

JW CreaGene Corp.



Technology Overview

1. Background of Technology

1) Development of immune anticancer therapy based on dendritic cell technology

Dispite advances in modern medicine today, cancer is the leading cause of death worldwide and very low survival rates have been reported. The majority of cancer patients worldwide died of after primary treatment, recurrence or systemic metastasis caused by microscopic residual cancer that was difficult to find in primary treatment or early metastasis.

Previous treatment methods for cancer include surgery, chemical treatments and radiation therapy, yet tumors located in anatomically tricky positions are difficult candidates for surgery. At the same time, chemical or radiation treatments come with many side effects and tolerance build-ups. As a result, the development of new forms of treatment is in need. In other words, a new form of treatment which can treat minor remaining cancer cells or initial metastatic cancer alongside traditional treatment methods, such as surgery, radiation and chemical treatment is required.

DC immune cell therapy utilizing dendritic cells cultivates and manipulates immune cells taken from the patient's body for re-administration. DC immune cell therapy induces powerful cancer immunity while not affecting normal cells. It is a viable and effective form of treatment which can prevent cancer metastasis and recurrence by using the memory immunity to attack and destroy only cancer cells. In addition, the treatment has none of the side effects found in chemical or radiation treatments because immune cells from the patient's own body are used in the creation of treatment. As such, the treatment contains no toxicity and outstanding stability, characteristics which are expected to be a significant breakthrough in the cancer treatment market.

2. Description on Dendritic Cell Technology

(A) Dendritic cell technology

As highly specialized immune cells, dendritic cells plays a key role in keeping the homeostasis of immune systems as a professional antigen-presenting cell.

Most of the dendritic cells present in the body are in an immature state, and they inhale antigens(virus, bacteria, disease-specific proteins, etc.) and provide the information to the cell surface. They function to treat disease by stimulating and regulating specific T-cell immune responses on the cancer or infective virus on the cell surface. The stages in which dendritic cells induce immunity can be organized in the following steps.

1) Dendritic cells sensitize to antigens will mature and express large quantities of homing receptors to move to the secondary immune system



2) Dendritic cell specific C-C chemokine(DC-CK1) are manifested to gather inactive T-cells to the area around

3) Deliver antigen information to T cells through direct interaction between antigens within MHC and T cell receptors

4) Proliferation of antigen-specific T cells and induced activity

(B) Cancer treatment using dendritic cells

JW CreaGene has been developed both mature DC(mDC) which induces immune response for cancer treatments, and toleragenic DC(tDC) which is known to control immune tolerance or regulation in autoimmune disease.

The CreaVax(JW CreaGene's Denderitic Cell therapy) is produced from patient's peripheral blood mononuclear cells(PBMC) by differentiating into dendritic cells after sensitizing with disease specific antigens. Once these autologous dendritic cells are injected to cancer patients, they move to the regional lymph nodes to modulate immune response such as induction of cancer-specific cytotoxic T lymphocytes(CTL) to kill tumor cells or immune tolerance against autoimmune antigen.

Cancer treatments developed by Creagene which utilize dendritic cell production technologies include kidney cancer treatment CreaVax-RCC Inj., prostate cancer treatment (CreaVax-PC Inj.), and liver cancer treatment CreaVax-Hcc Inj. Rheumatoid arthritis treatment CreaVax-RA Inj. also utilizes the immune regulatory functions of dendritic cells.

[DC vaccine preparation against cancer]





3. Differential Point, Superiority or Characteristics of Technology Applied

1) Differentiation of dendritic immune cells

CTL (Cytotoxic T Lymphocytes), which display immune capabilities that search and destroy cancer cells, is known to play a decisive role in suppressing virus infections and growth of cancer cells.

However, in the case of naturally occurring cancer cells, genetic mutations causes immunosurveillance functions within the body to respond irregularly, secrete substances which suppress immune responses, or obstruct the creation of antigens and prevents effective removal of cancer cells.

Dendritic cell immune treatments activate the T cells concerned with CTL (cyotoxic T Lymphocytes) within the body so that the body removes cancer cells on its own.

2) Superiority and characteristics of dendritic cell treatments

While dendritic cell treatments activate functions of declining immune cells to treatment cancer, they have no effect on normal cells. Dendritic cells treatment cancer by selectively attacking and destroying only cancer cells. If anticancer immune responses occur normally, even minor remaining cancer cells are removed via the memory immunity induced by the dendritic cells. At the same time, it possesses a long-term treatment effect by preventing recurrence in the future. Particularly, the treatment has none of the toxicity and side effects found in chemical treatments or radiation and allow cancer treatment without hospitalization while maintaining normal lifestyle. As a result, one of the treatment's biggest advantages is that it does not decrease the quality of life during treatment periods.

In addition, treatment efficacy can also be raised when combining with other methods of treatment, such as chemical or radiation treatment.

No.	Name of Patent	Application No.	Date of application /approval	Country	Status (Applied /approval)	Cost for patent (thousand, KRW)
1	Replication-competent recombinant	1998-032198	appl:98.08.07 appr:01.10.25	Korea	approval	330
I	Sabin type1 strain of poliovirus	09/284,349	appl:99.04.07 appr:04.02.24	USA	approval	5,000
2	Monoclonal Antibody 3-6-A Specific to Surface of Dendritic Cells among the Peripheral Blood Leukocytes	1998-24502	appl:98.06.27 appr:01.04.30	Korea	approval	500
2	Method for improving genetic stability of	2001-0006229	appl:01.02.08 appr:05.03.30	Korea	approval	1,434
5	recombinant single-stranded RNA virus	10/071,867	appl:02.02.07 appr:04.08.24	USA	approval	6,461
4	Phamaceutical Compositions Comprising Dendritic Cells for	2001-23098 2002-7017763	appl:01.04.27 appl:02.12.27	Korea	approval	1,305 1,368

Specific Patent



	Immunotherapy of Autoimmune Disease		appr:06.01.05			
			appl:02.04.26	PCT	applied	1 845
			app1.02.04.20		applied	1,045
		10/312,512	appl:02.12.27	USA	applied	1,094
		2801450.2	appl:02.12.27 appr:06.01.04	China	approval	3,136
		2002-584968	appl:02.12.26	Japan	applied	1,553
5	The preparation method of recombinant human interleukin-4	2001-0046115	appl:01.07.31 appr:04.07.28	Korea	approval	500
6	Vector for expression of mouse granulocyte-macrophage colony stimulating factor and a transformant transformed with the vector	2001-0086575	appl:01.12.28 appr:04.08.31	Korea	approval	800
7	Method for preparing mature dendritic cell-vaccine for immunotherapy	2002-0010000	appl:02.02.25 appr:05.05.10	Korea	approval	1,475
8	Novel recombinant poliovirus vectors and vaccine compositions capable of inducing cytotoxic T lymphocytes	2002-0017471	appl:02.03.29 appr:06.09.28	Korea	approval	1,338
		2002-0017470	appl:02.03.29 appr:04.11.09	Korea	approval	1,649
9	Novel Dendritic Cell-Specific Polynucleotides and Microarray Comprising the Same	PCT/KR03/00631	appl:03.03.28	РСТ	applied	1,745
		10/509,621	appl:04.09.29	USA	applied	4,418
10	Novel Recombinant Sabin Type 1	2002-0078158	appl:02.12.10 appr:05.06.09	Korea	approval	1,399
10	Poliovirus	10/926,333	appl:04.08.31 appr:06.11.21	USA	approval	4,884
		2005-0045234	appl:05.05.27 appr:07.06.26	Korea	approval	800
11	Method for measuring effectively the	PCT/KR2006/0020 29	appl:06.5.27	РСТ	applied	4,239
	human and out-bred animals	11/915,738	appl:07.11.27	USA	applied	5,000
		06 747 470.0	appl:07.12.21	EU	applied	4,000
		PCT/KR2006/0020 28	appl:06.5.27	РСТ	applied	4,283
12	expressing human prostate cancer- specific antigen and method for	10-2005-0045236	appl:05.05.27 appr:06.11.13	Korea	approval	500
12	analyzing prevention and treatment efficacy of dendritic cells-derived immune therapeutics using the above	10-2006-0062618	appl:06.07.04 appr:06.11.13	Korea	approval	500
		11/915,737	appl:07.11.27	USA	applied	5,000
	Animal models carrying tumors expressing human liver cancer-specific antigen and method for analyzing	10-2007-0048213	appl:07.05.17 appr:09.05.27	Korea	approval	1,547
13	prevention and treatment efficacy of dendritic cells-derived immune therapeutics using the above	PCT/KR2008/0014 20	appl:08.03.13	PCT	applied	4,568
14	Mesenchymal stem cell mediated autologous dendritic cells with increased immunosuppression	10-2007-0017970 10-2008-0117836	appl:07.02.22 appl:08.11.26	Korea	applied divided- applied	1,631



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* Please provide accurate information for Application No and Date of application/approval. It will be used for patent search.

X In case of Cost for patent, please consider administrative cost for patent application only.

* In case of PCT or overseas patent (application) except domestic patent, Please attach a certificate of

application/approval (or patent abstract) as a separate file.