Morgan Lewis

ASIA LIFE SCIENCES

ANTIBODY CLAIM STRATEGY
抗体专利权利要求的策略

May 2023

Presenters

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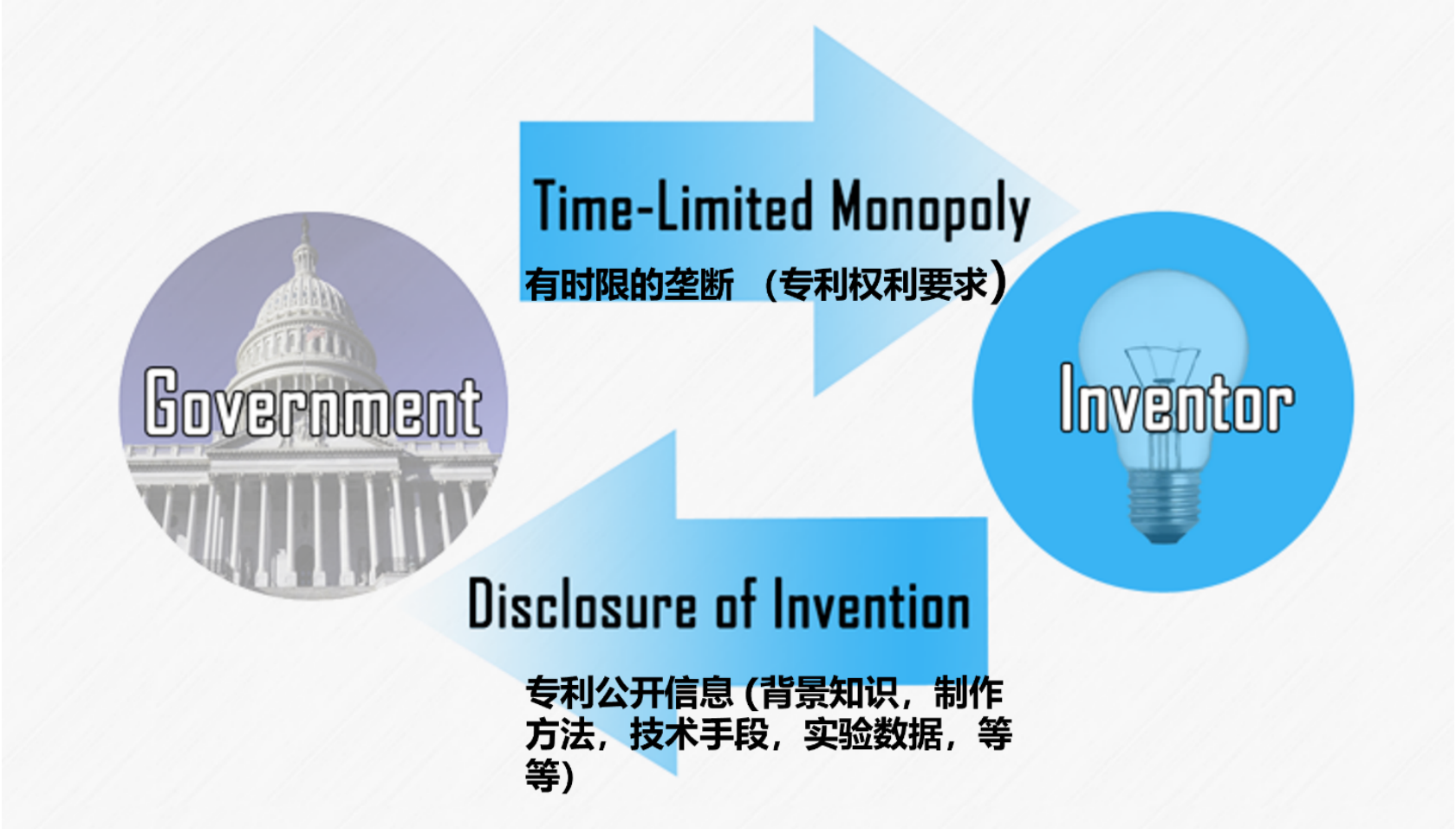
权利要求的策略

Disclosure 专利公开信息 vs. Claim 专利权利要求



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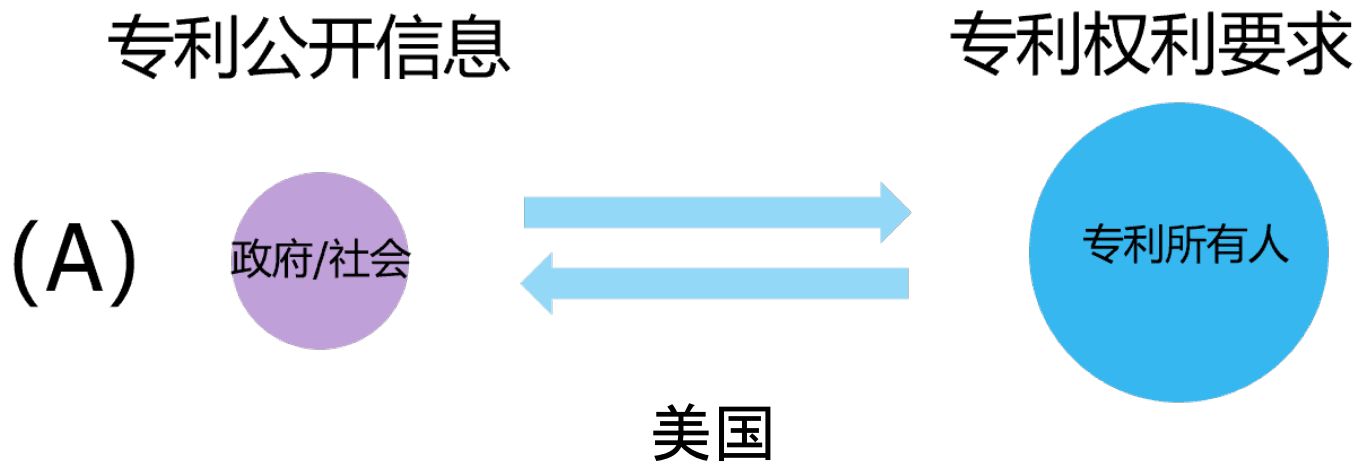


Enablement 可实施性
Written Description 书面描述

35 U.S.C. 112(a) - The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor or joint inventor of carrying out the invention.

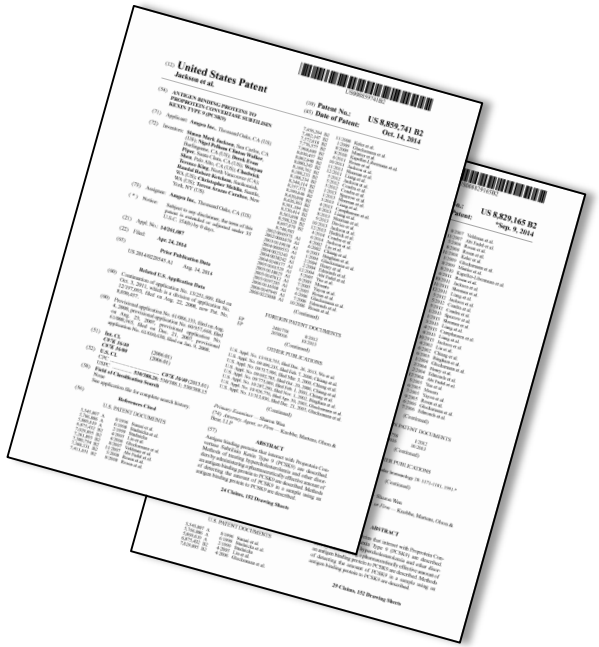
说明书应当包含发明的书面描述，并以全面、清晰、简明和准确的术语描述制造和使用发明的方式和过程，以使得本领域技术人员能够制造和使用该发明，并且说明书还应当提出发明人所想到的实施其发明的最佳实施方式。

Morgan Lewis

PART I: AMGEN V. SANOFI

Amgen Inc. v. Sanofi, Aventisub LLC (Fed. Cir. 2021)

Plaintiff 原告 / Appellant
上诉人 Amgen 安进



VS.

Defendant 被告 / Appellee 被上诉人
Sanofi 赛诺菲

阿利西尤单抗注射液（商品名：波立达®，Praluent®）PCSK9抑制剂

Amgen Inc. v. Sanofi, Aventisub LLC (Fed. Cir. 2021)

Facts: Amgen appealed from a decision of the District Court for the District of Delaware granting JMOL against Amgen of lack of enablement of claims 19 and 29 of Amgen's U.S. Patent 8,829,165 (the "'165 patent") and claim 7 of Amgen's U.S. Patent 8,859,741 (the "'741 patent"). Amgen Inc. v. Sanofi, 987 F. 3d 1080 (Fed. Cir. 2021)

诉讼经过：Amgen对特拉华州地区法院的判决提出上诉，该判决批准了有关第8,829,165号美国专利("'165号专利")权利要求19和29以及第8,859,741号美国专利("'741号专利")权利要求7在法律上缺乏可实施性的动议。

Issues: Whether Amgen's asserted claims to genera of antibodies meet the enablement requirement.

争议焦点：Amgen关于的抗体类属的权利主张是否具有可实施性。

Holding: The Federal Circuit affirmed the district court's judgment as a matter of law (JMOL) that Amgen's asserted claims to genera of antibodies were **invalid for lack of enablement**. The panel unanimously affirmed the District of Delaware's holding that undue experimentation would be required to practice the full scope of the claims-at-issue. Amgen filed a writ of certiorari to the US Supreme Court.

判决：联邦巡回上诉法院肯定了地区法院的判决，即Amgen的抗体属的权利主张因缺乏可实施性而无效。合议庭一致肯定了特拉华州地区法院的判决，即需要进行过度实验才能实现涉案权利要求所主张的全部范围。Amgen上诉到最高大法院。

***Current Status:** Amgen further appealed to the US Supreme Court on November 18, 2021. The US Supreme Court granted certiorari to review the issue of enablement on November 4, 2022. As of March 27, 2023, the Supreme Court heard oral arguments from both sides. Proceeding in progress.

当前状态：Amgen在2021年11月18日进一步向美国最高法院提出上诉。美国最高法院于2022年11月4日批准了复审申请，以审查关于可实施性的问题。截至2023年3月27日，最高法院已经听取了双方的口头辩论。复审审理目前正在正在进行中。

权利要求19&29： US 8,829,165; 以其功能宣称的抗体

19. The isolated monoclonal antibody of claim 1 wherein the isolated monoclonal antibody **binds to at least two of the following residues** S153, I154, P155, R194, D238, A239, I369, S372, D374, C375, T377, C378, F379, V380, or S381 of PCSK9 listed in SEQ ID NO:3.

权利要求19. 如权利要求1所述的分离的单克隆抗体，其中所述分离的单克隆抗体**结合以下PCSK9的SEQ ID NO:3序列残基中的至少两个**： S153、I154、P155、R194、D238、A239、I369、S372、D374、C375、T377、C378、F379、V380、或者 S381 SEQ ID NO:3 中列出的 PCSK9 的 。

29. A pharmaceutical composition comprising an isolated monoclonal antibody, wherein the isolated monoclonal antibody **binds to at least two of the following residues:** S153, I154, P155, R194, D238, A239, I369, S372, D374, C375, T377, C378, F379, V380, or S381 of PCSK9 listed in SEQ ID NO:3 and blocks the binding of PCSK9 to LDLR by at least 80%.

权利要求29. 一种药物组合物，包含分离的单克隆抗体，其中分离的单克隆抗体**结合以下PCSK9的SEQ ID NO:3序列残基中的至少两个**：S153, I154, P155, R194, D238, A239, I369, S372, D374, C375, T377, C378, F379, V380, 或 S381，并且阻断 PCSK9 与 LDLR 的结合至少 80%。

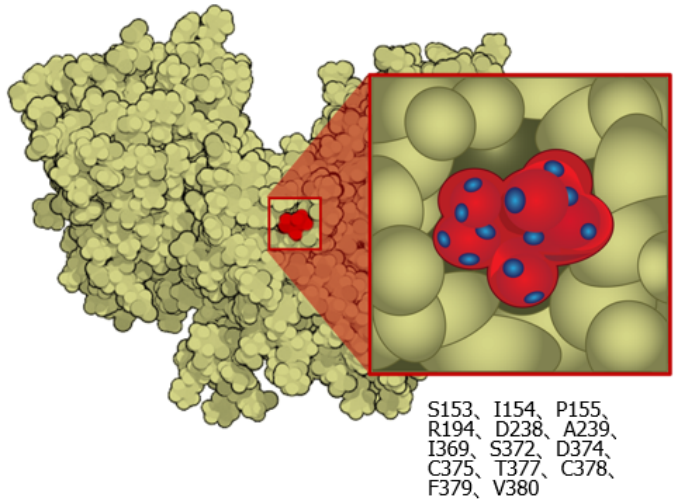
Holding: The Federal Circuit affirmed the district court's judgment as a matter of law that Amgen's asserted claims to genera of antibodies were invalid for lack of enablement. The panel unanimously affirmed the District of Delaware's holding that undue experimentation would be required to practice the full scope of the claims-at-issue.

判决：联邦巡回上诉法院肯定了地区法院的判决，即Amgen的抗体属的**权利主张因缺乏可实施性而无效**。合议庭一致肯定了特拉华州地区法院的判决，即需要进行过度实验才能实现涉案权利要求所主张的全部范围。

Amgen Inc. v. Sanofi, Aventisub LLC

Lack of Enablement: Undue Experimentation
缺乏可实施性：过度的实验

‘165 patent and ‘741 patent disclosed amino acid sequences for twenty-six PCSK9 antibodies, and three-dimensional structures for two of the antibodies.
Amgen的’165专利和’741专利披露了26种PCSK9抗体的氨基酸序列以及其中两种抗体的三维结构。



Amgen: The claims are enabled. A skilled person can make all antibodies within the scope of the claims by following a roadmap using anchor antibodies and well-known screening techniques, or by making conservative amino acid substitutions in the twenty-six examples.
Amgen：权利要求具备可实施性。熟练的技术人员可以通过使用锚定抗体和众所周知的筛选技术，或通过对二十六个示例进行保守的氨基酸替换来制造所有权利要求范围内的抗体。

vs.

Federal Circuit: No enablement because it requires undue experimentation to obtain all the claimed antibodies.
联邦巡回法院：权利要求不具备可实施性，因为获得所有权力声明中的抗体需要过度的实验。

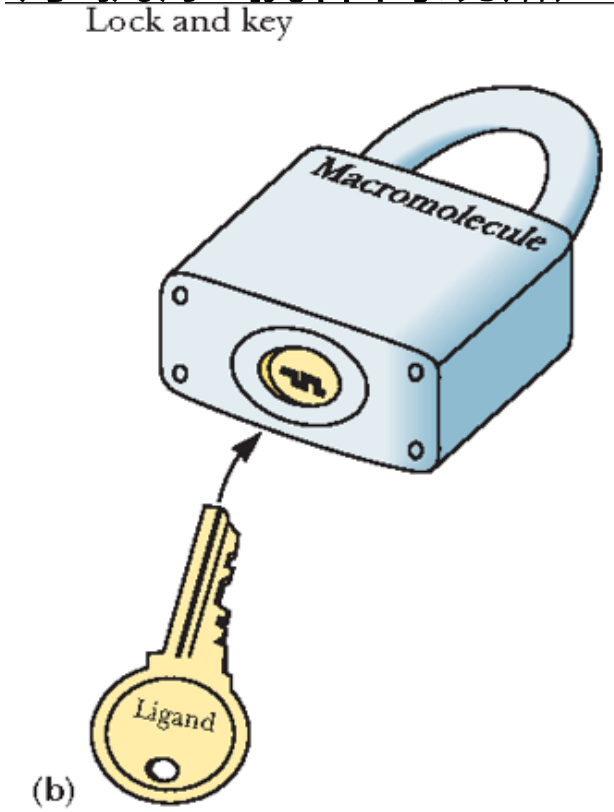
Amgen Inc. v. Sanofi, Aventisub LLC

Lack of Enablement: Undue Experimentation 缺乏可实施性：过度的实验

- **Amgen expressly claimed more than 32,000 combinations of residues and was required to enable every combination.**
- Amgen的权力要求中的抗体种类涵盖了超过 32,000 种可能的氨基酸残基组合，因此Amgen需要证明每种组合的可实施性
- **Determining where a particular antibody binds requires x-ray crystallography, a time-consuming and unpredictable methodology.**确定特定抗体的结合位置需要 X 射线晶体学，这是一种耗时且不可预测的方法
- **Performing amino acid substitutions according to the specification's instructions would lead to "millions of candidates" that must be tested.**
- 根据规范的说明进行氨基酸替换将导致必须测试的"数百万候选者"

Amgen Inc. v. Sanofi, Aventisub LLC

Old view of antigen-antibody: "Lock and Key"
过去关于抗原-抗体的观点："锁和钥匙"



VS.

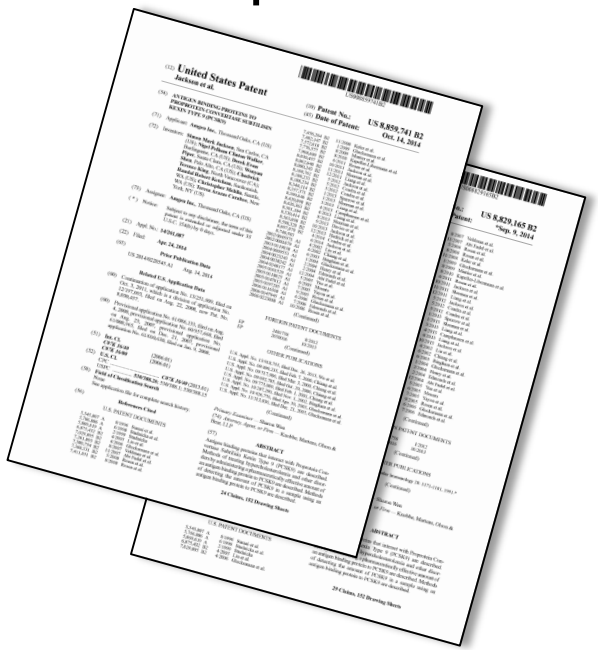
Post-*Amgen*: "A ring with a million Keys on it" 目前关于抗原-抗体的观点："钥匙圈上面有一百万个钥匙"

Morgan Lewis

PART II: JUNO V. KITE

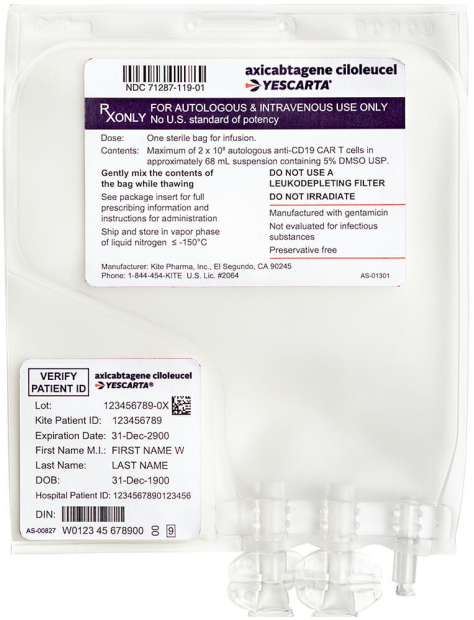
Juno Therapeutics, Inc., Sloan Kettering Institute For Cancer Research v. Kite Pharma, Inc. (Fed. Cir. 2021)

Plaintiff 原告 / Appellant 上诉人
Juno Therapeutics 朱诺医疗



VS.

Defendant 被告 / Appellee 被上诉人
Kite Pharma 凯特制药 （吉利德旗下公司）



阿基伦塞注射液（商品名：奕凯达®，Yescarta®）

Juno Therapeutics, Inc. v. Kite Pharma, Inc. (Fed. Cir. 2021)

Facts: Juno sued Kite, alleging that Kite's CD19-targeting Yescarta willfully infringed upon U.S. Patent No. 7,446,190 (the "'190 Patent"). During the trial, Kite defended by asserting the '190 Patent was invalid for lacking written description in support of the patent claims. The Jury's verdict unanimously found the '190 patent to be valid, with sufficient written description, and accordingly awarded Juno a total damage of $1.2 billion. Kite appealed to the Federal Circuit. Juno Therapeutics, Inc. v. Kite Pharma, Inc., No. 20-1758 (Fed. Cir. 2021)

诉讼经过：Juno起诉Kite，称Kite的CD19靶向疗法奕凯达®有意侵犯了美国专利号7,446,190（"'190专利"）。在审判期间，Kite称该'190专利缺乏书面描述而无效。陪审团一致裁定该'190专利有效，存在足够的书面描述以支持该专利的权力诉求，并相应地判给Juno总计12亿美元的赔偿。Kite上诉至联邦巡回法院。

Issues: Whether there was sufficient written description in the '190 patent for its patented CAR-T claims.

争议焦点：该'190专利是否具有足够的书面描述来支持其关于CAR-T的权利要求。

Holding: The Federal Circuit reversed the district court's judgment, invalidating the '190 patent for lacking written description and wiping out the $1.2 billion damage award for Juno.

判决：联邦巡回法院推翻了地方法院的判决，宣布该'190专利因缺乏书面描述无效，并取消对Juno的12亿美元赔偿。

***Current Status:** Juno appealed to the US Supreme Court on June 13, 2022. The US Supreme Court denied certiorari on November 7, 2022 and affirmed the denial on January 9, 2023, making the Federal Circuit's decision in favor of Kite now final.

当前状态：Juno于2022年6月13日向美国最高法院提出上诉。最高法院于2022年11月7日拒绝了复审申请并于2023年1月9日确认了此前的拒绝决定，这使得联邦巡回法院对Kite有利的裁决成为了终审裁决。

Juno Therapeutics, Inc. v. Kite Pharma, Inc. (Fed. Cir. 2021)

Claim 1. A nucleic acid polymer encoding a chimeric T cell receptor, said chimeric T cell receptor comprising: (a) a zeta chain portion comprising the intracellular domain of human CD3 ζ chain, (b) a costimulatory signaling region, and **(c) a binding element that specifically interacts with a selected target**, wherein the costimulatory signaling region comprises the amino acid sequence encoded by SEQ ID NO:6.

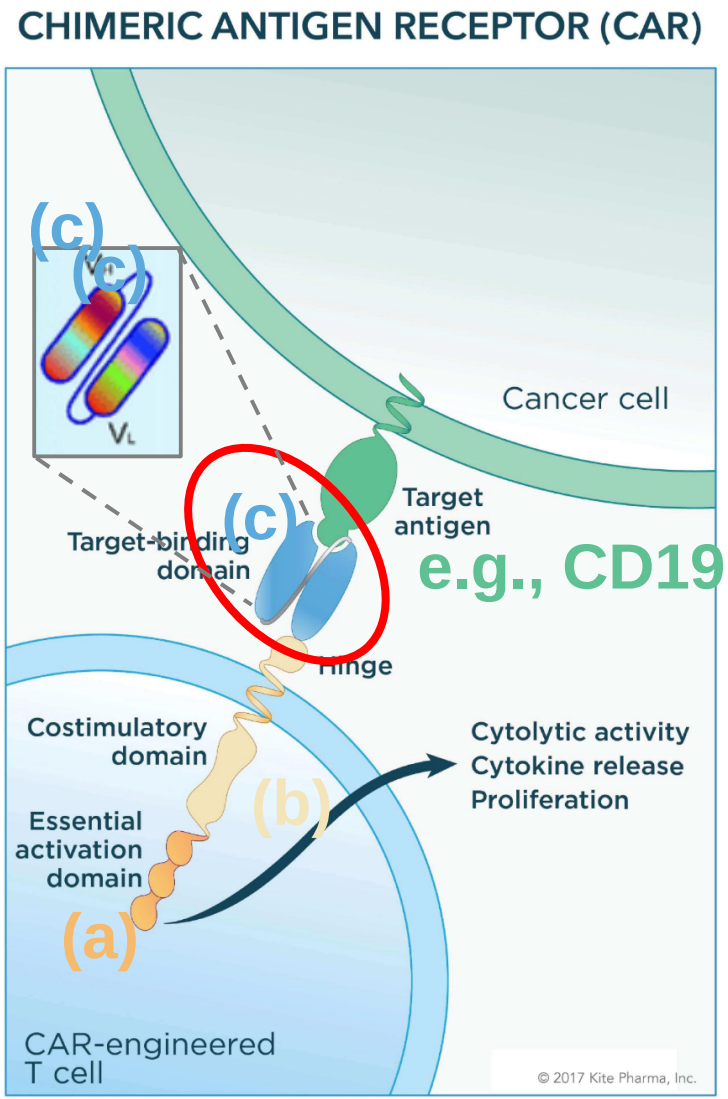
权利要求1. 一个编码CAR-T的核酸聚合物，所述CAR-T包括：（a）ζ链部分，包括人类CD3 ζ链的胞内域，(b）共刺激信号区域，和 **（c）特异性与所选靶标相互作用的结合元素**，其中，共刺激信号区域包括由SEQ ID NO:6编码的氨基酸序列。

Claim 3. The nucleic acid polymer of claim 2, wherein the antibody is **a single chain antibody**.

权利要求3. 根据权利要求2的核酸聚合物，其中所述抗体是单链抗体。

Claim 5. The nucleic acid polymer of claim 3, wherein **the single chain antibody binds to CD19**.

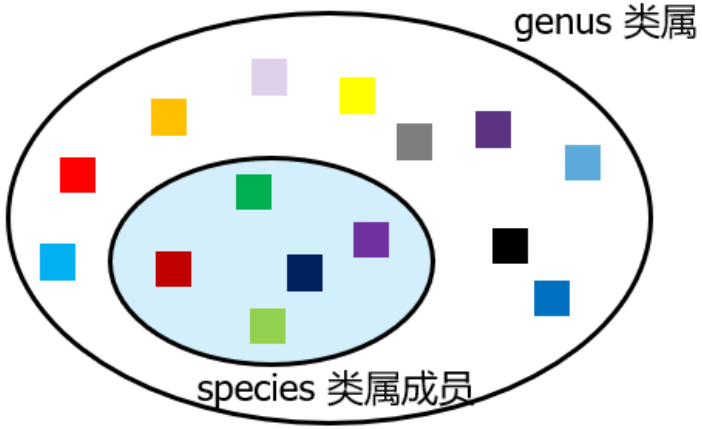
权利要求5. 根据权利要求3的核酸聚合物，其中所述单链抗体结合于**CD19**。



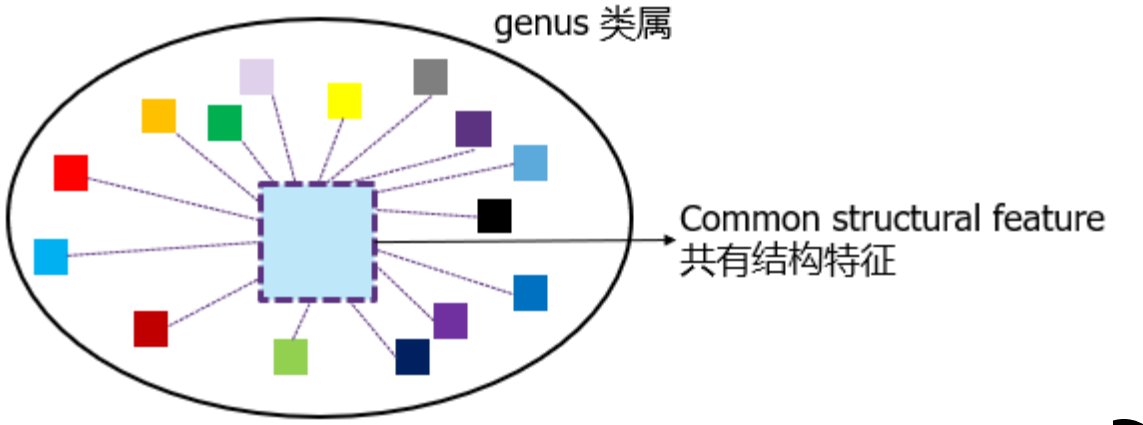
Juno Therapeutics, Inc. v. Kite Pharma, Inc. (Fed. Cir. 2021)

Two ways for an applicant to establish written description for a genus claim 建立一般类属权利要求的书面说明的两种方式：

(A) establishing **a representative number of species** falling within the scope of the claimed genus 确定落入所要求类属范围内的**一定数量的代表性类属成员**



(B) establishing **structural features common to the members of the genus** so that a skilled person can visualize or recognize the species of the genus 确定**类属成员的共有结构特征，使得熟**练的技术人员能够描述或识别类属成员。



Juno Therapeutics, Inc. v. Kite Pharma, Inc. (Fed. Cir. 2021)

(A) Representative Number of Species 一定数量的代表性类属成员

The ’190 patent discloses two example scFvs species: one derived from J591, which targets a PSMA antigen on prostate cancer cells, and another derived from SJ25C1, which targets CD19.

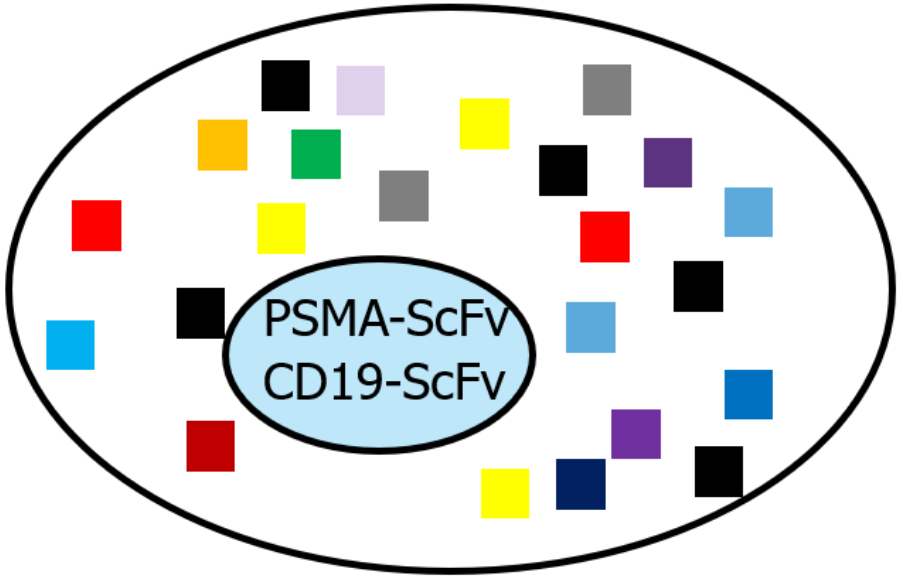
‘190专利”披露了两个scFv的具体范例：一个源自于J591针对靶向前列腺癌细胞上的PSMA抗原，另一个源自于SJ25C1针对靶向CD19。

Juno and Kite agreed the number of possible sequences for scFvs in the claim scope is in the range of millions of billions.

Juno和Kite认为权利要求涵盖的可能的scFv氨基酸序列数目在万兆级别的数量级范围内。

Federal Circuit: “The disclosure of one scFv that binds to CD19 and one scFv that binds to a PSMA antigen on prostate cancer cells in the manner provided in this patent does **not provide information sufficient to establish that a skilled artisan would understand how to identify the species of scFvs capable of binding to the limitless number of targets as the claims require**.”

联邦巡回法院：“本专利提供的只有一个与CD19结合和另一个与前列腺癌细胞上的PSMA抗原结合的scFv的披露。这些信息不足以能使得熟练的技术人员能够识别结合于无限数量的靶标上的scFv类属成员。”



Juno Therapeutics, Inc. v. Kite Pharma, Inc. (Fed. Cir. 2021)

(B) Common Structural Feature 共有结构特征

Juno argues that scFvs have the same general, common structure consisting of a variable region derived from the light chain of an antibody and a variable region derived from the heavy chain of an antibody. The Federal Circuit rejected this argument.

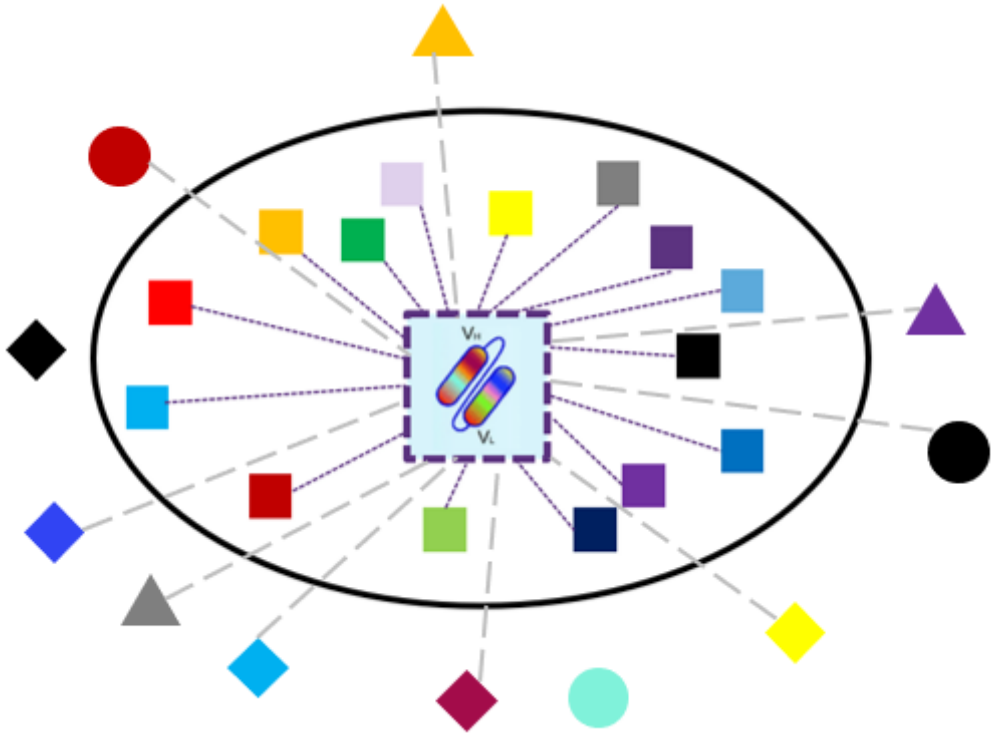
Juno认为scFv具有相同的普遍、共同结构，包括来源于抗体轻链的可变区和来源于抗体重链的可变区。联邦巡回法院驳回了这个观点。

Federal Circuit: "The '190 patent not only fails to disclose structural features commo to scFvs capable of binding specific targets, it also fails to disclose a way to distinguish those scFvs capable of binding from scFvs incapable of binding those targets".

联邦巡回法院："'190专利'不仅未披露与能够结合特定靶标的scFv的共有结构特征，而且也未披露如何区分具有结合能力的scFv和不具有结合能力的scFv的方法。"

In other words, there is no correlation between the commonality Juno asserted and the functionality of the claimed scFvs species. As such, the asserted commonality, according to the Court, does not constitute a common structural feature.

换句话说，Juno主张的scFv的结构相似性与scFv的功能（结合抗原）并不相关。因此，Juno所谓的结构相似性并不能构成"共有结构特征"。

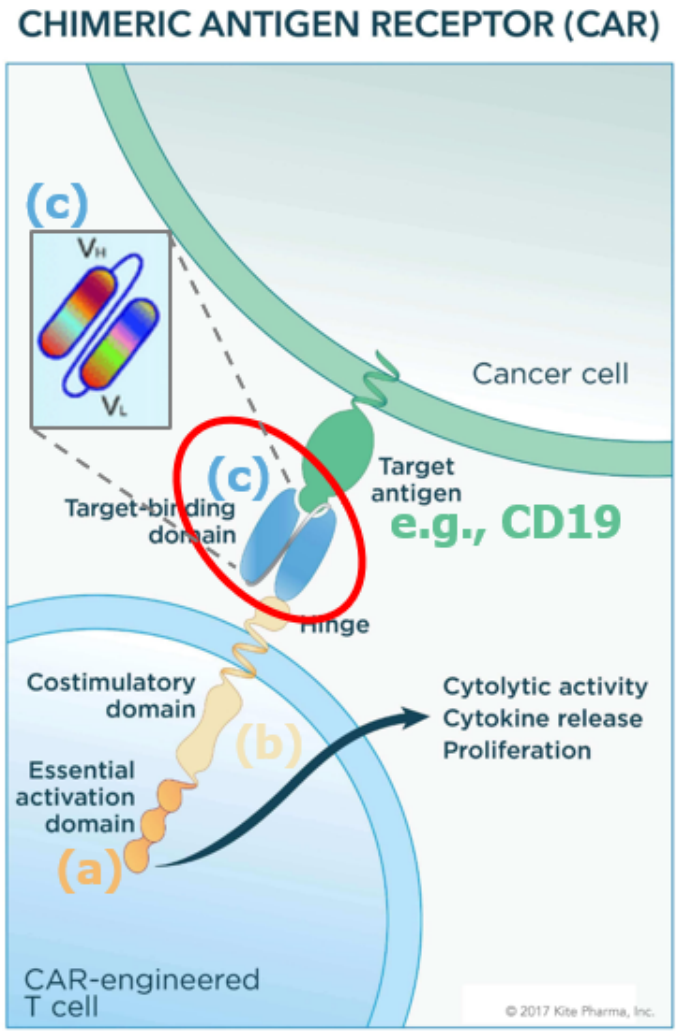


Juno Therapeutics, Inc. v. Kite Pharma, Inc. (Fed. Cir. 2021)

Was the Federal Circuit justified in focusing the debate on the genus of scFv while disregarding other domains?
联邦巡回法院将争议的核心集中在scFv而回避其他CAR-T结构区域的论证方法是否合理？

Claim 1. A nucleic acid polymer encoding a chimeric T cell receptor, said chimeric T cell receptor comprising: (a) a zeta chain portion comprising the intracellular domain of human CD3 ζ chain, (b) a costimulatory signaling region, and (c) a binding element that specifically interacts with a selected target, **wherein the costimulatory signaling region comprises the amino acid sequence encoded by SEQ ID NO:6**.

权利要求1. 一个编码CAR-T的核酸聚合物，所述CAR-T包括：（a）ζ链部分，包括人类CD3 ζ链的胞内域，(b）共刺激信号区域，和（c）特异性与所选靶标相互作用的结合元素，**其中，共刺激信号区域包括由SEQ ID NO:6编码的氨基酸序列**。



Morgan Lewis

PART III: CLAIMING STRATEGY

权利要求的策略

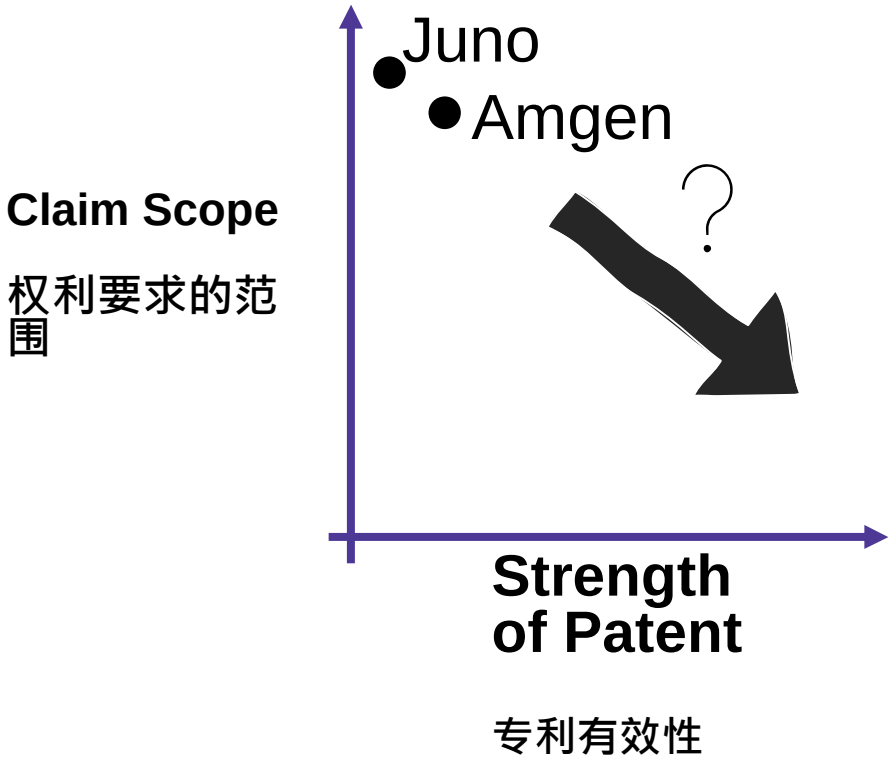
Claiming Strategy 权利要求的策略

Claim Scope
权利要求的范围

- Freedom to operate or not 自由实施
- Patent protection for future modification or improvement 未来 技术升级的专利保护
- Protection against competitor product 针对竞争对手产品的专利保护

Strength of Patent
专利有效性

- Examination 专利审查
- Litigation 专利诉讼



Strategies for Claiming Antibodies 抗体权利要求的策略

Sequence & Structure序列与结构

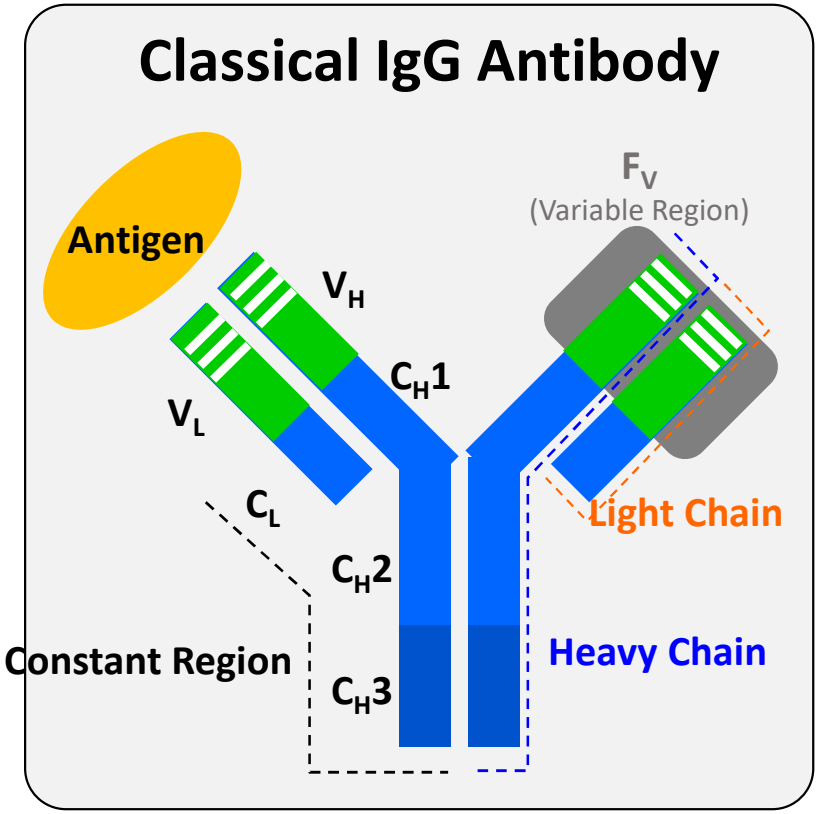
> Claim directed to entire heavy and light chain sequences. 针对整个重链和轻链序列的权利要求

Example 例子

An antibody that binds antigen X, comprising a heavy chain as set forth in SEQ ID NO: 1 and a light chain as set forth in SEQ ID NO: 2. 一种结合抗原X的抗体，其包含如SEQ ID NO: 1所示的重链和如SEQ ID NO: 2所示的轻链。

> Full-length heavy and/or light chain variable region (VH/VL). 全长重链和/或轻链可变区

> Heavy and/or light chain CDRs 重链和/或轻链可变区



Strategies for Claiming Antibodies 抗体权利要求的策略

1. A composition comprising an anti-PVRIG antibody, wherein said antibody comprises:

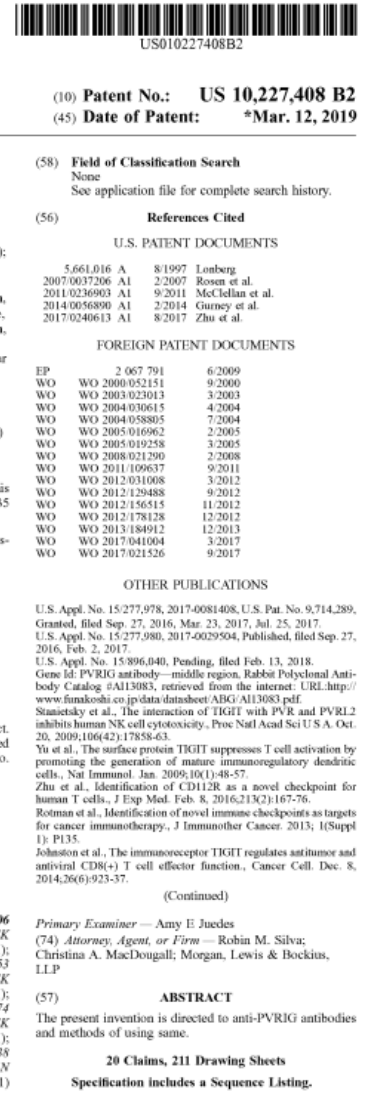
   i) the vhCDR1, vhCDR2, and vhCDR3 from SEQ ID NO:1434 and

   ii) the vlCDR1, vlCDR2, and vlCDR3 from SEQ ID NO:1453.

权利要求1. 一种包含PVRIG抗体的药物组合物，该抗体包括：

   i) 蛋白质序列编号1434包含的的vhCDR1, vhCDR2, 和vhCDR3；以及

   ii)蛋白质序列编号1453包含的的vlCDR1, vlCDR2, vlCDR3。



US010227408B2

(12) **United States Patent**
White et al.

(10) **Patent No.: US 10,227,408 B2**
(45) **Date of Patent: *Mar. 12, 2019**

(54) **ANTI-PVRIG ANTIBODIES AND METHODS OF USE**

(71) Applicant: **Compugen, Ltd.**, Holon (IL)

(72) Inventors: **Mark White**, Antioch, CA (US); **Sandeep Kumar**, San Bruno, CA (US); **Christopher Chan**, South San Francisco, CA (US); **Spencer Liang**, San Mateo, CA (US); **Lance Stapleton**, Oakland, CA (US); **Andrew W. Drake**, Mountain View, CA (US); **Yosi Gozlan**, Tel Aviv (IL); **Ilan Vaknin**, Tel Aviv (IL); **Shirley Sameah-Greenwald**, Kfar Saba (IL); **Liat Dassa**, Tel Aviv (IL); **Zohar Tiran**, Oranit (IL); **Gad S. Cojocaru**, Tel Aviv (IL); **Leonard Presta**, San Francisco, CA (US); **Richard Theolis**, Santa Cruz, CA (US)

(73) Assignee: **Compugen Ltd.**, Holon (IL)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 172 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **15/048,967**

(22) Filed: **Feb. 19, 2016**

(65) **Prior Publication Data**

US 2016/0244521 A1 Aug. 25, 2016

Related U.S. Application Data

(60) Provisional application No. 62/235,823, filed on Oct. 1, 2015, provisional application No. 62/141,120, filed on Mar. 31, 2015, provisional application No. 62/118,208, filed on Feb. 19, 2015.

(51) **Int. Cl.**

C07K 16/00	(2006.01)
C12P 21/08	(2006.01)
C07K 16/28	(2006.01)
G01N 33/574	(2006.01)
C07K 7/06	(2006.01)
C12N 15/113	(2010.01)

(52) **U.S. Cl.**

CPC ***C07K 16/2803*** (2013.01); ***C07K 7/06*** (2013.01); ***G01N 33/57484*** (2013.01); *C07K 2317/21* (2013.01); *C07K 2317/33* (2013.01); *C07K 2317/34* (2013.01); *C07K 2317/53* (2013.01); *C07K 2317/55* (2013.01); *C07K 2317/56* (2013.01); *C07K 2317/565* (2013.01); *C07K 2317/70* (2013.01); *C07K 2317/74* (2013.01); *C07K 2317/76* (2013.01); *C07K 2317/92* (2013.01); *C07K 2319/30* (2013.01); *C07K 2319/32* (2013.01); *C12N 15/1138* (2013.01); *C12N 2310/14* (2013.01); *G01N 2333/47* (2013.01)

(58) **Field of Classification Search**
None
See application file for complete search history.

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U.S. Appl. No. 15/896,040, Pending, filed Feb. 13, 2018.
Gene Id: PVRIG antibody—middle region, Rabbit Polyclonal Antibody Catalog #AI13083, retrieved from the internet: URL:http://www.funakoshi.co.jp/data/datasheet/ABG/AI13083.pdf.
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Yu et al., The surface protein TIGIT suppresses T cell activation by promoting the generation of mature immunoregulatory dendritic cells., Nat Immunol. Jan. 2009;10(1):48-57.
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Primary Examiner — Amy E Juedes
(74) *Attorney, Agent, or Firm* — Robin M. Silva; Christina A. MacDougall; Morgan, Lewis & Bockius, LLP

(57) **ABSTRACT**

The present invention is directed to anti-PVRIG antibodies and methods of using same.

20 Claims, 211 Drawing Sheets

Specification includes a Sequence Listing.

Strategies for Claiming Antibodies抗体权利要求的策略

Sequence & Structure 序列与结构

- Homologous sequences 同源序列
  - 70%, 80%, 90%, 95% identical/similar相同/相似

  Example例子:

  An antibody that binds antigen X, comprising a heavy chain having at least 95% sequence identity to SEQ ID NO: 1 and a light chain having at least 95% sequence identity to SEQ ID NO: 2. 一种结合抗原X的抗体，其包含与SEQ ID NO: 1具有至少95%序列同一性的重链和与SEQ ID NO: 2具有至少95%序列同一性的轻链。
- Substitutions 氨基酸替换
- Fragments碎片

Strategies for Claiming Antibodies抗体权利要求的策略

25. A method of activating T-cells of a patient with cancer comprising administering an anti-PVRIG antibody to said patient, wherein said anti-PVRIG antibody comprises:

i) a heavy chain variable domain comprising a sequence exhibiting at least 90% identity to SEQ ID NO:1434, wherein each individual vhCDR from SEQ ID NO:1434 comprises no more than 1 substitution, and wherein the vhCDR3 comprises no substitutions, and

ii) a light chain variable domain comprising a sequence exhibiting at least 90% identity to SEQ ID NO:1453, wherein each individual vlCDR from SEQ ID NO:1453 comprises no more than 1 substitution, and wherein the vlCDR3 comprises no substitutions, and

wherein a subset of said T-cells of said patient are activated.

权利要求25. 一种激活癌症病人T－细胞的方法，包括了给该病人施用PVRIG抗体，其中所述抗 PVRIG 抗体包括：

i) 重链可变结构域，其序列与 SEQ ID NO: 1434 具有至少 90% 的相似度，其中来自 SEQ ID NO: 1434 的每个单独的 vhCDR 包含不超过 1 个氨基酸替换，并且其中 vhCDR3 不包含任何氨基酸替代，和

ii)轻链可变结构域，其序列与SEQ ID NO:1453具有至少 90% 的相似度，其中来自SEQ ID NO:1453的每个单独的vlCDR包含不超过1个氨基酸替代，并且其中vlCDR3不包含任何氨基酸替代，和

其中所述患者的所述T细胞的子集被激活。


US011220542B2

(12) **United States Patent**
White et al.

(10) **Patent No.: US 11,220,542 B2**
(45) **Date of Patent: Jan. 11, 2022**

(54) **ANTI-PVRIG ANTIBODIES AND METHODS OF USE**

(71) Applicant: **Compugen Ltd.**, Holon (IL)

(72) Inventors: **Mark White**, Antioch, CA (US); **Sandeep Kumar**, San Bruno, CA (US); **Christopher Chan**, South San Francisco, CA (US); **Spencer Liang**, San Mateo, CA (US); **Lance Stapleton**, Oakland, CA (US); **Andrew W. Drake**, Mountain View, CA (US); **Yosi Gozlan**, Tel Aviv (IL); **Ilan Vaknin**, Tel Aviv (IL); **Shirley Sameah-Greenwald**, Kfar Saba (IL); **Liat Dassa**, Tel Aviv (IL); **Zohar Tiran**, Oranit (IL); **Gad S. Cojocaru**, Tel Aviv (IL); **Leonard Presta**, San Francisco, CA (US); **Richard Theolis**, Santa Cruz, CA (US)

(73) Assignee: **Compugen Ltd.**, Holon (IL)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **15/277,980**

(22) Filed: **Sep. 27, 2016**

(65) **Prior Publication Data**

US 2017/0029504 A1 Feb. 2, 2017

Related U.S. Application Data

(62) Division of application No. 15/048,967, filed on Feb. 19, 2016.

(60) Provisional application No. 62/118,208, filed on Feb. 19, 2015, provisional application No. 62/141,120, filed on Mar. 31, 2015, provisional application No. 62/235,823, filed on Oct. 1, 2015.

(51) **Int. Cl.**

C07K 16/28	(2006.01)
C07K 7/06	(2006.01)
G01N 33/574	(2006.01)
C12N 15/113	(2010.01)

(52) **U.S. Cl.**

CPC ***C07K 16/2803*** (2013.01); ***C07K 7/06*** (2013.01); ***G01N 33/57484*** (2013.01); *C07K 2317/21* (2013.01); *C07K 2317/33* (2013.01); *C07K 2317/34* (2013.01); *C07K 2317/53* (2013.01); *C07K 2317/55* (2013.01); *C07K 2317/56* (2013.01); *C07K 2317/565* (2013.01); *C07K 2317/70* (2013.01); *C07K 2317/74* (2013.01); *C07K 2317/76* (2013.01); *C07K 2317/92* (2013.01); *C07K 2319/30* (2013.01); *C07K 2319/32* (2013.01); *C12N 15/1138* (2013.01); *C12N 2310/14* (2013.01); *G01N 2333/47* (2013.01)

(58) **Field of Classification Search**

None

See application file for complete search history.

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2017/0240613	A1	8/2017	Zhu et al.

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Gene ID: PVRIG antibody—middle region, Rabbit Polyclonal Antibody Catalog #AI13083, retrieved from the internet: URL:http://www.funakoshi.co.jp/data/datasheet/ABG/AI13083.pdf.
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Primary Examiner — Amy E Juedes

(57) **ABSTRACT**

The present invention is directed to anti-PVRIG antibodies and methods of using same.

42 Claims, 234 Drawing Sheets

Specification includes a Sequence Listing.

Strategies for Claiming Antibodies抗体权利要求的策略

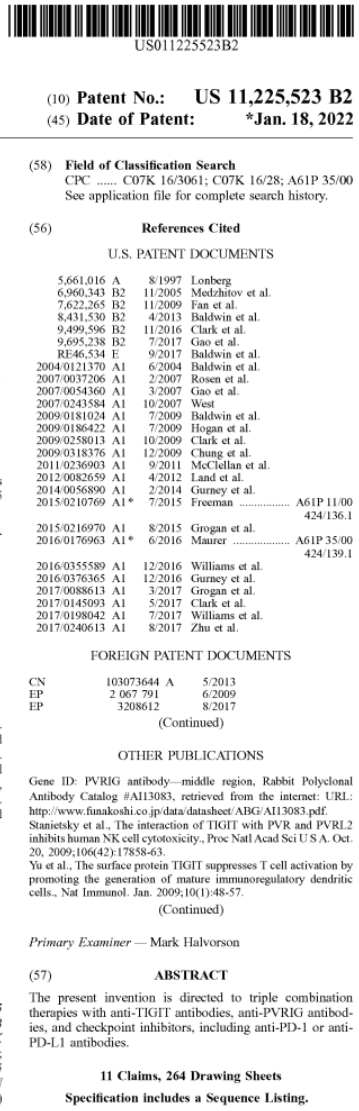
Combination Therapy Claims 联合疗法权利要求

e.g .,A combination comprising components A, B and C…

一个包含了组件A、B和C成员的组合

1. A method of treatment for cancer in a patient comprising administering the triple combination comprising an anti-TIGIT antibody, an anti-PVRIG antibody and an anti-PD-1 antibody, wherein said anti-PVRIG antibody is an antibody chosen from at least one of CHA.7.518.1.H4(S241P) and CHA.7.538.1.2.H4(S241P).

权利要求1. 一种治疗患者癌症的方法，包括给予三联组合物，所述三联组合物包括抗TIGIT抗体、抗PVRIG抗体和抗PD-1抗体，其中所述抗PVRIG抗体是从CHA.7.518.1.H4(S241P)和CHA.7.538.1.2.H4(S241P)中选择的至少一种抗体。



US011225523B2

(12) **United States Patent**
Liang et al.

(10) **Patent No.: US 11,225,523 B2**
(45) **Date of Patent: *Jan. 18, 2022**

(54) **TRIPLE COMBINATION ANTIBODY THERAPIES**

(71) Applicant: **Compugen Ltd.**, Holon (IL)

(72) Inventors: **Spencer Liang**, Belmont, CA (US); **Ling Leung**, Foster City, CA (US); **Sarah Whelan**, Mountain View, CA (US); **Maya Kotturi**, Belmont, CA (US); **Eran Ophir**, Yehuda (IL); **Arthur Machlenkin**, Givaat Brener (IL); **Zoya Alteber**, Nes Ziyona (IL); **Meir Azulay**, Givatayim (IL); **Sandeep Kumar**, San Bruno, CA (US); **Radhika Desai**, Brisbane, CA (US); **Christopher Chan**, South San Francisco, CA (US); **Kathryn Logronio**, Pleasanton, CA (US)

(73) Assignee: **Compugen Ltd.**, Holon (IL)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 505 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **15/996,369**

(22) Filed: **Jun. 1, 2018**

(65) **Prior Publication Data**

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(60) Provisional application No. 62/513,960, filed on Jun. 1, 2017, provisional application No. 62/515,452, filed on Jun. 5, 2017, provisional application No. 62/538,563, filed on Jul. 28, 2017, provisional application No. 62/547,051, filed on Aug. 17, 2017, provisional application No. 62/582,756, filed on Nov. 7, 2017, provisional application No. 62/618,005, filed on Jan. 16, 2018.

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A61K 39/395	(2006.01)
C07K 16/30	(2006.01)
A61P 35/00	(2006.01)
A61K 38/17	(2006.01)
C07K 16/24	(2006.01)
C07K 16/42	(2006.01)
G01N 33/574	(2006.01)

(52) **U.S. Cl.**

CPC ***C07K 16/3061*** (2013.01); ***A61K 39/395*** (2013.01); ***A61P 35/00*** (2018.01); ***C07K 16/28*** (2013.01); ***C07K 16/2803*** (2013.01); *A61K 38/1709* (2013.01); *A61K 2300/00* (2013.01); *C07K 16/24* (2013.01); *C07K 16/2875* (2013.01); *C07K 16/4283* (2013.01); *G01N 33/57484* (2013.01)

(58) **Field of Classification Search**

CPC C07K 16/3061; C07K 16/28; A61P 35/00

See application file for complete search history.

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EP	3208612	8/2017

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Yu et al., The surface protein TIGIT suppresses T cell activation by promoting the generation of mature immunoregulatory dendritic cells., Nat Immunol. Jan. 2009;10(1):48-57.

(Continued)

Primary Examiner — Mark Halvorson

(57) **ABSTRACT**

The present invention is directed to triple combination therapies with anti-TIGIT antibodies, anti-PVRIG antibodies, and checkpoint inhibitors, including anti-PD-1 or anti-PD-L1 antibodies.

11 Claims, 264 Drawing Sheets

Specification includes a Sequence Listing.

Strategies for Claiming Antibodies抗体权利要求的策略

Function功能

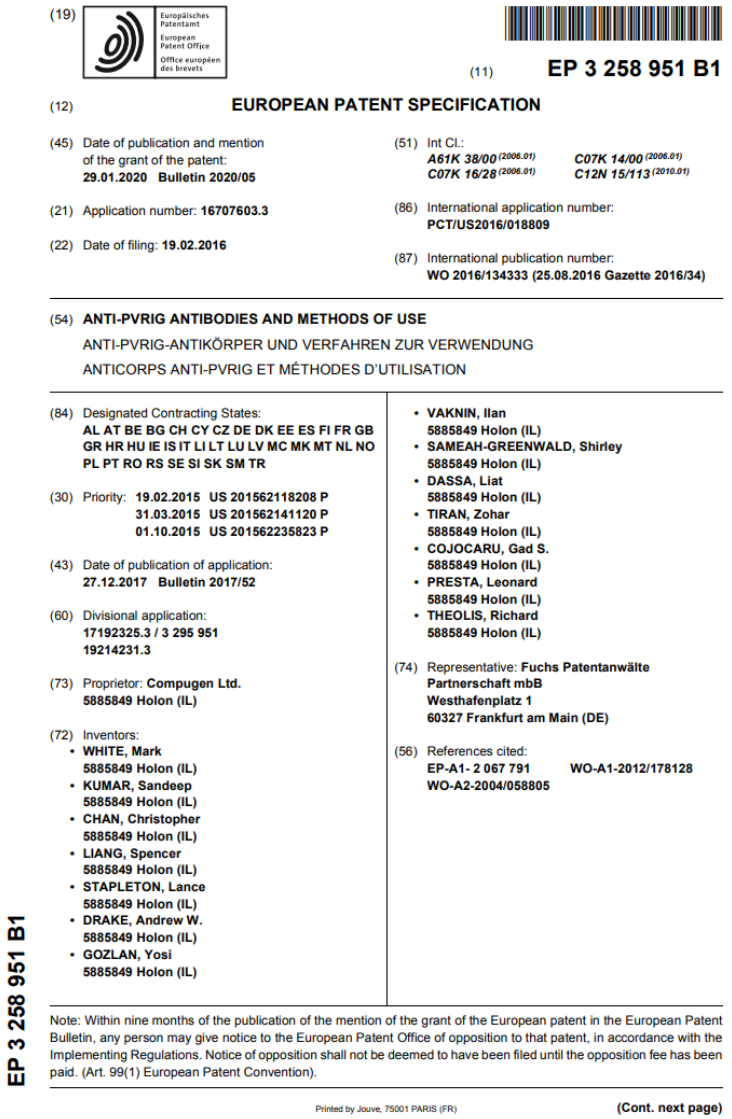
- Binding affinity (e.g., Kd, K_{off}) 结合亲和力
- Effect of binding interaction 结合相互作用的影响
- Treatment of disease/disorder **疾病/障碍的治**疗
- Competition for binding with other antibodies 竞争与其他抗体的结合

  Example: An antibody that binds antigen X, and competes with reference antibody Y for binding to antigen X. 结合抗原 X **并与参考抗体** Y 竞争结合抗原 X **的抗体**

Strategies for Claiming Antibodies抗体权利要求的策略

1.An anti-PVRIG (Poliovirus Receptor Related Immunoglobulin Domain Containing Protein) antibody for use in the treatment of cancer, wherein the antibody activates T cells and/or NK cells.

1. 一种用于治疗癌症的抗 PVRIG（脊髓灰质炎病毒受体相关免疫球蛋白结构域）抗体，其中该抗体激活 T 细胞和/或 NK 细胞。



(19) Europäisches Patentamt / European Patent Office / Office européen des brevets

(11) EP 3 258 951 B1

(12) EUROPEAN PATENT SPECIFICATION

(45) Date of publication and mention of the grant of the patent:
29.01.2020 Bulletin 2020/05

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(22) Date of filing: **19.02.2016**

(51) Int Cl.:
A61K 38/00 *(2006.01)* ***C07K 14/00*** *(2006.01)*
C07K 16/28 *(2006.01)* ***C12N 15/113*** *(2010.01)*

(86) International application number:
PCT/US2016/018809

(87) International publication number:
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(54) **ANTI-PVRIG ANTIBODIES AND METHODS OF USE**
ANTI-PVRIG-ANTIKÖRPER UND VERFAHREN ZUR VERWENDUNG
ANTICORPS ANTI-PVRIG ET MÉTHODES D'UTILISATION

(84) Designated Contracting States:
AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HR HU IE IS IT LI LT LU LV MC MK MT NL NO PL PT RO RS SE SI SK SM TR

(30) Priority: **19.02.2015 US 201562118208 P**
31.03.2015 US 201562141120 P
01.10.2015 US 201562235823 P

(43) Date of publication of application:
27.12.2017 Bulletin 2017/52

(60) Divisional application:
17192325.3 / 3 295 951
19214231.3

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- **LIANG, Spencer**
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- **STAPLETON, Lance**
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Strategies for Claiming Antibodies抗体权利要求的策略

Steps to Functionally Claim an Antibody:功能性权利要求抗体的步骤

- Identify all inventive antibodies 描述所有创造性抗体
- Determine similarities and difference of one or more characteristics 确定一个或多个特征的异同
  - IGHV germline genes, HCDR3 lengths, canonical structures, binding epitopes, identity of heavy/light chain, etc. 免疫球蛋白重链基因种系基因、HCDR3长度、典型结构、结合表位、轻重链特征等
- Assess percentage of known antibodies represented by the diversity of each characteristic评估每个特征的多样性所代表的已知抗体的百分比

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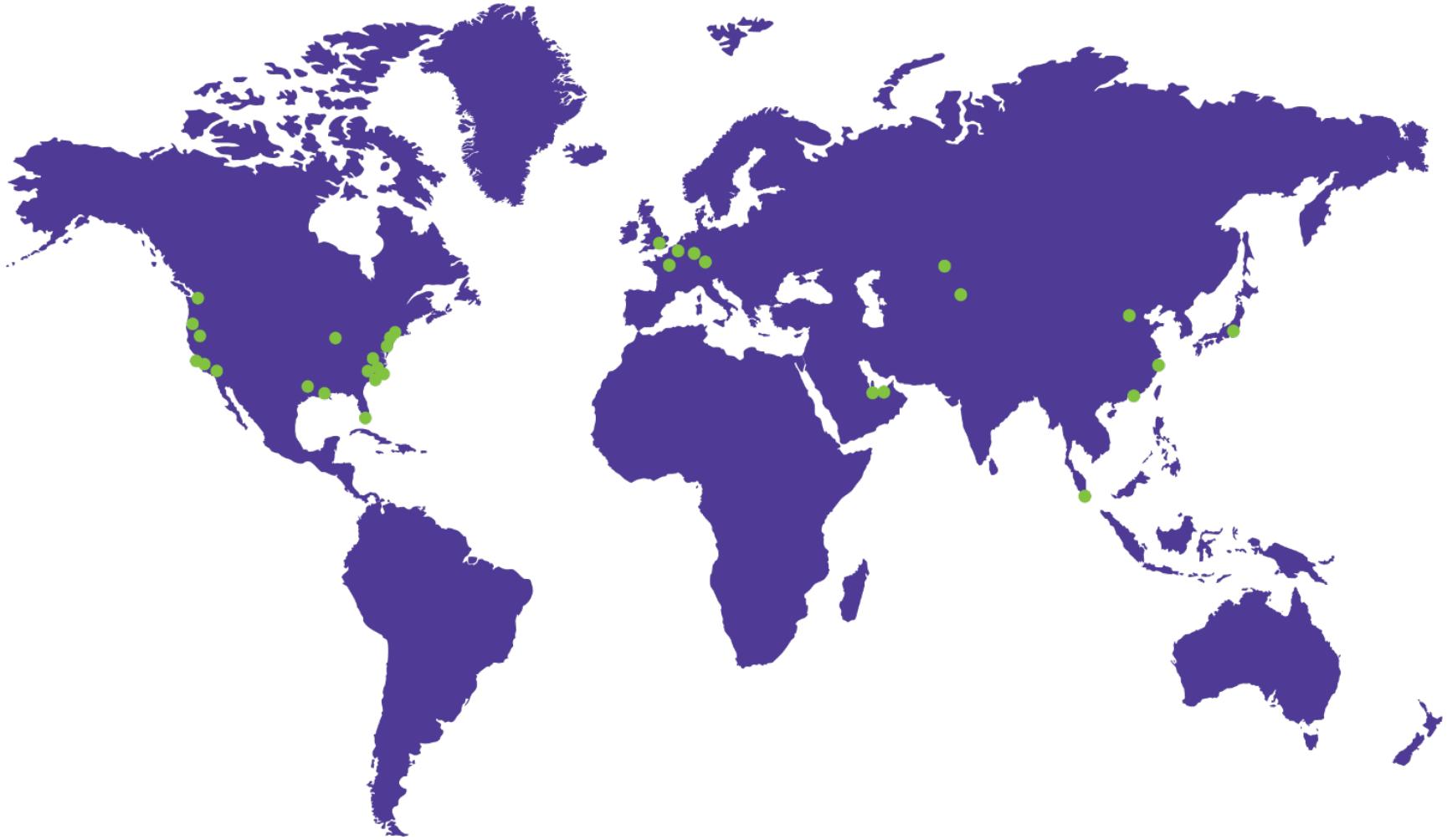

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