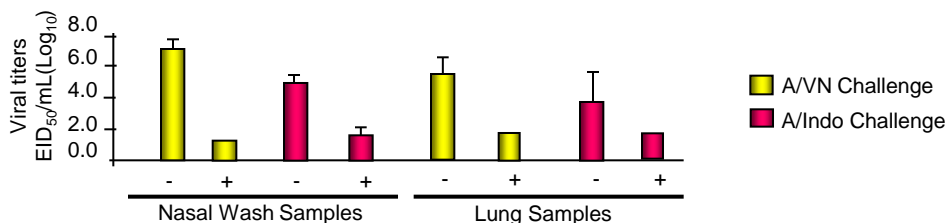


Fig. 3. Viral load in nasal wash and lung samples following A/VN and A/Indo Challenge



Competitive advantages

- Identified the safety in phase I clinical trial
- Manufactured in compliance with the European Pharmacopoeia
- Manufactured in Hwasun plant with current production capacity of 20 million dose/year and maximum capacity of 50 million dose/year

Partnering Interests:

Export/Co-development and

Tech-transfer

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MG4101 - NK cell therapy

Compound: Allogeneic human natural killer cell therapy

Indication: Cancer

Development Stage: Phase I clinical studies in KR

Intellectual Property: KR 2008-74069, KR 2008-47716, PCT/KR2009/004228

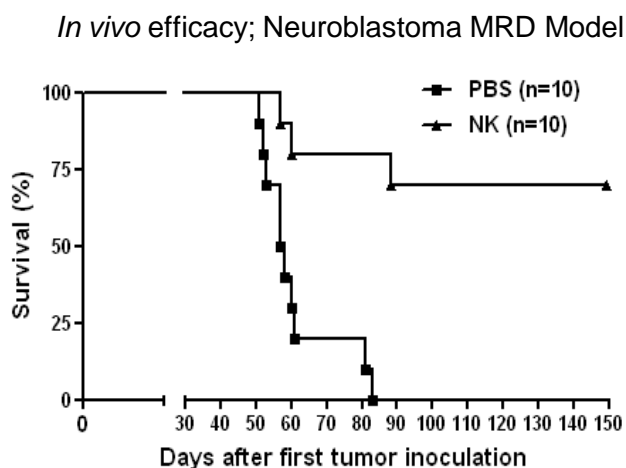
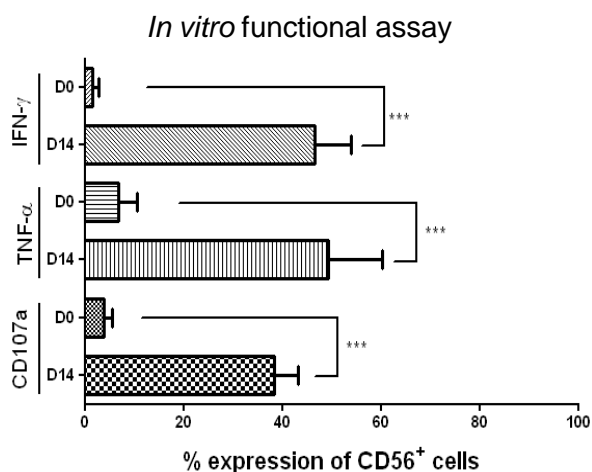
Introduction

Natural killer (NK) cells are specialized lymphocytes that provide a first line of defense through their ability to kill infected or transformed cells. Alloreactivity of NK cells was known to improve the clinical outcome of cancer patients who underwent hematopoietic stem cell transplantation (HSCT). With these concept, adoptive transfer of NK cells (termed NK cell therapy) has been applied to treat various types of cancers. The most difficult hurdle of NK cell therapy is the limitation of NK cell expansion and activation *ex vivo*.

We have established a novel method for the expansion and activation of NK cells from healthy volunteers and prepared for clinical application under good manufacturing practice (GMP) guidance. Highly pure population of CD16⁺/CD56⁺ NK cells were obtained while contaminants such as T cells, B cells, or monocytes were analyzed by less than one percent. Expanded NK cells showed potent efficacy on killing tumor cells. Effector cytokines such as IFN- γ and TNF- α were efficiently secreted 10-fold more compared to resting NK cells. Adhesion molecules, DNAM-1; activating receptors, NKG2D; and natural cytotoxicity receptors (NCRs), NKp30, NKp44, and NKp46 were up-regulated by *ex vivo*-expansion resulting in the enhancement of cytolytic activity against tumor cells.

Development Summary

- Developed cost-effective NK cell expansion process and analytical methods.
- Confirmed *in vitro* cytotoxic activity against various cancer cell lines.
- Demonstrated *in vivo* anti-cancer activity using mouse models of neuroblastoma, lymphoma and glioblastoma (see figures below).
- Completed stability and toxicity study of *ex vivo*-expanded NK cells.



Competitive advantages

- Simple and efficient process for preparation of highly purified (> 95%) and activated allogeneic human NK cell from healthy donors.
- By using allogeneic NK cells, higher anti-tumor effect with less adverse effect (e.g. GvHD) is expected.
- Applicable for various cancer types.

Partnering Interests:

Clinical study partnership

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