# Reduce the risk of missing genetically engineered sequence patents

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October 2018







# Agenda

Latest trends in immuno-oncology research	01
Introduction to GENESEQ	02
Searching for CAR sequences in GENESEQ on SequenceBase	03
Due diligence research in Derwent Innovation	04



# Breaking news: The 2018 Nobel Prize in physiology or medicine goes to....

- Professor Tasuku Honjo, Kyoto University and Professor James Allison, MD Anderson Cancer Center
  - □ For the discovery of immune checkpoint inhibitor PD-1 (programmed cell death 1)





# What is immuno-oncology (IO)?

- Tumor cells are different to normal cells. Therefore, one might expect the immune system to recognise and destroy tumor cells. However, this does not always happen.
- Immuno-oncology is the study of the immune system in relation to cancer. It is helping us to understand how tumors escape the body's immune response.
- Cancer immunotherapies such as anti-PD-1 antibodies are being developed to enable the immune system to recognise and kill cancer cells.





### Immuno-oncology patent families 2008-2018



Volume of DWPI families in six checkpoint inhibitor targets (CTLA-4, PD-1, PD-L1, Ox40, TIM3 and LAG3) and CAR T-cell therapy from 2008-May 2018.

Projecting 2018 partial volumes, we see continuing growth rates of between 124% for CAR T and 234% for PD-L1 closely followed by PD-1 at 220% growth over 2017.

Source: Derwent Innovation (DWPI)

Derwent

Powering IP Innovation

Chart taken from Clarivate's webinar (May 2018): Innovation trends in immuno-oncology



# **Chimeric Antigen Receptor (CAR) T-cell therapy**

- Adoptive cell immunotherapy was named as "Advance of the Year" at ASCO 2018 in June.<sup>1</sup>
- T-cells are collected from a cancer patient and genetically engineered to produce a chimeric antigen receptor (CAR) which binds to a tumor-specific antigen. Inside the patient, CAR-T cells will recognise and destroy tumor cells.



- of children and young adults with B-cell lymphoblastic leukemia in ELIANA trial **treated with CAR-T therapy** tisagenlecleucel who **achieved complete remission** or complete remission with incomplete blood count recovery at three months.<sup>2</sup>
- 1. https://www.asco.org/research-progress/reports-studies/clinical-cancer-advances-2018/advance-year
- 2. Maude S.L. et al, N Engl J Med 2018, 378(5): 439 "Tisagenlecleucel in children and young adults with B-cell lymphoblastic leukemia"



# Anatomy of a Chimeric Antigen Receptor (CAR)

- CARs are composed of:
  - an extracellular binding domain (e.g. singlechain variable fragments (scFv) derived from tumor antigen-reactive antibodies)
  - a hinge region,
  - a transmembrane domain, and
  - $\hfill\square$  CD37 chain intracellular signaling domain.
- CARs also contain co-stimulatory domains, like CD28 and/or 4-1BB.
- Current research is investigating "smart T cells" with built-in safety controls (e.g. suicide genes).





### **CAR-T patent challenges**

- Ongoing legal dispute regarding "obviousness" of combining certain sequences, in particular a version of CD28 which includes the "MYPPPY" amino acid motif.
- Important to know the precise sequences being used in a chimeric antigen receptor.
- Not all sequences in a patent are necessarily included in the electronic sequence listing,



\*for some of the patents in the 'Sequences in text' only category, sequence listings files are available via manual searching using the PN on WIPO, but are not present in the auto-download of SL data from WIPO



### **GENESEQ Sequence Capture – WO docs Q3 2017**

# **Challenges of sequence searching**

- Using public or proprietary sequence databases which rely on electronic sequence listings and original, local language descriptions can be costly:
  - **High risk of missing important patent documents** and therefore exposing your company to liabilities or wasting R&D resources.
  - Waste precious time and effort trying to assess the relevance of specific sequences or documents.
    - Spend money on expensive translations, possibly to find that the document is not relevant.



# **GENESEQ** offers...

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Global Coverage

- Manual Capture
  - Including sequences not found in SEQ ID listings
- **Manual Annotation** 
  - All in plain English

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FIG. 23

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The present invention relates to pharmaceutical compositions and methods for treating rheumatic disease. The composition comprises a soluble cytotoxic T lymphocyte antigen 4 (CTLA4) mutant molecule that blocks endogenous B7 molecules from binding their ligands. Soluble CTLA4 molecules are constructed by fusing variable (V)-like extracellular domains of CTLA4 to immunoglobulin (Ig) constant domains resulting in CTLA4Ig. The composition is useful for treating rheumatic disease especially rheumatoid arthritis, and for alleviating a symptom associated with a rheumatic disease from joint swelling, pain, tenderness, and structural damage The composition can optionally be used with other pharmaceutical agents for treating immune ystem disorders which include autoimmune diseases (e.g. systemic lupus erythematosus, Addison's disease, diabetes mellitus, multiple sclerosis, Crohn's disease, ulcerative colitis, Sjogren's syndrome, scleroderma and sympathetic ophthalmia), graft-related diseases (e.g. graft-versus-host disease), immunoproliferative diseases (e.g. psoriasis, T cell lymphoma, Hashimoto's thyroiditis, pernicious anaemia and good pasture's syndrome). The present sequence represents a mutant of the human CTLA4 receptor. Note: The present sequence is not given in the patent but is created by the indexer from the sequence provided in Fig 23 and the information given in claim 12

protein

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lolecule type

Organism Length

Sequence

Feature table

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Key Location Feature Peptide 1..26 label: O Protein 27..212 label: M

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- label: Oncostatin\_M\_Signal\_peptide label: Mature\_CTLA4\_receptor
- 2 label: Mature\_CTLA4\_receptor note: "Substitution of wild type Ser to any amino acid"



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### Search example – CD3zeta and CD28

- CD3 zeta (164 amino acids)
- MKWKALFTAAILQAQLPITEAQSFGLLDPKLCYLLDGILFIYGVILTALFLRVKFSRSAD APAYQQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPQRRKNPQEGL YNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
- CD28 (220 acids)
- MLRLLLALNLFPSIQVTGNKILVKQSPMLVAYDNAVNLSCKYSYNLFSREFRASLHKGLDSAVEVCVVYGNYSQQLQV YSKTGFNCDGKLGNESVTFYLQNLYVNQTDIYFCKIEV**MYPPPY**LDNEKSNGTIIHVKGKHLCPSPLFPGPSKPFWVL VVVGGVLACYSLLVTVAFIIFWVRSKRSRLLHSDYMNMTP RRPGPTRKHYQPYAPPRDFAAYRS

# IP due diligence on genetic sequence patents using Derwent Innovation

Bob Stembridge Senior IP Analyst

October, 2018







# Agenda

Introduction to Derwent Innovation	01
Transferring GENESEQ results into Derwent Innovation	02
General insights	03
Legal status & ownership	04



# **Introduction to Derwent Innovation**











# **Transferring GENESEQ results into Derwent Innovation**





### **Export from GENESEQ, import into Derwent Innovation**

- Data can be exported from GENESEQ in numerous formats, including Excel, to perform further analyses that can be shared with colleagues or clients
- The Text export option is specifically for exporting lists of deduplicated patent numbers
- The list of patent numbers can either be uploaded or copied into Derwent Innovation







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# **General insights**





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# Legal status and ownership





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Key Summary Data Patent: Alive DWPI Family: Alive View Details INPADOC Family: Alive View Details Original Assignee: Keji Biological Medicine (shanghai) Co. Ltd., S Optimized Assignee: SHANGHAI YIKELAI BIOLOGICAL MEDICINE TEC Ultimate Parent: SHANGHAI YIKELAI BIOLOGICAL MEDICINE TEC	Publication Date: 2017-06- Expiration Date: 2033-04-0 Remaining Life: 5296 days	20 01 (estimated) • View factors (14 year(s), 5 montn(s))	ee tracellul:	Publication Date 2016-03-24 ar spacer comprising at least part ncer	Display 100 ▼ records per page Current IPC C07K 19/00 of the extracellular domain of
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EARCH	Communication of the second se	DWPI Title: New cell comprising constitutive expression construct encoding fusion protein comprising antigen binding protein that binds tumor antigen and polypeptide target for cellular therapeutic, useful for treating solid tumor e.g. ovarian cancer
QUICK SEARCH		
PATENT	22 US20180244796A1 DWPI Drawing:	CARSGEN THERAPEUTICS LTD CARSGEN THERAPEUTICS LTD 2018-08-30 C07K 16/30 Title: FULLY HUMAN ANTI-MESOTHELIN ANTIBODIES AND IMMUNE EFFECTOR CELLS TARGETING MESOTHELIN DWPI Title: New human antibody used for preparing targeted antitumor drugs, or agent for diagnosing tumors which express mesothelin
ALL CONTENT NATIVE JAPANESE		e.g. pancreatic cancer and ovarian cancer, comprises heavy chain variable region and light chain variable region
SEARCH HISTORY	23 <u>W02014180306A1</u>	SHANGHAI YIJIE BIOTECHNOLOGY CO SHANGHAI YIJIE BIOTECHNOLOGY2014-11-13 C12N 15/09 LTD CO LTD
MARKED LIST	DWPI Drawing:	Title: NUCLEIC ACID OF CODED GPC3 CHIMERIC ANTIGEN RECEPTOR PROTEIN AND T LYMPHOCYTE EXPRESSING GPC3 CHIMERIC ANTIGEN RECEPTOR PROTEIN DWPI Title: New nucleic acid capable of resisting chimeric antigen receptor protein of glypican-3 encoded and expressed on surface of human T lymphocyte
	24 W02015172339A1 DWPI Drawing:	CARSGEN THERAPEUTICS LTD CARSGEN THERAPEUTICS LTD 2015-11-19 C12N 15/62 Title: NUCLEIC ACID FOR CODING CHIMERIC ANTIGEN RECEPTOR PROTEIN AND T LYMPHOCYTE FOR EXPRESSION OF CHIMERIC ANTIGEN RECEPTOR PROTEIN DWPI Title: New nucleic acid capable of encoding chimeric antigen receptor protein expressed on surface of human T lymphocyte, useful for treating cancer e.g. bladder cancer and ovarian cancer
	25 W02015172339A8 DWPI Drawing:	CARSGEN THERAPEUTICS LTD CARSGEN THERAPEUTICS LTD 2016-02-04 C12N 15/62 Title: NUCLEIC ACID FOR CODING CHIMERIC ANTIGEN RECEPTOR PROTEIN AND T LYMPHOCYTE FOR EXPRESSION OF CHIMERIC ANTIGEN RECEPTOR PROTEIN DWPI Title: New nucleic acid capable of encoding chimeric antigen receptor protein expressed on surface of human T lymphocyte, useful for treating cancer e.g. bladder cancer and ovarian cancer
	26 <u>W02016042461A1</u> DWPI Drawing:	MOLMED SPA     MOLMED SPA     2016-03-24     C07K 14/725       Title: CHIMERIC ANTIGEN RECEPTORS     DWPI Title: New chimeric antigen receptor (CAR) comprises an extracellular spacer comprising at least part of the extracellular domain of human low affinity nerve growth factor or a derivative for use in treating cancer
	27 <u>WO2016073629A1</u> DWPI Drawing:	UNIV TEXAS UNIVERSITY OF TEXAS 2016-05-12 C07K 16/28 Title: CHIMERIC ANTIGEN RECEPTORS (CAR) TO SELECTIVELY TARGET PROTEIN COMPLEXES DWPI Title: New chimeric antigen receptor polypeptide used in pharmaceutical composition for treating cancer, comprising antigen binding Print Watch Records Analyze = Edit Custom Fields Order = Export Save Add

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Add to Work File 🔻   Mark Record   Watch Record   Download 🔻   Trans	slate 🔻   Citation Map   Highlight   Print	Navigate: Preferred	Documents 🔻	encoding fusion protein comprising antigen binding protein that binds
Key Summary Data Patent: S Alive DWPI Family: Alive View Details	Publication Date: 2014-11- Expiration Date: - () Vie	-13 w factors	×	LTD 2018-08-30 C07K 16/30
INPADOC Family: S Alive View Details Original Assignee: SHANGHAI YIJIE BIOTECHNOLOGY CO. LTD, CN Optimized Assignee: SHANGHAI YIJIE BIOTECHNOLOGY CO LTD Ultimate Parent: SHANGHAI YIJIE BIOTECHNOLOGY CO LTD	Remaining Life: -			umor drugs, or agent for diagnosing tumors which express mesothelin riable region and light chain variable region
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Assignee/Applicant ? Standardized: SHANGHAI YIJIE BIOTECHNOLOGY CO LTD Original: SHANGHAI YIJIE BIOTECHNOLOGY CO. LTD, TU, Yan, Rm 301, Bu Xuhui District, Shanghai 200032, CN	ilding 6, #333 Guiping Rd.	GPC3-24 DD		LTD 2016-02-04 C12N 15/62 PROTEIN AND T LYMPHOCYTE FOR EXPRESSION OF CHIMERIC ANTIGEN receptor protein expressed on surface of human T lymphocyte, useful fr
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Gazette Date Code Description		
2016-03-01 WWE WIPO INFORMATION: ENTRY INTO NATIONAL PHASE US 14889778	生要盐水组	LTD 2015-11-19 C12N 15/62
+ 2015-12-07 ENP ENTRY INTO THE NATIONAL PHASE IN: KR 20157034790 A	<b>立即从分期的</b>	PROTEIN AND T LYMPHOCYTE FOR EXPRESSION OF CHIMERIC ANTIGEN
2015-11-09 NENP NON-ENTRY INTO THE NATIONAL PHASE IN: DE	BB	
2015-11-06 ENP ENTRY INTO THE NATIONAL PHASE IN: JP 2016512212 A	GPC3- 8 Z/EL	receptor protein expressed on surface of human I lymphocyte, useful for
2014-12-31 121 EP: THE EPO HAS BEEN INFORMED BY WIPO THAT EP WAS DESIGNATED IN THIS APPLICATION EP 14794936 A1	CC	
	DD DD	LTD 2016-02-04 C12N 15/62
		PROTEIN AND T LYMPHOCYTE FOR EXPRESSION OF CHIMERIC ANTIGEN
Get Family Legal Status		- recentor protein expressed on surface of human T lymphocyte useful for
Family		
		±
Family ?		2016-03-24 C07K 14/725
+ Expand INPADOC Family (10) INPADOC Family: Alive		racellular spacer comprising at least part of the extracellular domain of
Record 23 of 38	Go to page	Go ating cancer
100 I I I I I I I I I I I I I I I I I I		
27 <u>WO2016073629A1</u>	UNIV TEXAS UNIVERSITY OF T	EXAS 2016-05-12 C07K 16/28
DWPI Drawing:	Title: CHIMERIC ANTIGEN RECEPTORS (CAR) TO SELECTIVE	ELY TARGET PROTEIN COMPLEXES
	DWPI Title: New chimeric antigen receptor polypeptide use	ed in pharmaceutical composition for treating cancer, comprising antigen binding
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WO2014180306A	1Family Legal Sta	atus Report - 10 me	embers found				💡 Blu	eprints for Success ((i)) 🗘	Clarivate (K
				<b>_</b>	ion 🗨 Fee	dback 🕐 Help	INC 2010-03-24	C07K 10/52	4
Jump Publication	Title		Filed	ApplNo	te: Preferre	ed Documents 🔻	encoding fusion protein comp	rising antigen binding protein that I	binds
<u>Status</u> WO20141803	06A1 NUCLEIC ACID OF CO PROTEIN AND T LYMI RECEPTOR PROTEIN	DDED GPC3 CHIMERIC ANTIGEN RECEPTOR PHOCYTE EXPRESSING GPC3 CHIMERIC ANTIGEN	2014-05-06	WO2014CN76913A		×	for treating solid tumor e.g.	ovarian cancer	
Status US201602152	61A1 Nucleic Acid Of Code Lymphocyte Expressi	d GPC3 Chimeric Antigen Receptor Protein And T ing GPC3 Chimeric Antigen Receptor Protein	2016-03-01	US14889778A			LTD 2018-08-30 EFFECTOR CELLS TARGETING	C07K 16/30 3 MESOTHELIN	
Status EP2995682A4	NUCLEIC ACID OF CO PROTEIN AND T LYMI RECEPTOR PROTEIN	DDED GPC3 CHIMERIC ANTIGEN RECEPTOR PHOCYTE EXPRESSING GPC3 CHIMERIC ANTIGEN	2014-05-06	EP2014794936A			umor drugs, or agent for diag riable region and light chain	nosing tumors which express meso variable region	othelin
<u>Status</u> CN107460201	A Nucleic acid for enco protein and T-lympho receptor protein	ding GPC (Glypican)-3 chimeric antigen receptor ocyte for expressing GPC-3 chimeric antigen	2013-05-08	CN201710672717A		QUICK VIEW	NOLOGY2014-11-13	C12N 15/09	
Status CN104140974	B 编码GPC-3嵌合抗原受体	本蛋白的核酸及表达GPC-3嵌合抗原受体 蛋白的T淋巴细胞	2013-05-08	CN201310164725A			OR PROTEIN AND T LYMPHOC	YTE EXPRESSING GPC3 CHIMERIC	ANTIGEN
<u>Status</u> CN104140974	A Nucleic acid for codir protein and T lympho receptor protein	ng GPC-3 (glypican-3) chimeric antigen receptor ocytes for expression of GPC-3 chimeric antigen	2013-05-08	CN201310164725A		Zoom (+)	receptor protein of glypican-3	encoded and expressed on surface	e of
<u>Status</u> KR201600328	7A NUCLEIC ACID OF CO PROTEIN AND T LYMI RECEPTOR PROTEIN	DDED GPC3 CHIMERIC ANTIGEN RECEPTOR PHOCYTE EXPRESSING GPC3 CHIMERIC ANTIGEN	2014-05-06	KR20157034790A	生理盐水组 AA		LTD 2015-11-19	C12N 15/62	
Status KR1857229B1	NUCLEIC ACID OF CO PROTEIN AND T LYM RECEPTOR PROTEIN	DDED GPC3 CHIMERIC ANTIGEN RECEPTOR PHOCYTE EXPRESSING GPC3 CHIMERIC ANTIGEN	2014-05-06	KR20157034790A	空载体対類組 BB GPC3- δ Z組		PROTEIN AND T LYMPHOCYTE receptor protein expressed o	FOR EXPRESSION OF CHIMERIC A n surface of human T lymphocyte,	.NTIGEN useful for
Status JP2016523518	A GPC3キメラ抗原受容 容体蛋白質を発現する1	客体蛋白氏をコードする核酸及び GPC3キメラ抗原受 『リンパ球	2014-05-06	JP2016512212A	CC GPC3-Z#1 DD		ITD 2016-02-04	C12N 15/62	
Status EP2995682A1	NUCLEIC ACID OF CO PROTEIN AND T LYMI RECEPTOR PROTEIN	DDED GPC3 CHIMERIC ANTIGEN RECEPTOR PHOCYTE EXPRESSING GPC3 CHIMERIC ANTIGEN	2014-05-06	EP2014794936A		4	PROTEIN AND T LYMPHOCYTE receptor protein expressed o	FOR EXPRESSION OF CHIMERIC A	NTIGEN
Codes All <u>Positive</u> shown:	<u>Negative</u> Positiv	e actions are shown in green, Negative actions in r	red, neutral in l	black					
WO2014180306A1: Gazette	Date Code	Description(remarks) List all possible c	odes forWO		14		2016-03-24	C07K 14/725	
2016-03-	01 WWE +	WIPO INFORMATION: ENTRY INTO NATIONAL PH	HASE (US1488	39778)			racellular anacor comprising	at least part of the outracellular do	main of
2015-12-	07 ENP	ENTRY INTO THE NATIONAL PHASE IN: ( KR201	57034790)		&fromDocDel	-true&recultee Go	ating cancer	at least part of the extracentiar do	main or
2015-11-	09 NENP	NON-ENTRY INTO THE NATIONAL PHASE IN: ( 1	DF)		anombocber				
	<b>2</b> 7	W02016073629A1 DWPI Drawing:	UNIV TEXAS Title: CHIME DWPI Title:	RIC ANTIGEN RECEPT New chimeric antigen	UNIVER ORS (CAR) TO receptor polyp	SITY OF TEXAS SELECTIVELY TAR peptide used in pha	2016-05-12 GET PROTEIN COMPLEXES armaceutical composition for t	C07K 16/28 treating cancer, comprising antigen	binding
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# Summary

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