CTL IP Series

IP Series #2: What Makes Patents Commercially Relevant?

….will begin shortly.

11/9/2022

CTL CENTER FOR TECHNOLOGY LICENSING AT CORNELL UNIVERSITY

Weill Cornell Medicine
Enterprise Innovation

CTL IP Series

IP Series #2: What Makes Patents Commercially Relevant?

November 9, 2022

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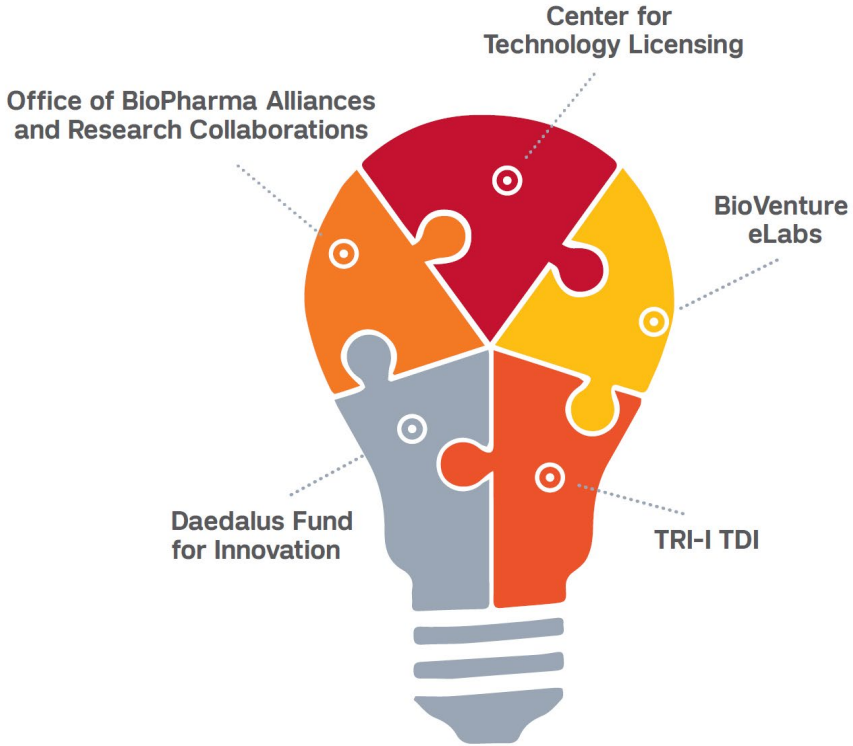
CTL CENTER FOR TECHNOLOGY LICENSING AT CORNELL UNIVERSITY

Weill Cornell Medicine
Enterprise Innovation

Weill Cornell Medicine Enterprise Innovation (est. 2021)

A consolidation and reorganization of key innovation and eShip offices and resources exclusively focused on the needs of the medical/graduate school

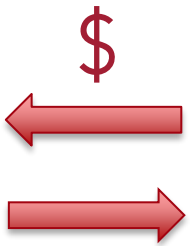


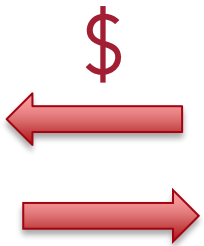
Weill Cornell

Webinar Overview

- Brief Overview Technology Transfer
- Introduction to Patents
  - What
  - Process, Timeline, and Costs
  - Anatomy
- Commercially Relevant Claim Scope: What, Why, and Working Examples
  - Claim Breadth
  - Freedom to Operate
  - Enforcement

Innovation Transfer at Its Most Basic





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What Do We Mean By “Innovation, Inventions, Assets & Technologies”?*

Therapeutics:

- Small Molecules
- Biologics
- Cell/Gene Therapy
- Novel Targets

Medical Devices:

- Imaging Equipment/Methods
- Surgical Devices/Implants
- Equipment

Diagnostics:

- Molecular
- Histological
- Imaging
- mAb based

Digital Health:

- Therapeutics
- “alerts”
- Clinical work-flow aides
- AI/Machine Learning Algorithms

Research Tool:

- Mouse models
- Research mAbs
- New research methodologies

Data:

- Clinical care models/workflows/training
- Unique structured data sets
- INDs

Weill Cornell Medicine

*in the healthcare/life sciences field

What Do We Mean By “Intellectual Property”*?

Patents:

- Must proactively apply and be awarded
- Covers patent-eligible subject matter
- 20 years of protection

Therapeutics, Devices, Diagnostics

Copyright:

- Automatically exists/registration
- Covers the physical manifestation of work
- 95 years from publication

Software, Workflows, Questionnaires

Trademark:

- Exists upon use in commerce/registration
- Covers recognizable sign, design, or expression to identify service or product
- Perpetual (as long as used in commerce)

Technical Information:

- Assays/Protocols
- Unpublished data
- Sequence Information
- Biological/Disease Insight
- Perpetual

All Technology Types

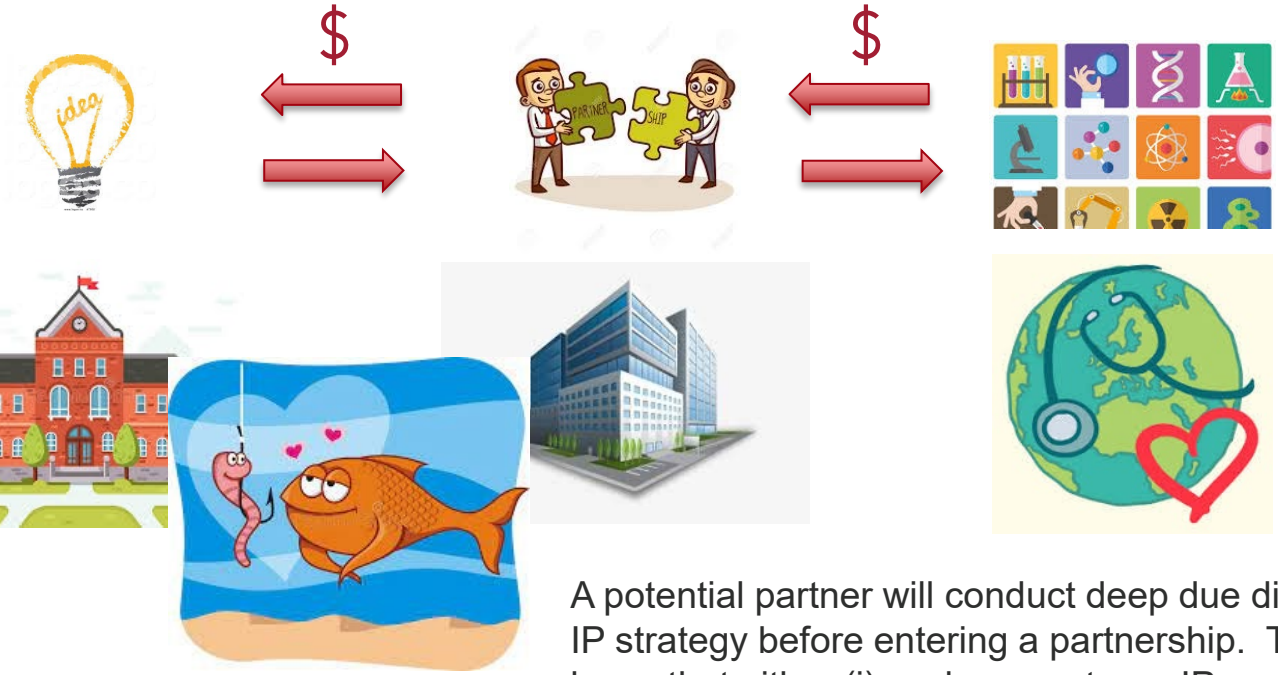
Tangible Material:

- Mice
- Antibodies
- Vectors
- Reagents
- Software
- Perpetual

All Technology Types

*in the healthcare/life sciences field

What does an academic institution use intellectual property for?



A potential partner will conduct deep due diligence on the IP strategy before entering a partnership. They need to know that either (i) we have a strong IP position; or (ii) they can build a strong position using our foundational IP

PATENTS: “Congress shall have the power to promote the progress of science…by securing for limited time to…inventors the exclusive right to their…discoveries”*

What is It?

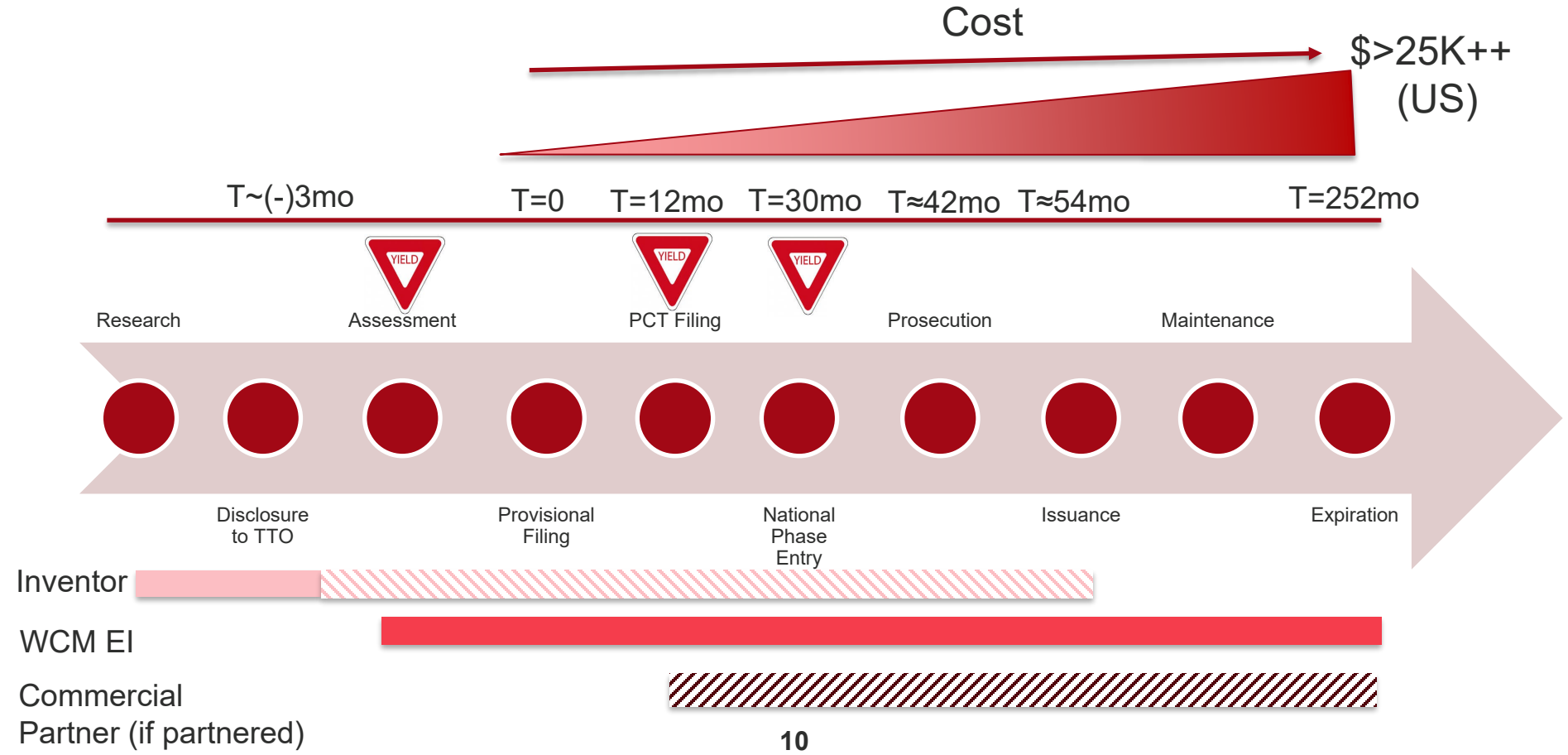
- **Legal monopoly** granted in return for public disclosure of an invention
- Gives the right to **exclude others** from practicing the invention
- Only enforceable once issued
- Patents **valid from 20 years** from application date (not issue date)
- Inventorship is **legally defined** and distinct from authorship

What is Patentable?

- Any **new and useful** process, machine, method/manufacture, or composition *excluding* any abstract idea, laws of nature, and natural phenomena (including products of nature)
- Must be **novel** (e.g. completely new) and **non-obvious** (e.g. more than a logical increment or combination) over “prior art”
- Must be **described and enabled** (e.g. one “skilled in the art” can make and use the invention)

*US Constitution Section 8 Clause 8

Overview of Process, Timeline, and Cost for Obtaining a Patent



Anatomy of a Patent: Title Page

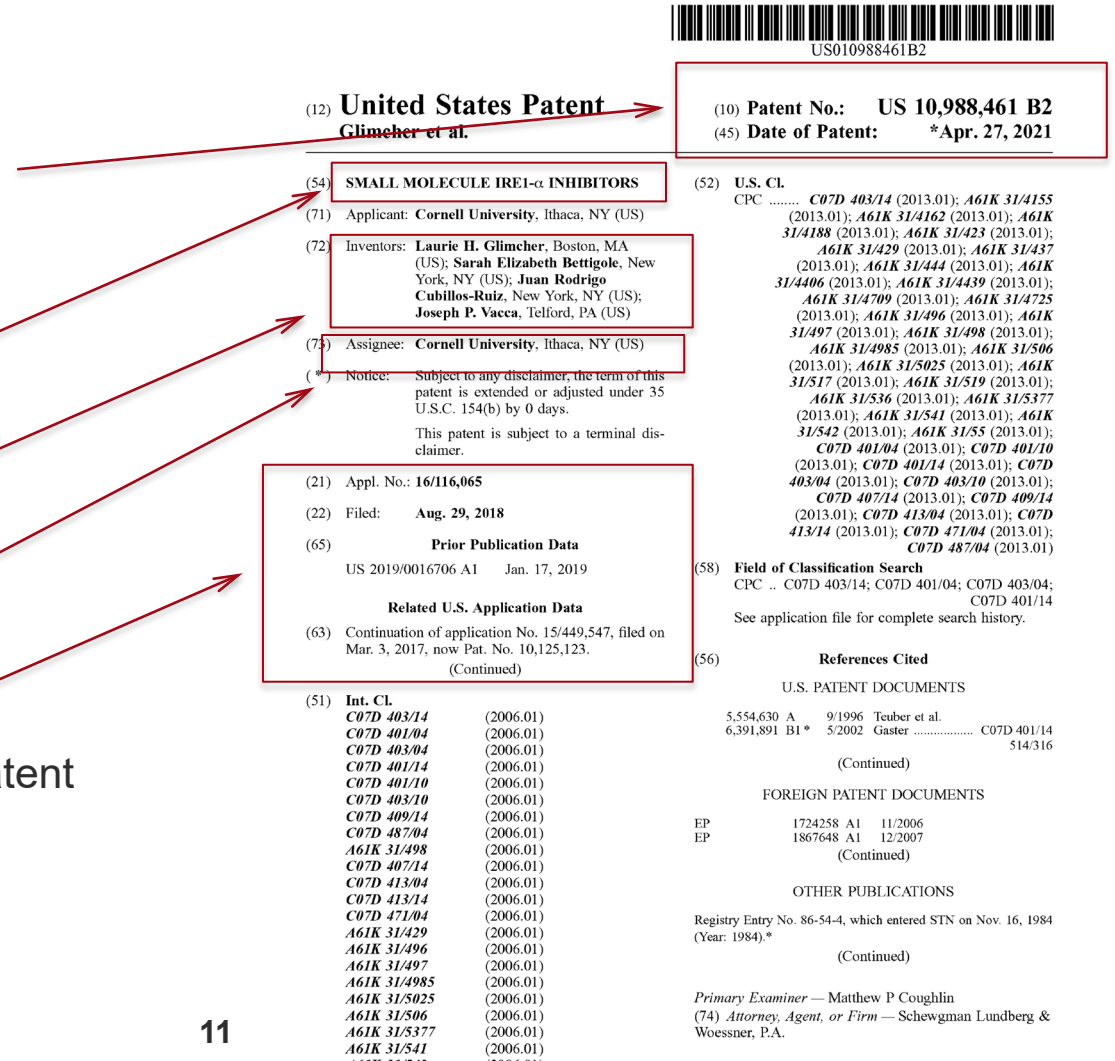
Patent Number
Issue Date

Title

Inventors

Assignee (Owner)

“Family History” of the Patent



US010988461B2

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

(10) **Patent No.: US 10,988,461 B2**
(45) **Date of Patent: *Apr. 27, 2021**

(54) **SMALL MOLECULE IRE1-α INHIBITORS**

(71) Applicant: **Cornell University**, Ithaca, NY (US)

(72) Inventors: **Laurie H. Glimcher**, Boston, MA (US); **Sarah Elizabeth Bettigole**, New York, NY (US); **Juan Rodrigo Cubillos-Ruiz**, New York, NY (US); **Joseph P. Vacca**, Telford, PA (US)

(73) Assignee: **Cornell University**, Ithaca, NY (US)

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

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **16/116,065**

(22) Filed: **Aug. 29, 2018**

(65) **Prior Publication Data**

US 2019/0016706 A1 Jan. 17, 2019

Related U.S. Application Data

(63) Continuation of application No. 15/449,547, filed on Mar. 3, 2017, now Pat. No. 10,125,123.
(Continued)

(51) **Int. Cl.**

C07D 403/14	(2006.01)
C07D 401/04	(2006.01)
C07D 403/04	(2006.01)
C07D 401/14	(2006.01)
C07D 401/10	(2006.01)
C07D 403/10	(2006.01)
C07D 409/14	(2006.01)
C07D 487/04	(2006.01)
A61K 31/498	(2006.01)
C07D 407/14	(2006.01)
C07D 413/04	(2006.01)
C07D 413/14	(2006.01)
C07D 471/04	(2006.01)
A61K 31/429	(2006.01)
A61K 31/496	(2006.01)
A61K 31/497	(2006.01)
A61K 31/4985	(2006.01)
A61K 31/5025	(2006.01)
A61K 31/506	(2006.01)
A61K 31/5377	(2006.01)
A61K 31/541	(2006.01)

(52) **U.S. Cl.**
CPC ***C07D 403/14*** (2013.01); ***A61K 31/4155*** (2013.01); ***A61K 31/4162*** (2013.01); ***A61K 31/4188*** (2013.01); ***A61K 31/423*** (2013.01); ***A61K 31/429*** (2013.01); ***A61K 31/437*** (2013.01); ***A61K 31/444*** (2013.01); ***A61K 31/4406*** (2013.01); ***A61K 31/4439*** (2013.01); ***A61K 31/4709*** (2013.01); ***A61K 31/4725*** (2013.01); ***A61K 31/496*** (2013.01); ***A61K 31/497*** (2013.01); ***A61K 31/498*** (2013.01); ***A61K 31/4985*** (2013.01); ***A61K 31/506*** (2013.01); ***A61K 31/5025*** (2013.01); ***A61K 31/517*** (2013.01); ***A61K 31/519*** (2013.01); ***A61K 31/536*** (2013.01); ***A61K 31/5377*** (2013.01); ***A61K 31/541*** (2013.01); ***A61K 31/542*** (2013.01); ***A61K 31/55*** (2013.01); ***C07D 401/04*** (2013.01); ***C07D 401/10*** (2013.01); ***C07D 401/14*** (2013.01); ***C07D 403/04*** (2013.01); ***C07D 403/10*** (2013.01); ***C07D 407/14*** (2013.01); ***C07D 409/14*** (2013.01); ***C07D 413/04*** (2013.01); ***C07D 413/14*** (2013.01); ***C07D 471/04*** (2013.01); ***C07D 487/04*** (2013.01)

(58) **Field of Classification Search**
CPC .. C07D 403/14; C07D 401/04; C07D 403/04; C07D 401/14
See application file for complete search history.

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(Continued)

Primary Examiner — Matthew P Coughlin
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Anatomy of a Patent:
The Inside (e.g. Specifications)

Background: a brief summary of the state of the art and its deficiencies

Summary: Overall description of the invention

Drawings: Summary of supporting data and figures

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a continuation of U.S. patent application Ser. No. 15/449,547, Filed Mar. 3, 2017, which claims the benefit under 35 U.S.C. § 119(e) of U.S. Provisional Patent Application Ser. No. 62/303,951, filed Mar. 4, 2016, and of U.S. Provisional Patent Application Ser. No. 62/303,236, filed Mar. 3, 2016, the disclosures of both of which are incorporated herein in their entirety by reference.

BACKGROUND

Aggressive tumors have evolved strategies that enable them to thrive under constant adverse conditions. Cancer cells respond to hypoxia, nutrient starvation, oxidative stress, and high metabolic demand by adjusting their protein folding capacity via the endoplasmic reticulum (ER) stress response pathway. Cancer patients would benefit from the development of new strategies and therapeutics.

SUMMARY

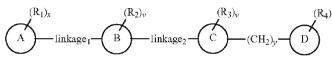
Described herein are IRE1α inhibitors, compositions containing such inhibitors, and methods of treatment that include administration of such compounds.

The inventors have discovered that XBP1 can promote tumor progression by confounding the development of protective antitumor immunity in the ovarian cancer tumor microenvironment. Without XBP1, tumor resident dendritic cells fail to accumulate intracellular lipids, which normally disrupt effective antigen cross-presentation. This pathological lipid accumulation is fundamentally driven by reactive oxygen species-mediated lipid peroxidation, which directly destabilizes protein-folding chaperones within the endoplasmic reticulum to induce a state of ER stress and XBP1 activation. Additionally, the inventors have found that IRE1α-mediated XBP signaling is involved in myeloid cell production of immunosuppressive prostaglandins such as prostaglandin E2 (PGE2).

These findings have led to the development of novel small-molecule IRE1α inhibitors with the ability to induce two parallel and mutually reinforcing anti-tumor mechanisms, namely the direct inhibition of tumor growth and the simultaneous induction of robust anti-tumor immunity. Such a compound is highly desirable, as no effective, targeted therapies currently exist for either TNBC or ovarian cancer.

Described herein are novel IRE1α kinase inhibitors that exhibit such immune-modulatory properties and/or that allosterically block IRE1alpha endoribonuclease function. The identified direct IRE1α inhibitors have unique chemical structures, unique binding mechanisms, inhibitory activity, and off-target effects.

One aspect of the invention is a compound of formula I:



I

phenyl group, where the A ring has x R_1 substituents;
C is phenyl or pyridinyl;
D is heterocyclyl ring;
$linkage_1$ is a single bond between A and B;
$linkage_2$ is a C_1-C_3 alkylamido, amidoalkyl, amino, urea, alkylurea, or ureaalkyl with a first and second terminal atom;
y is an integer of 0-3, and when y is 0, the linkage between the rings is a single bond;
x is an integer of 0-4;
v is an integer of 0-2;
R_1 substituents on the A ring are selected from amino, optionally substituted C_1-C_4 alkyl, optionally substituted ether, optionally substituted C_1-C_4 alkoxy, oxy, hydroxy, —NH—SO_2-phenyl-(R_5), and cyano;
R_2 substituents on the B ring are selected from amino, and optionally substituted C_1-C_4 alkyl;
R_3 substituents on the C ring are selected from halo, CF_3, optionally substituted C_1-C_4 alkyl, and optionally substituted heteroaryl; and
R_4 substituents on the D ring are selected from optionally substituted C_1-C_4 alkyl, optionally substituted C_1-C_4 alkoxy, (optionally substituted C_1-C_4 alkylene)-OH, hydroxy, optionally substituted aryl, optionally substituted benzyl, and optionally substituted benzaldehyde;
R_5 is halo; or
a pharmaceutically acceptable salt thereof.

Another aspect of the invention is compound selected from any of the compounds in Tables 1-4, the Examples or a pharmaceutically acceptable salt thereof.

Another aspect of the invention is a composition that includes a carrier and any of the compounds of formula I, pharmaceutically acceptable salts thereof, or any combination of such compounds.

Another aspect of the invention is a composition that includes a carrier and any of the compounds in the Examples, pharmaceutically acceptable salts thereof, or any combination thereof.

Another aspect of the invention is a method that includes administering one or more of such compositions to a mammal. For example, the mammal can be in need of administration of the composition. Such a mammal can, for example, have cancer, a neurodegenerative disease, inflammation, a metabolic disorder, liver dysfunction, brain ischemia, heart ischemia, or an autoimmune disease such as systemic lupus erythematosus. In some cases, the mammal has triple negative breast cancer or ovarian cancer.

The compositions and methods described herein can include one or more agents such as vitamin E, an antioxidant, and/or hydralazine. Such agents can sequester lipid peroxidation byproducts, and can be effective treatments for controlling ER stress responses and sustained IRE1α/XBP1 signaling in tumor-associated dendritic cells exposed, for example, to ovarian cancer-derived ascites.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. **1**A is the structure of vitamin E (VitE).

FIG. **1**B is the structure of hydralazine (Hlz), a representative member of lipid peroxidation-sequestering hydrazines.

FIG. **1**C is RT-qPCR analyses of markers of ER stress after culturing purified tumor-resident DCs in the absence (grey bars) or presence (green bars) of 25% cell-free ovarian cancer ascites supernatants for 18 hours. Data are normalized to Actb expression in each sample.

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Anatomy of a Patent:
The Inside (e.g. Specifications)

Detailed Description: The detailed written description of the invention

- Must **teach** how to make and use the full scope of the claimed invention (e.g. enablement)
- Can describe all possible uses/forms of the invention
- Must disclose the "best mode" of the invention
- Must provide evidence of possession of the invention

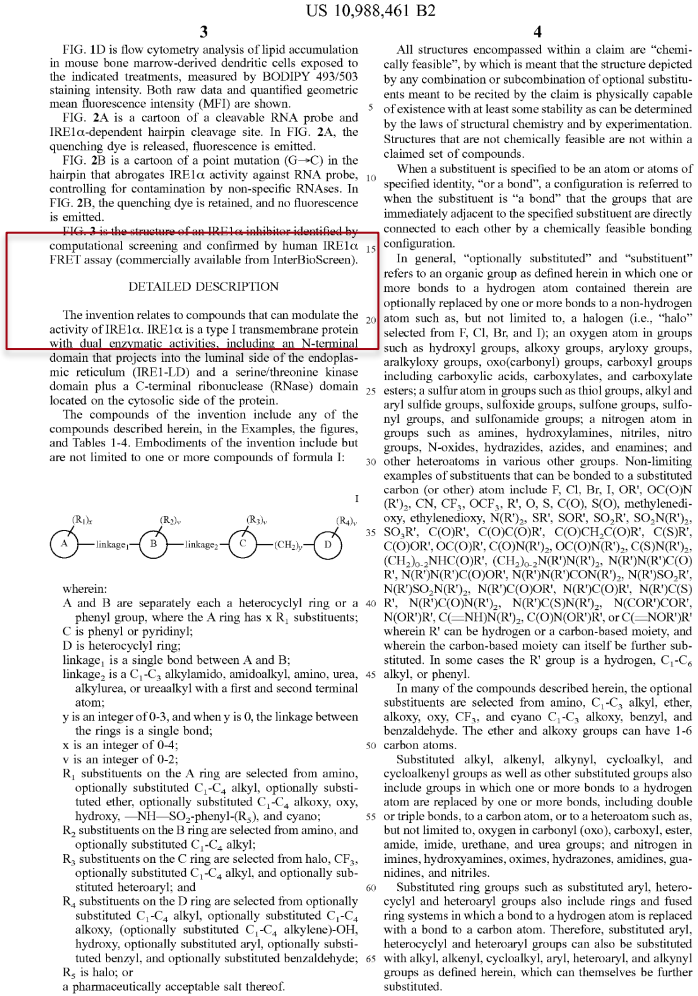

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FIG. 1D is flow cytometry analysis of lipid accumulation in mouse bone marrow-derived dendritic cells exposed to the indicated treatments, measured by BODIPY 493/503 staining intensity. Both raw data and quantified geometric mean fluorescence intensity (MFI) are shown.

FIG. 2A is a cartoon of a cleavable RNA probe and IRE1α-dependent hairpin cleavage site. In FIG. 2A, the quenching dye is released, fluorescence is emitted.

FIG. 2B is a cartoon of a point mutation (G→C) in the hairpin that abrogates IRE1α activity against RNA probe, controlling for contamination by non-specific RNAses. In FIG. 2B, the quenching dye is retained, and no fluorescence is emitted.

FIG. 3 is the structure of an IRE1α inhibitor identified by computational screening and confirmed by human IRE1α FRET assay (commercially available from InterBioScreen).

DETAILED DESCRIPTION

The invention relates to compounds that can modulate the activity of IRE1α. IRE1α is a type I transmembrane protein with dual enzymatic activities, including an N-terminal domain that projects into the luminal side of the endoplasmic reticulum (IRE1-LD) and a serine/threonine kinase domain plus a C-terminal ribonuclease (RNase) domain located on the cytosolic side of the protein.

The compounds of the invention include any of the compounds described herein, in the Examples, the figures, and Tables 1-4. Embodiments of the invention include but are not limited to one or more compounds of formula I:

I

wherein:

A and B are separately each a heterocyclyl ring or a phenyl group, where the A ring has x R_1 substituents;

C is phenyl or pyridinyl;

D is heterocyclyl ring;

$linker_1$ is a single bond between A and B;

$linker_2$ is a C_1-C_3 alkylamido, amidoalkyl, amino, urea, alkylurea, or ureaalkyl with a first and second terminal atom;

y is an integer of 0-3, and when y is 0, the linkage between the rings is a single bond;

x is an integer of 0-4;

v is an integer of 0-2;

R_1 substituents on the A ring are selected from amino, optionally substituted C_1-C_4 alkyl, optionally substituted ether, optionally substituted C_1-C_4 alkoxy, oxy, hydroxy, —NH—SO_2-phenyl-(R_4), and cyano;

R_2 substituents on the B ring are selected from amino, and optionally substituted C_1-C_4 alkyl;

R_3 substituents on the C ring are selected from halo, CF_3, optionally substituted C_1-C_4 alkyl, and optionally substituted heteroaryl; and

R_4 substituents on the D ring are selected from optionally substituted C_1-C_4 alkyl, optionally substituted C_1-C_4 alkoxy, (optionally substituted C_1-C_4 alkylene)-OH, hydroxy, optionally substituted aryl, optionally substituted benzyl, and optionally substituted benzaldehyde;

R_5 is halo; or

a pharmaceutically acceptable salt thereof.

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All structures encompassed within a claim are "chemically feasible", by which is meant that the structure depicted by any combination or subcombination of optional substituents meant to be recited by the claim is physically capable of existence with at least some stability as can be determined by the laws of structural chemistry and by experimentation. Structures that are not chemically feasible are not within a claimed set of compounds.

When a substituent is specified to be an atom or atoms of specified identity, "or a bond", a configuration is referred to when the substituent is "a bond" that the groups that are immediately adjacent to the specified substituent are directly connected to each other by a chemically feasible bonding configuration.

In general, "optionally substituted" and "substituent" refers to an organic group as defined herein in which one or more bonds to a hydrogen atom contained therein are optionally replaced by one or more bonds to a non-hydrogen atom such as, but not limited to, a halogen (i.e., "halo" selected from F, Cl, Br, and I); an oxygen atom in groups such as hydroxyl groups, alkoxy groups, aryloxy groups, aralkyloxy groups, oxo(carbonyl) groups, carboxyl groups including carboxylic acids, carboxylates, and carboxylate esters; a sulfur atom in groups such as thiol groups, alkyl and aryl sulfide groups, sulfoxide groups, sulfone groups, sulfonyl groups, and sulfonamide groups; a nitrogen atom in groups such as amines, hydroxylamines, nitriles, nitro groups, N-oxides, hydrazides, azides, and enamines; and other heteroatoms in various other groups. Non-limiting examples of substituents that can be bonded to a substituted carbon (or other) atom include F, Cl, Br, I, OR', OC(O)N(R')$_2$, CN, CF_3, OCF_3, R', O, S, C(O), S(O), methylenedioxy, ethylenedioxy, N(R')$_2$, SR', SOR', SO_2R', SO_2N(R')$_2$, SO_3R', C(O)R', C(O)C(O)R', C(O)CH_2C(O)R', C(S)R', C(O)OR', OC(O)R', C(O)N(R')$_2$, OC(O)N(R')$_2$, C(S)N(R')$_2$, $(CH_2)_{0-2}$NHC(O)R', $(CH_2)_{0-2}$N(R')N(R')$_2$, N(R')N(R')C(O)R', N(R')N(R')C(O)OR', N(R')N(R')CON(R')$_2$, N(R')SO_2R', N(R')SO_2N(R')$_2$, N(R')C(O)OR', N(R')C(O)R', N(R')C(S)R', N(R')C(O)N(R')$_2$, N(R')C(S)N(R')$_2$, N(COR')COR', N(OR')R', C(=NH)N(R')$_2$, C(O)N(OR')R', or C(=NOR')R' wherein R' can be hydrogen or a carbon-based moiety, and wherein the carbon-based moiety can itself be further substituted. In some cases the R' group is a hydrogen, C_1-C_6 alkyl, or phenyl.

In many of the compounds described herein, the optional substituents are selected from amino, C_1-C_3 alkyl, ether, alkoxy, oxy, CF_3, and cyano C_1-C_3 alkoxy, benzyl, and benzaldehyde. The ether and alkoxy groups can have 1-6 carbon atoms.

Substituted alkyl, alkenyl, alkynyl, cycloalkyl, and cycloalkenyl groups as well as other substituted groups also include groups in which one or more bonds to a hydrogen atom are replaced by one or more bonds, including double or triple bonds, to a carbon atom, or to a heteroatom such as, but not limited to, oxygen in carbonyl (oxo), carboxyl, ester, amide, imide, urethane, and urea groups; and nitrogen in imines, hydroxyamines, oximes, hydrazones, amidines, guanidines, and nitriles.

Substituted ring groups such as substituted aryl, heterocyclyl and heteroaryl groups also include rings and fused ring systems in which a bond to a hydrogen atom is replaced with a bond to a carbon atom. Therefore, substituted aryl, heterocyclyl and heteroaryl groups can also be substituted with alkyl, alkenyl, cycloalkyl, aryl, heteroaryl, and alkynyl groups as defined herein, which can themselves be further substituted.

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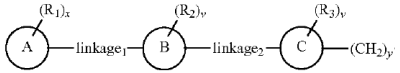
Anatomy of a Patent: The Claims

Claims: Defines the extent of protection offered by the patent (e.g. what is legal scope of the invention)

Limitations: defines limiting parameters of claimed invention (wherein, comprising, consisting, dependent claims, etc)

What is claimed is:

1. A compound of formula I,



wherein:

A is a heteroaromatic ring, where the A ring substituents;

B is pyrazolyl, imidazolyl, or triazolyl;

C is phenyl or pyridinyl;

D is a six- or seven-membered saturated he ring;

$linkage_1$ is a single bond between A and B;

$linkage_2$ is a urea, alkylurea, or ureaalkyl with second terminal atom;

I

$(R_4)_v$

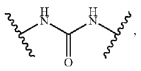
y is an integer of 1-3;
x is an integer of 0-4;
v is an integer of 0-2;
R_1 substituents on the A ring are selected from amino, optionally substituted C_1-C_4 alkyl, optionally substituted ether, optionally substituted C_1-C_4 alkoxy, hydroxy, —NH—SO_2-phenyl-(R_5), and cyano;
R_2 substituents on the B ring are selected from amino, and optionally substituted C_1-C_4 alkyl;
R_3 substituents on the C ring are selected from halo, CF_3, optionally substituted C_1-C_4 alkyl, and optionally substituted heteroaryl; and
R_4 substituents on the D ring are selected from optionally substituted C_1-C_4 alkyl, optionally substituted C_1-C_4 alkoxy, (optionally substituted C_1-C_4 alkylene)-OH, hydroxy, optionally substituted aryl, optionally substituted benzyl, and optionally substituted benzaldehyde; and
R_5 is halo; or
a pharmaceutically acceptable salt thereof.

2. The compound of claim **1**, wherein the A ring is a fusion of two rings.

3. The compound of claim **1**, wherein the A ring is indazole, imadazopyridine, imadazopyrazine, imadazopyridazine, pyrrolopyridine, hexahydrothienopyrimidine, imidazole, pyrazole, pyrazine, pyridine, pyrimidine, phenylpyrimidinamine, quinolinyl, isoquinolinyl, tetrahydroquinolinyl, and quinazolinyl.

4. The compound of claim **1**, wherein the C ring is phenyl.

5. The compound of claim **1**, wherein the $linkage_2$ is:



wherein a hydrogen atom on Ring B is replaced by the first terminal atom of $linkage_2$ and a hydrogen atom on Ring C is replaced by the second terminal atom of $linkage_2$.

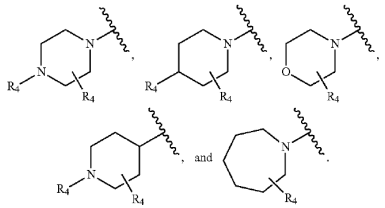
6. The compound of claim **1**, wherein the R_1 substituents on the A ring are selected from the group consisting of amino and optionally substituted C_1-C_3 alkyl.

7. The compound of claim **6**, wherein the R_1 substituents on the A ring are selected from the group consisting of —NH_2 and CH_3.

8. The compound of claim **1**, wherein x=0, 1 or 2.

9. The compound of claim **1**, wherein v is 1 and the R_3 substituent on the C ring is CF_3.

10. The compound of claim **1**, wherein D is selected from the group consisting of:



11. The compound of claim **1**, wherein v is 1.

12. The compound of claim **1**, wherein R_4 is selected from the group consisting of H, optionally substituted C_1-C_4 alkyl, (optionally substituted C_1-C_4 alkylene)-OH, hydroxy, optionally substituted aryl, and optionally substituted benzyl.

13. The compound of claim **12**, wherein R_4 is selected from H and optionally substituted C_1-C_4 alkyl.

14. A composition comprising a carrier and a compound of claim **1**.

15. The composition of claim **14**, further comprising vitamin E, an antioxidant, hydralazine, or any combination thereof.

16. The compound of claim **1**, wherein the ring C is a divalent phenyl ring.

17. The compound of claim **1**, wherein the B ring is pyrazolyl.

* * * * *

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Shocking Statements…

You can get an issued patent on (almost) anything

Probably doesn't matter if there is not commercially relevant claim scope

…the point is not to just have a patent (or patent application) but to have an IP strategy that attracts a commercial partner. They are looking for commercially relevant claim scope.

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What does "*commercially relevant claim scope*" mean?

Claims are Patentable and Valid

Claims Cover the (anticipated) Product with Reasonable Scope

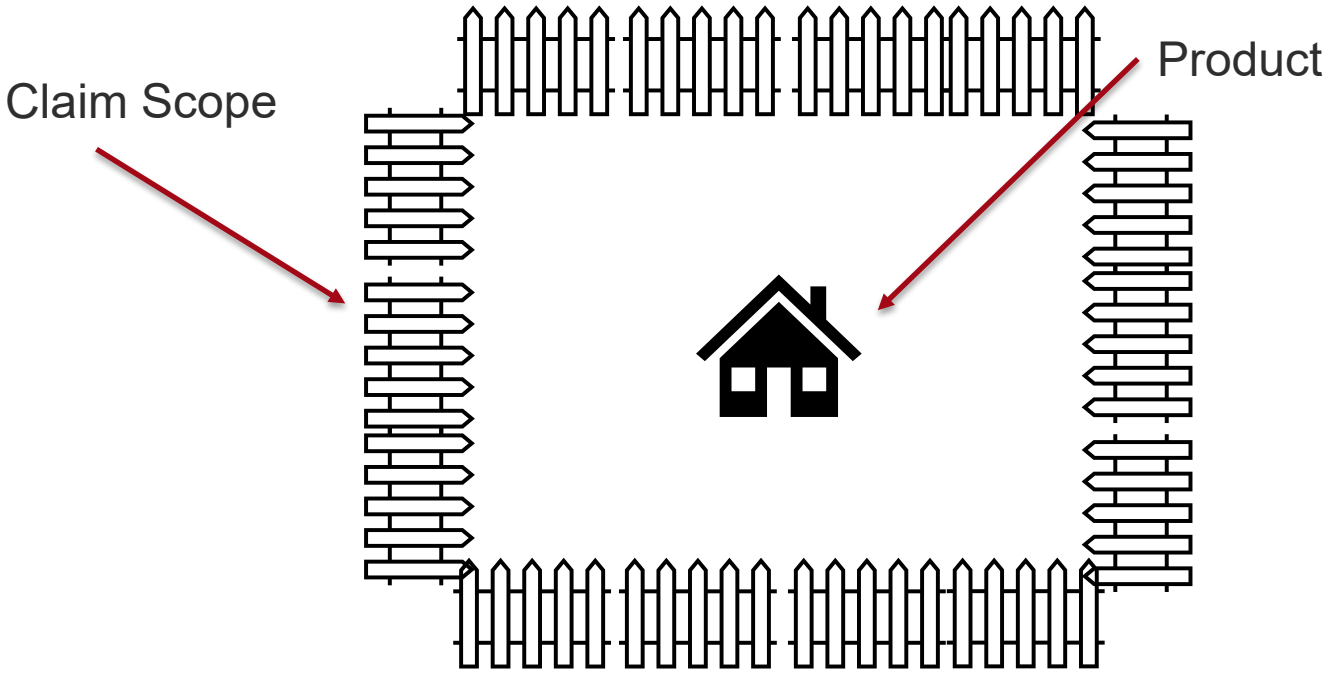
Claims are Difficult to Engineer Around

There is Freedom to Operate *(e.g. practice the invention without infringing third party rights)*

Claims are Enforceable

Easy to Detect if Someone is Practicing the Claims

Claims Cover the Product with Reasonable Claim Scope



“Big Yard”

- Reserves area “around” the product for further R&D and follow-on product development by patent owner
- Deters competitors from innovating in space close to product
- Limits “Design-Around”

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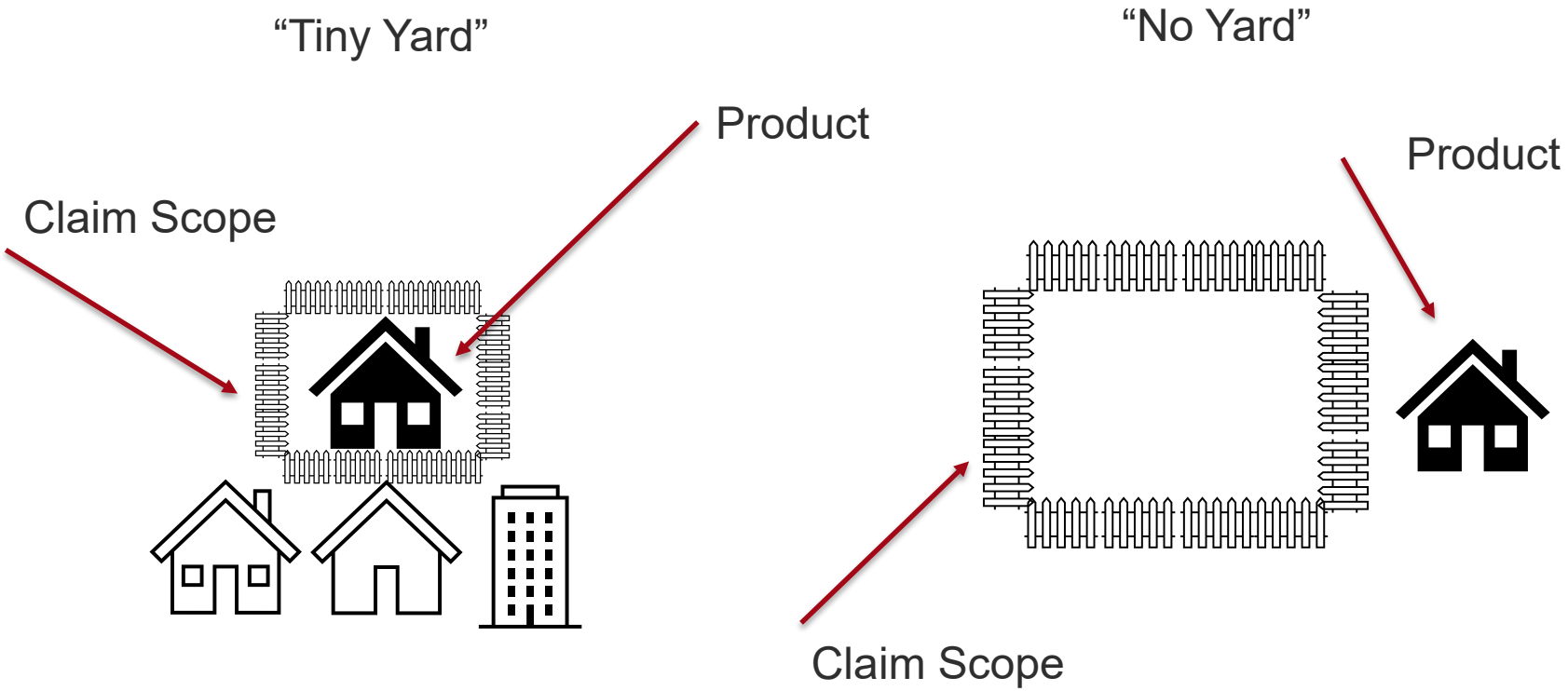
When Claims Don't Cover the Product with Reasonable Scope



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Hypothetical Example House Claims

"Big Yard"	A living dwelling *comprising* a free-standing permanent structure wherein the permanent structure includes at least one entrance
"Tiny Yard"	A living dwelling *consisting of* a free-standing permanent single-story structure wherein the permanent single-story structure is black and includes one door, two windows, and a chimney
"No Yard"	A living dwelling *consisting of* a canvas tent

Example “Bigger Yard” vs “Smaller Yard” Pharmaceutical Patent

What is claimed is:

1. A pharmaceutical composition comprising:

a lipid-based nanoparticle comprising a synthetic messenger ribonucleic acid (mRNA) encoding a defensin polypeptide in an amount effective to permit production of the defensin polypeptide in a cell, wherein the synthetic mRNA comprises a translatable region that contains at least one nucleoside modification, and wherein 75-100% of uridine nucleotides in the synthetic mRNA are modified.

2. The pharmaceutical composition of claim **1**, wherein the at least one nucleoside modification is selected from the group consisting of pyridin-4-one ribonucleoside, 5-aza-uridine, 2-thio-5-aza-uridine, 2-thiouridine, 4-thio-pseudouridine, 2-thio-pseudouridine, 5-hydroxyuridine, 3-methyluridine, 5-carboxymethyl-uridine, 1-carboxymethyl-pseudouridine, 5-propynyl-uridine, 1-propynyl-

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The invention claimed is:

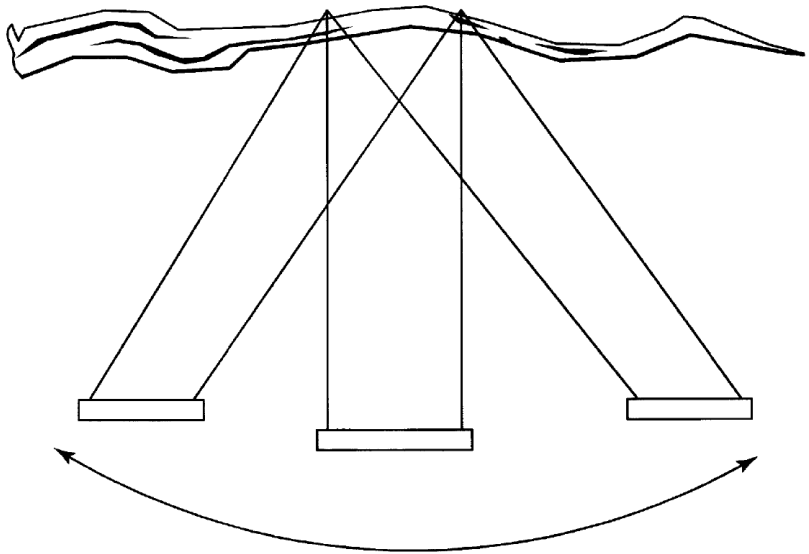
1. A method for enhancing exon skipping in an mRNA of interest, comprising contacting the mRNA with an antisense oligonucleotide that is specific for a splicing sequence in the mRNA and an effective amount of dantrolene, Ryanodine, or RyCal S107, or a pharmaceutically acceptable salt, hydrate, solvate, or isomer thereof.

US 946412B2; US 10188633B2

Example of Claims That May be Circumventable in Exercise Method Device Patent

United States Patent
Olson

(10) **Patent No.: US 6,368,227 B1**
(45) **Date of Patent: Apr. 9, 2002**



1. A method of swinging on a swing, the method comprising the steps of:

a) suspending a seat for supporting a user between only two chains that are hung from a tree branch;

b) positioning a user on the seat so that the user is facing a direction perpendicular to the tree branch;

c) having the user pull alternately on one chain to induce movement of the user and the swing toward one side, and then on the other chain to induce movement of the user and the swing toward the other side; and

d) repeating step c) to create side-to-side swinging motion, relative to the user, that is parallel to the tree branch.

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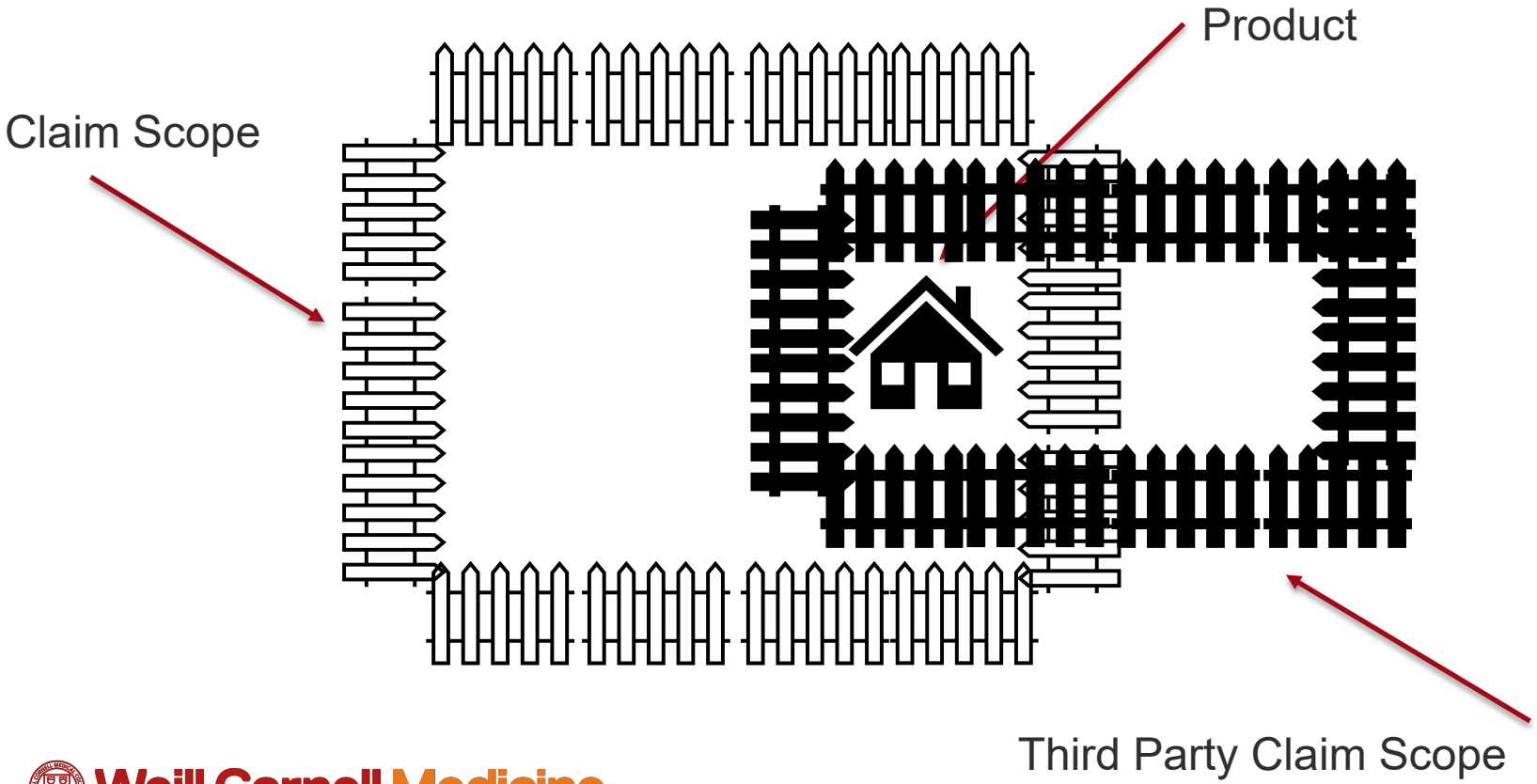
Freedom to Operate



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Hypothetical Example House Claims

“Claim Scope”	A living dwelling comprising a free-standing permanent structure wherein the permanent structure includes at least one entrance
“Third Party Claim Scope”	A method if manufacturing a living dwelling comprising a free-standing permanent structure wherein the permanent structure includes at least one entrance using a heavy construction equipment

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Example of Claims with Poetntial Freedom to Operate Issues in Pharmaceutical Patent

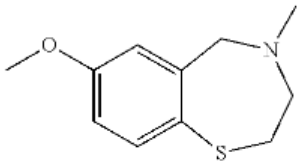
The invention claimed is:

1. A method for enhancing exon skipping in an mRNA of interest, comprising contacting the mRNA with an antisense oligonucleotide that is specific for a splicing sequence in the mRNA and an effective amount of ~~dantrolene, Ryanodine, or~~ RyCal S107, or a pharmaceutically acceptable salt, hydrate, solvate, or isomer thereof.

RyCalS107: CoM Covered US 8710045B2 owned by Third Party (expires 2025)

10. The compound of claim 8, wherein the compound is S107

S107



or its pharmaceutically acceptable salt.

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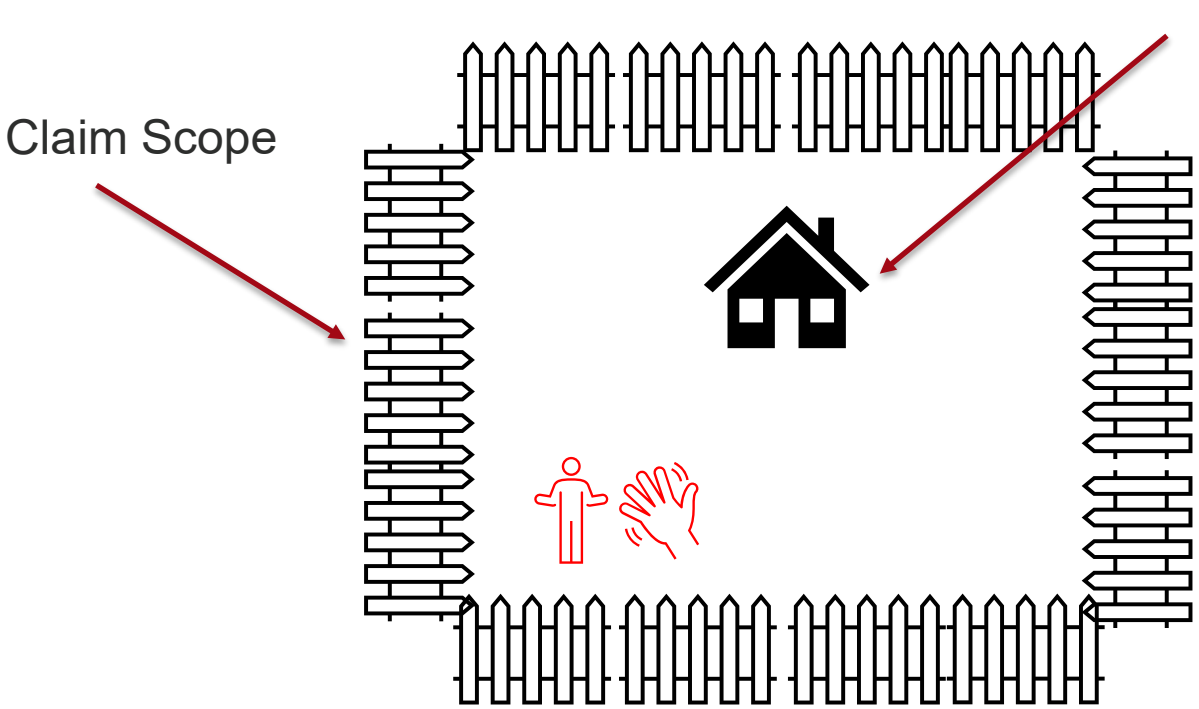
US 10188633B2

Claims Are Enforceable



Reminder

Patents give the owner the right to *exclude others* from:

- Making
- Using
- Selling

the claimed invention

Need to be able to “see” someone inside the “fence” to enforce patent rights.

Example of Claims with Likely Enforcement Issues in Veterinary Medical Device Method of Use Patent

US005443036A

United States Patent [19]

Amiss et al.

[11] **Patent Number:** **5,443,036**

[45] **Date of Patent:** **Aug. 22, 1995**

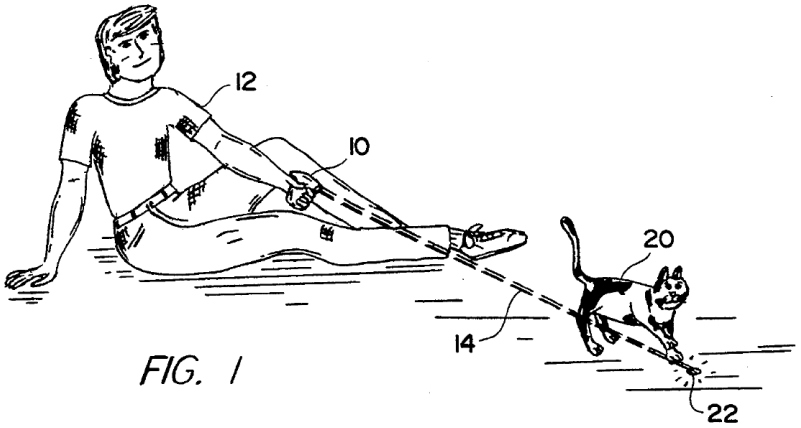


FIG. 1

What is claimed is:

1. A method of inducing aerobic exercise in an unrestrained cat comprising the steps of:

(a) directing an intense coherent beam of invisible light produced by a hand-held laser apparatus to produce a bright highly-focused pattern of light at the intersection of the beam and an opaque surface, said pattern being of visual interest to a cat; and

(b) selectively redirecting said beam out of the cat's immediate reach to induce said cat to run and chase said beam and pattern of light around an exercise area.

Example of Claims with Potential Enforcement Issues in Biotech Patent

What is claimed is:

1. A method of selecting a Ras antagonist, the method comprising:

(a) combining in a reaction mixture a mutant Ras, a competition probe, and a test compound; and

(b) detecting a decrease in binding between the mutant Ras and the competition probe as compared to binding of the competition probe to the mutant Ras in an absence of the test compound; wherein:

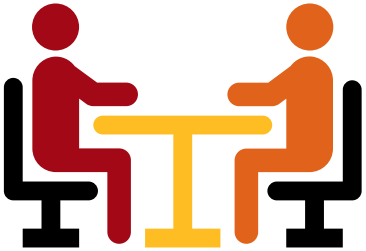
i. the mutant Ras comprises a truncated or full-length sequence according to SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, or SEQ ID NO: 4, that is mutated to have up to 20 mutations including mutation of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, or SEQ ID NO: 4 at amino acid residue 62, 92, or 95 to cysteine;

ii. the competition probe is capable of binding and covalently modifying the mutant Ras; and

iii. the decrease in binding between the mutant Ras and the competition probe is indicative of Ras antagonist activity of the test compound.

US 9810690B2

When and How to Engage



- ☑ (well) **BEFORE** Public Disclosure
- ☑ During Initiation of Commercially Translatable Research Programs
- ☑ Participation in educational and mentorship opportunities offered by WCM EI and CTL
- ☑ *Anytime* with Questions re Innovation, Intellectual Property, and Commercialization

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https://innovation.weill.cornell.edu/

https://ctl.cornell.edu/

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Thank you for joining us today!

Keep an eye out for upcoming events:

- **November 14 3-5:30PM:** 6th Annual Symposium on eShip and Drug Development In-Person/Hybrid at Weill Cornell Medicine in NYC
- **November 17, 12-1:30PM:** CTL Women Innovator Initiative Webinar Series: Imposter Syndrome, Overwhelm, and Getting Unstuck
- **November 18 2-4PM:** CTL@WCM Office Hours with Jamie Brisbois
- **December 6 5:30-8:30PM:** eLabs Accelerating BioVenture Innovation Pitch Day at Griffis Faculty Club in NYC
- **January: CTL IP Series #3:** Navigating Software and Copyright

Visit https://ctl.cornell.edu/our-events/ for more information and to register

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