Intellectual property for bioentrepreneurship in Africa

Jenny Molloy | molloy@icgeb.org

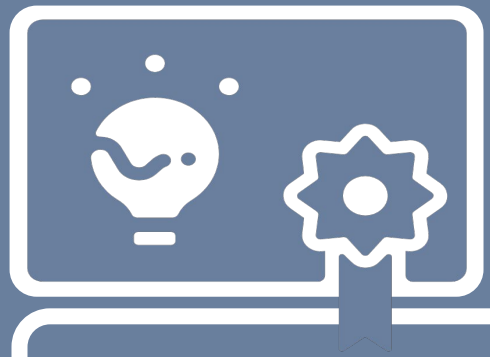
Group Leader, Biomanufacturing

International Centre for Genetic Engineering & Biotechnology (ICGEB)

Senior Research Associate, University of Cambridge

Former Fellow, World Economic Forum Global Future Council on Synthetic Biology

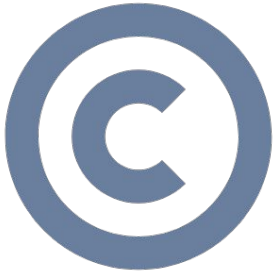
Member, OECD Expert Group on Synthetic Biology

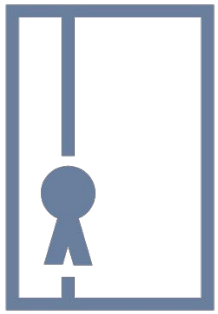


Intellectual Property

Part 1: Main types of Intellectual Property

IP

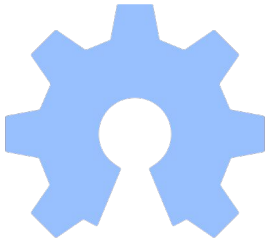


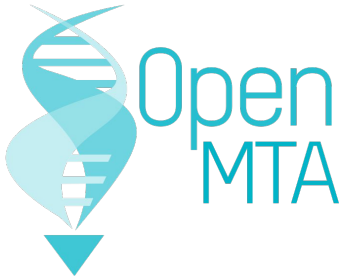


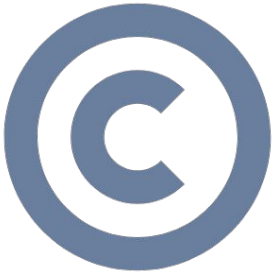


Open







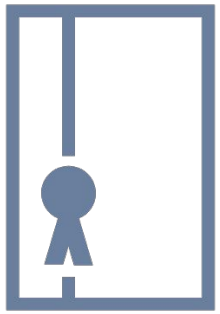


A **copyright** is an exclusive right granted by law for a limited period to an author, designer, etc. for his/her original work

How do I get copyrights?
You do need to apply for a copyright - you have it automatically.

What does it apply to in biotech?
Most written documents and designs e.g. scientific articles, figures. However, copyright does not cover facts and ideas, only their “creative expression”. I can write the same facts using different words and I will not be infringing your copyright.

What does it restrict?
Copying (obviously!). This includes photocopying, translating, showing in a presentation, using sections in a textbook or another paper. There are exceptions in some countries for “fair use” but they vary.



A **patent** gives its owner the right to exclude others from making, using, selling, and importing an invention for a limited period of time, usually twenty years.

How do I get a patent?
You need to apply for a patent in every country you want one. Your invention has to be i) a patentable thing; ii) novel and not previously published; iii) non-obvious to someone “skilled in the art” e.g. another biotechnologist, iv) have industrial applicability; v) be legal.

What does it apply to in biotech?
Protocols, genetically modified organisms, equipment, uses of enzymes, uses of DNA parts and many other inventions.

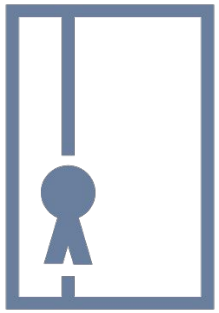
What does it restrict?
If a patent is in place in a country, the patent owner can stop anyone else manufacturing and selling or importing the invention. In most countries (but not all) there are exemptions which allow research and personal use of the patented invention.



A trademark is a recognizable sign, design, or expression which identifies products or services of a particular source from those of others

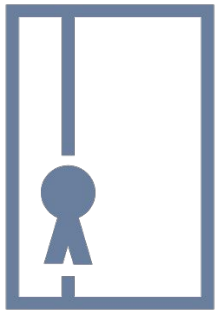
How do I get a trademark?
Apply in each country you want a trademark and pay a fee. You can't trademark a name/design that is already trademarked or is protected.

What does it apply to in biotech?
Brands for companies - typically trademarks are not a form of IP that impacts anyone's ability to use knowledge that matters.



Patents are one option among many - a tool in the toolbox!

- Contracts e.g. material transfer agreement
- Partnership building through shared know-how and consulting
- Club goods model
- Donation to the public domain
- Open disclosure and licensing



Once you have a patent - you can share it in a number of ways

- Exclusive licensing
- Non-exclusive licensing
- Socially responsible licensing
- Pool
- Pledge

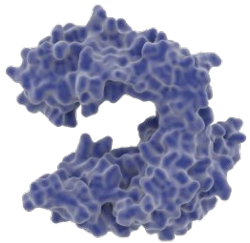
Good things about patents for people who want to use the technologies!

1. They only last 20 years, then the inventions are in the public domain and anyone can use or sell them.
2. They are jurisdictional i.e. if someone patents ***only*** in the US then the invention can be manufactured and sold in any other country but not imported into the US.
3. Patents have to be filed in each country almost at the same time and each country requires a fee, therefore many patents from countries that file the most patents are never filed in developing and emerging economies to reduce costs, leaving the invention open to manufacture and sale there.
4. They are difficult to read but they have to contain enough information for someone “skilled in the art” to reproduce the invention so they have great detail on biotechnology protocols and inventions.

Consider patents as a great source of information alongside scientific papers!

LENS.ORG

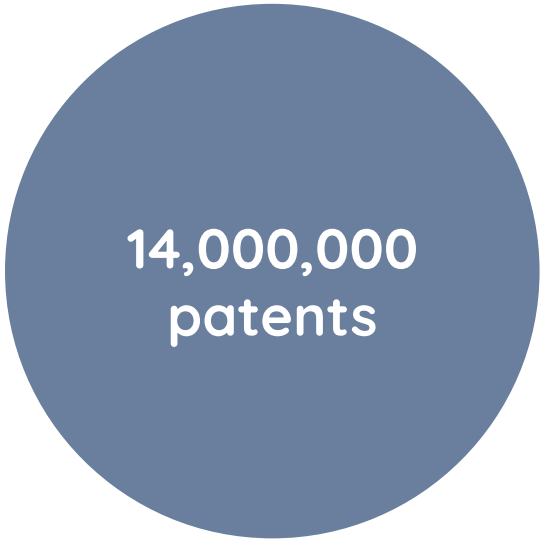
Solving The Problem Of Problem Solving ™



Search millions of scientific papers and patents at https://lens.org

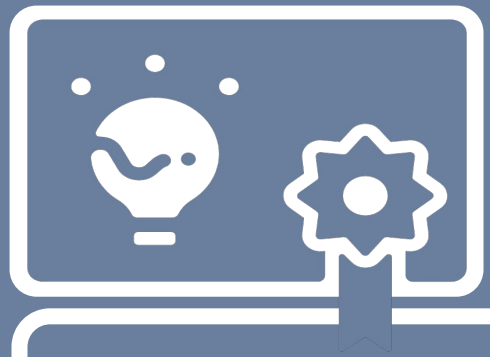
The Open Enzyme Collection is making use of technologies whose patents have expired and “born open” technologies to ensure that you can use, reuse, build on them and commercialise new innovations. Find links at: https://openbioeconomy.org

Freedom to operate landscape



1% registered in the global South

Data: lens.org
99% have rights in fewer than 20 countries



Intellectual Property

Part 2: Open Intellectual Property

What does "Open" mean?



subject **only**, at most, to the requirement to attribute and/or share-alike. *opendefinition.org*

Open approaches provide mechanisms for organizing knowledge production that favour:



(a) **universal versus restricted access** e.g. availability of specific molecular tools unencumbered by intellectual property;



(b) **universal versus restricted participation** e.g. greater involvement of beneficiaries in shaping projects using those tools;



(c) **collaborative versus centralized production** e.g. multiple partners working together for a common goal

Smith, M., Engler, N. J., Christian, G., Diga, K., Rashid, A., & Flynn-Dapaah, K. (2008). Open ICT4D (working draft). International Development Research Centre http://openict4d.wikidot.com/open-ness-to-open-ict4d.



In science there is an **Open Access** movement for authors to waive some of their copyrights and give more people the ability to read, use and build up research.

How do I do that?
Using licences that confer rights on the users. You can give away or keep different parts of your copyright, often using Creative Commons licenses e.g. CC-BY licences allow anyone to use your content as long as they attribute you (which should happen in science anyway or it is plagiarism)

Why does this matter?
Copyright monopolies restrict access to scientific knowledge for many groups of people: scientists cannot read papers without paying, lecturers cannot copy resources for students or include figures in teaching materials. Some authors end up not being able to use their own figures in textbooks because they gave away copyright to a publisher! Open Access hopes to change this situation.



Free and open source are approaches whereby inventors choose to freely share their ideas in a way that other people can use and even sell.

How do I do that?
The simplest way is to publish without applying for a patent, this blocks anyone else getting a patent as your publication is “prior art”. You could also patent and then use various means to allow others to use part or all of the invention. However, in many cases open source solutions are not patentable and the main advantage of open source approaches

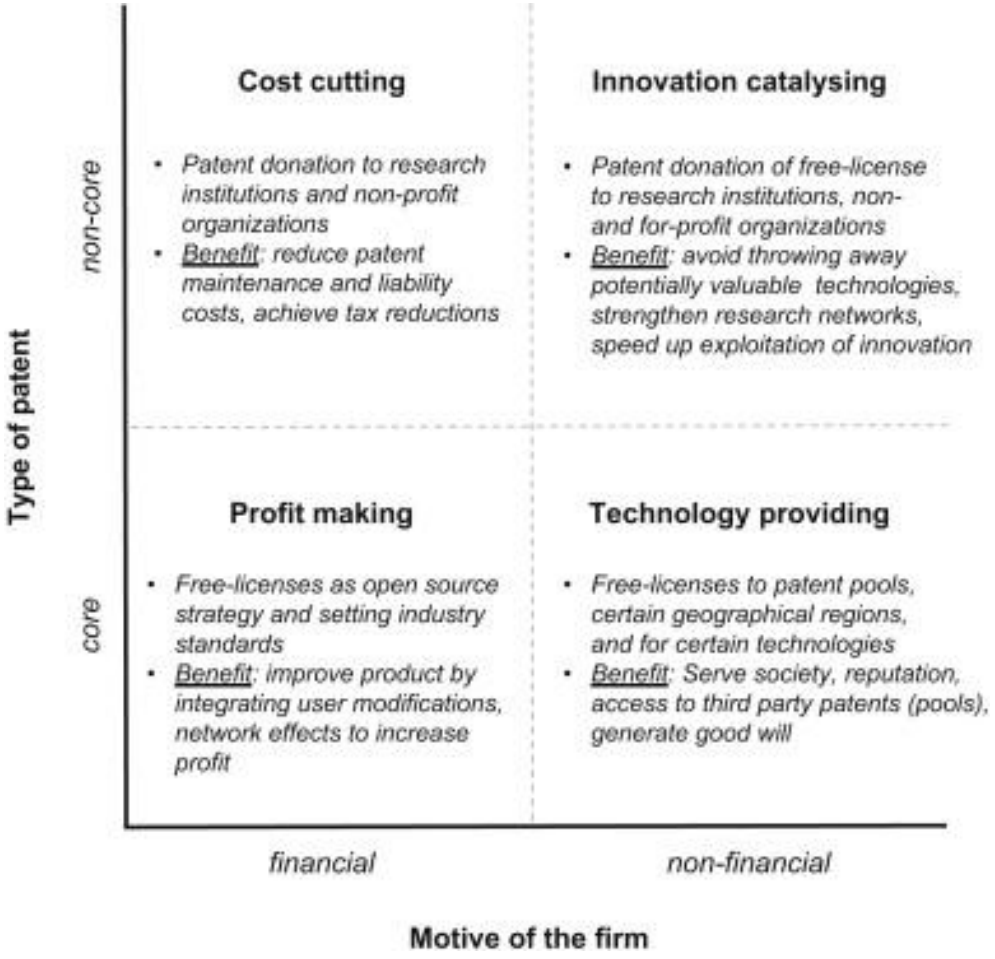
Why does it matter?
Patents grant a monopoly and for some technologies they are restrictive in who can access that technology, this is particularly debated in Access to Medicines. Free and open source approaches strive to go beyond making something legally accessible and also make it documented enough to be reproducible and allow people to build more easily on existing technologies with new inventions and innovations. The hope is that this will enable more people globally to practice and benefit from science and technology.

Why might you give your IP away for free?

MEDICINES 4 KIDS

a4K PHARMA





Ziegler, N., Gassmann, O., & Friesike, S. (2014). Why do firms give away their patents for free?. *World Patent Information*, *37*, 19-25.



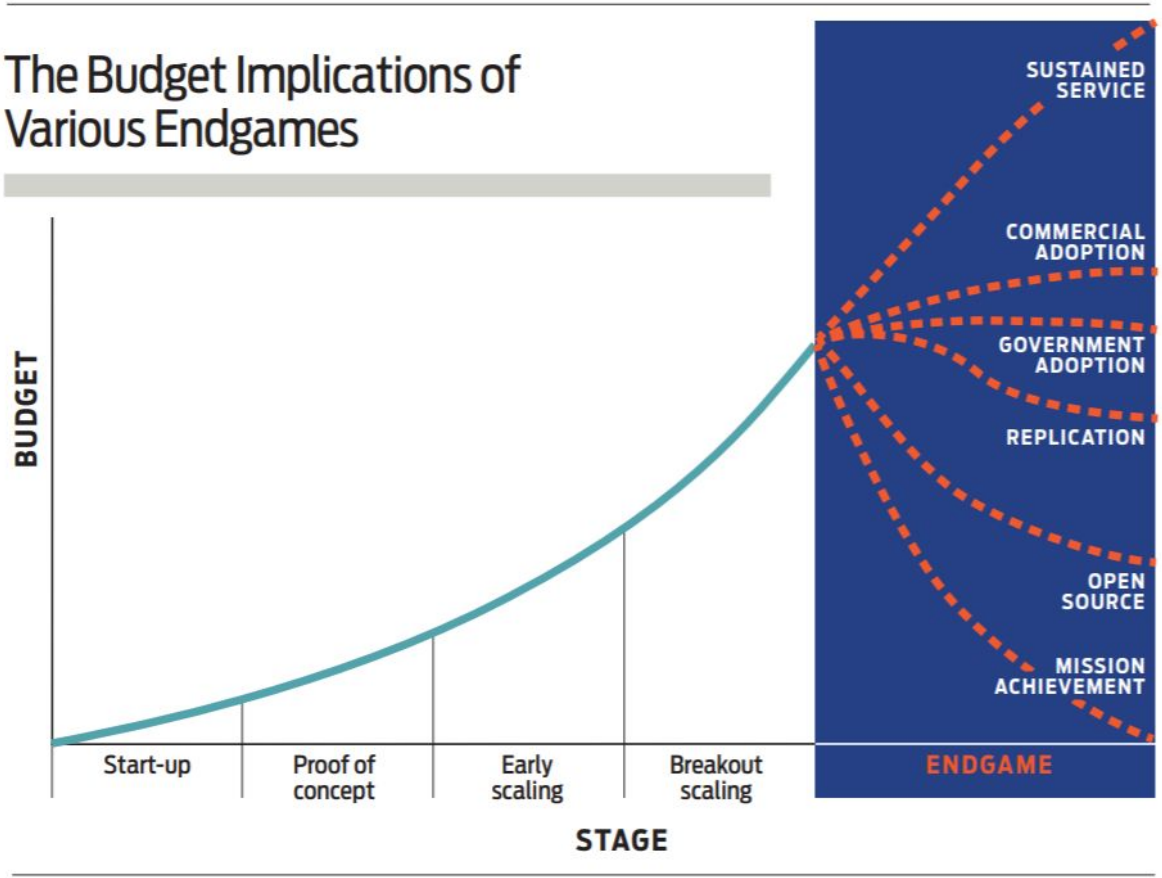
aled edwards @aledmedwards · Nov 15

Our @M4KPharma MTA asks academic recipients of our compounds to publish, not to patent, and to feel free to use the results for their careers. All tech transfer offices so far edited our MTA asking for the right to patent. I'm at a university, is this really our role in society?

2 15 18

How does open apply in your business?

Question your value proposition and your mission



Gugelev, Alice, and Andrew Stern. "What's your Endgame." *Stanford Social Innovation Review* 13.1 (2015): 40-47.

In what context and by what mechanisms can open source sharing help generate impact?

Why open source approaches?



accelerating R&D

reducing friction in access to knowledge and materials



user innovation

more diverse ideas, expanding pool of developers



focusing on value-add

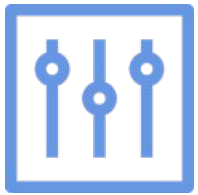
know-how, collaborations and community, using the technologies, building trust and buy-in

Why not open source approaches?



need for capital

open source can be a route to profit but it is often not a route to maximising profits - monopoly is quite effective at this



need to defend or control

some projects use patents to maintain values of quality and equitable distribution under certain conditions.



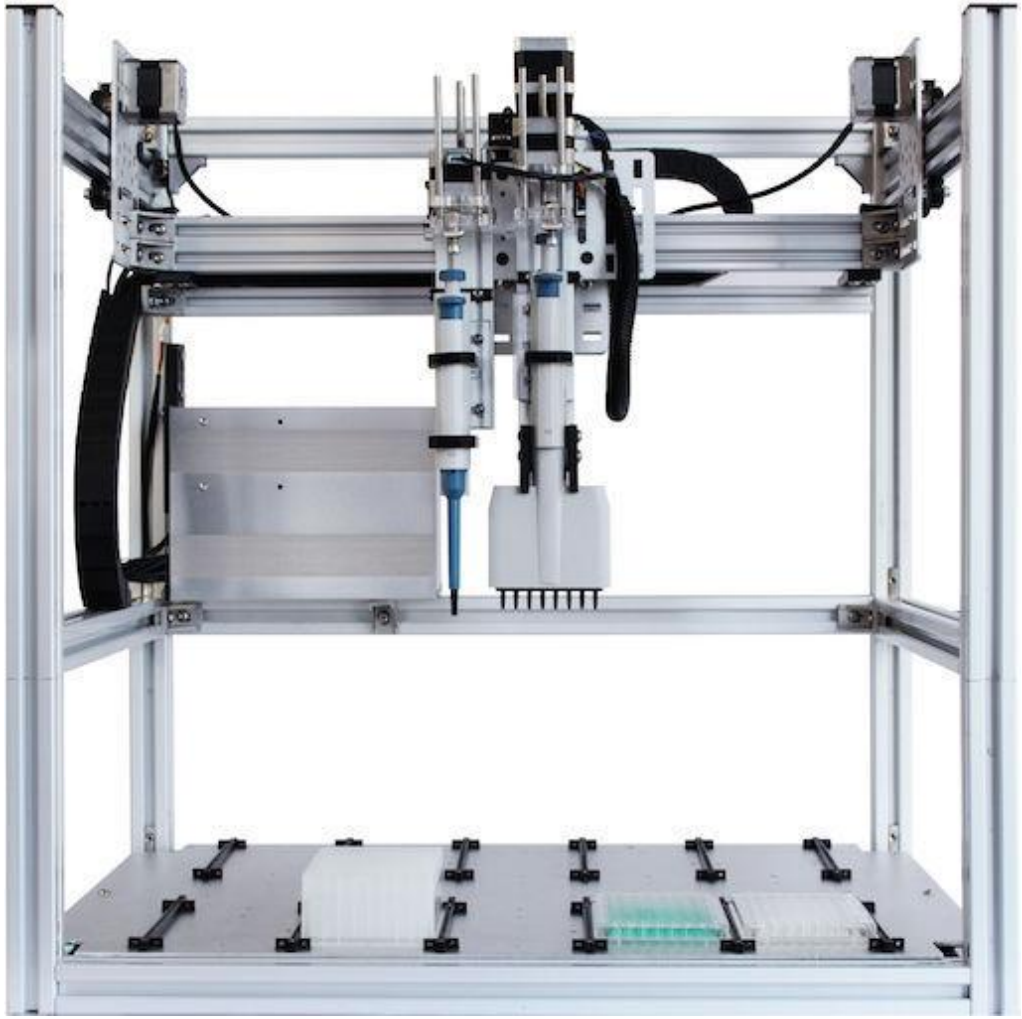
it won’t be used

if it is a distraction or no one will adapt or use it, the effort needed to document an open hardware project is wasted.

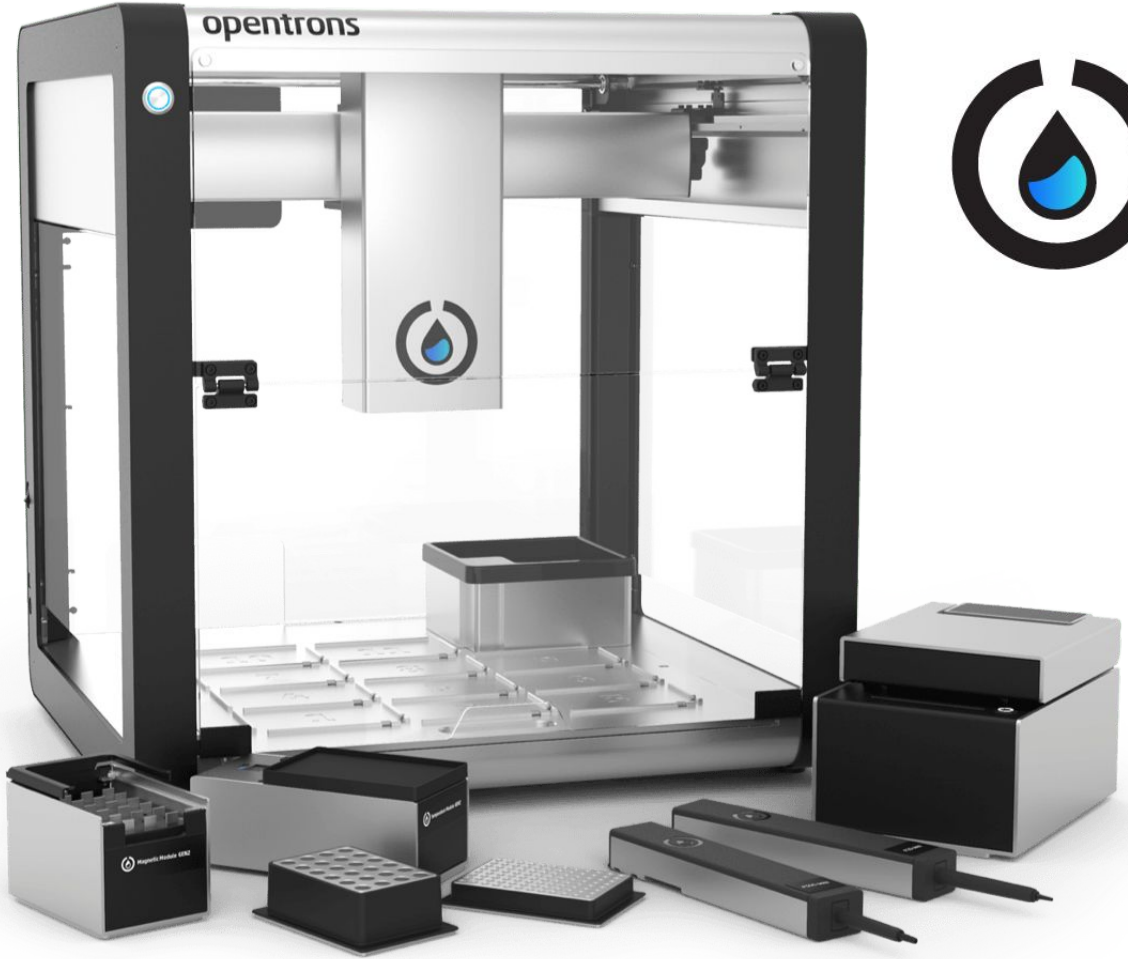
CASE STUDY

Automation with **OpenTrons**

Increasing supply options



opentrons



opentrons



Opentrons

Lab robots for Biologists

Brooklyn, NYC https://opentrons.com info@opentrons.com Verified

Overview Repositories 62 Packages People 9 Projects

Pinned

opentrons Public

Software for writing protocols and running them on the Opentrons OT-2

TypeScript 235 121

ot2 Public

Open source hardware documentation for the OT-2 liquid handling robot

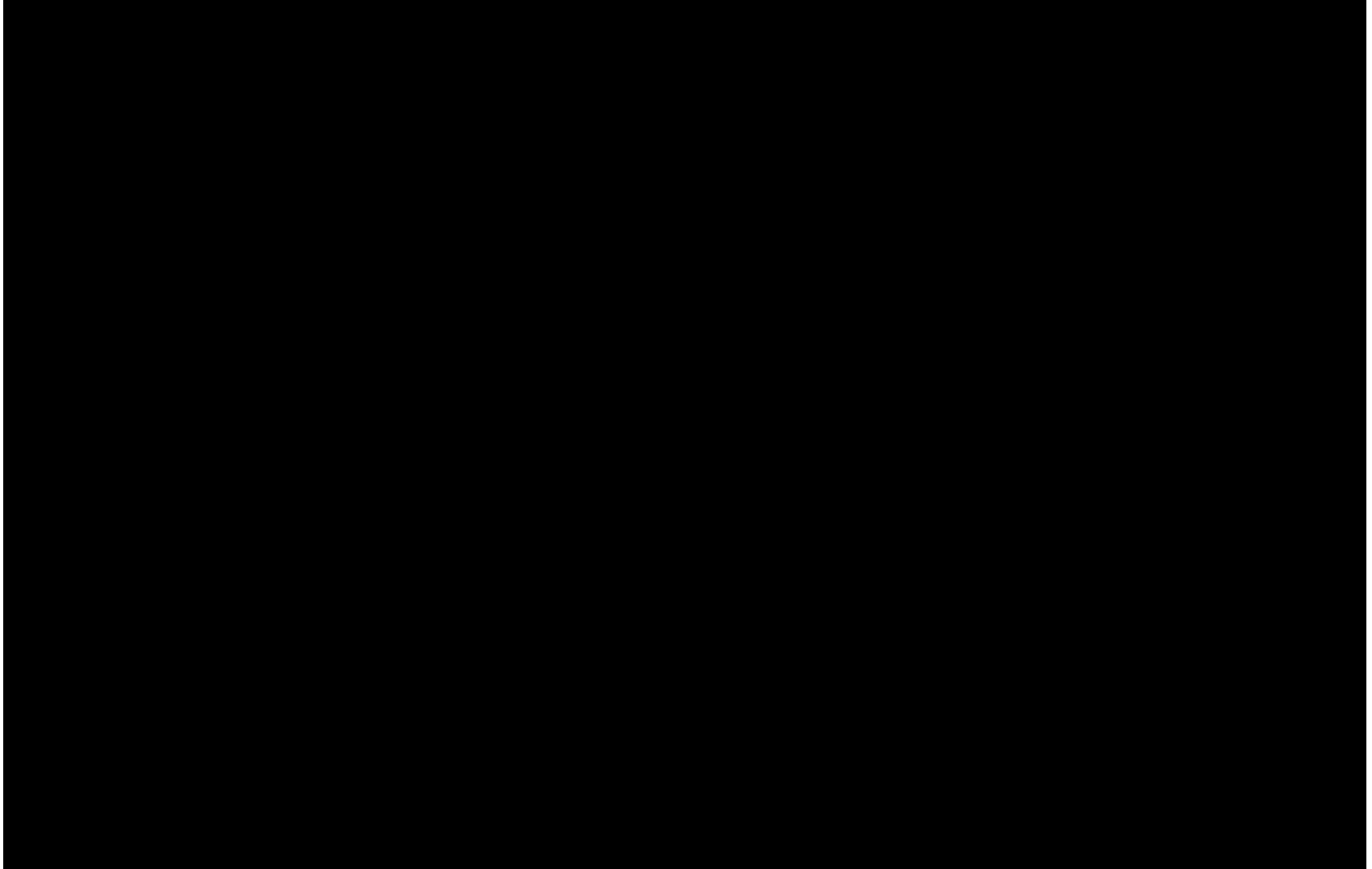
33 12

SmoothiewareOT Public

Forked from Smoothieware/Smoothieware

Opentrons' fork of the modular, opensource, high performance G-code interpreter and CNC controller written in Object-Oriented C++

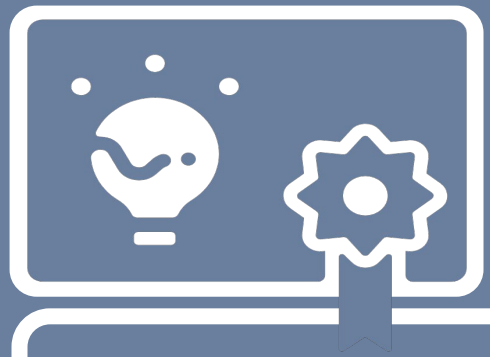
C++ 5 5



MedTech

Lab platform Opentrons closes $200M series C to build out robotics, diagnostics, cell engineering services

by Andrea Park | Sep 23, 2021 10:10am



Intellectual Property

Part 3: Material Transfer Agreements

Introduction to Material Transfer Agreements

Material Transfer Agreements are NOT IP but they are legal contracts and they are very important for biotechnology because if you want biological material from a university or company it would typically come with an MTA.



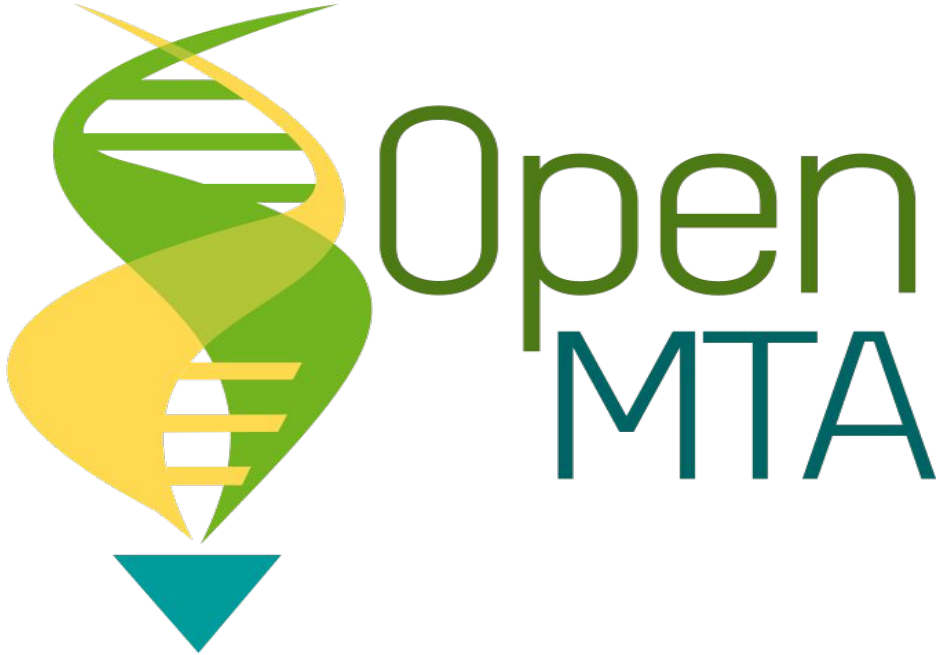
\+ Facilitate the exchange of materials

\+ Protect the interests of the researchers and their institutions

\- Often a source of delay and transaction costs, they are rarely enforced and often applied to materials of low commercial value which have no patent protection.

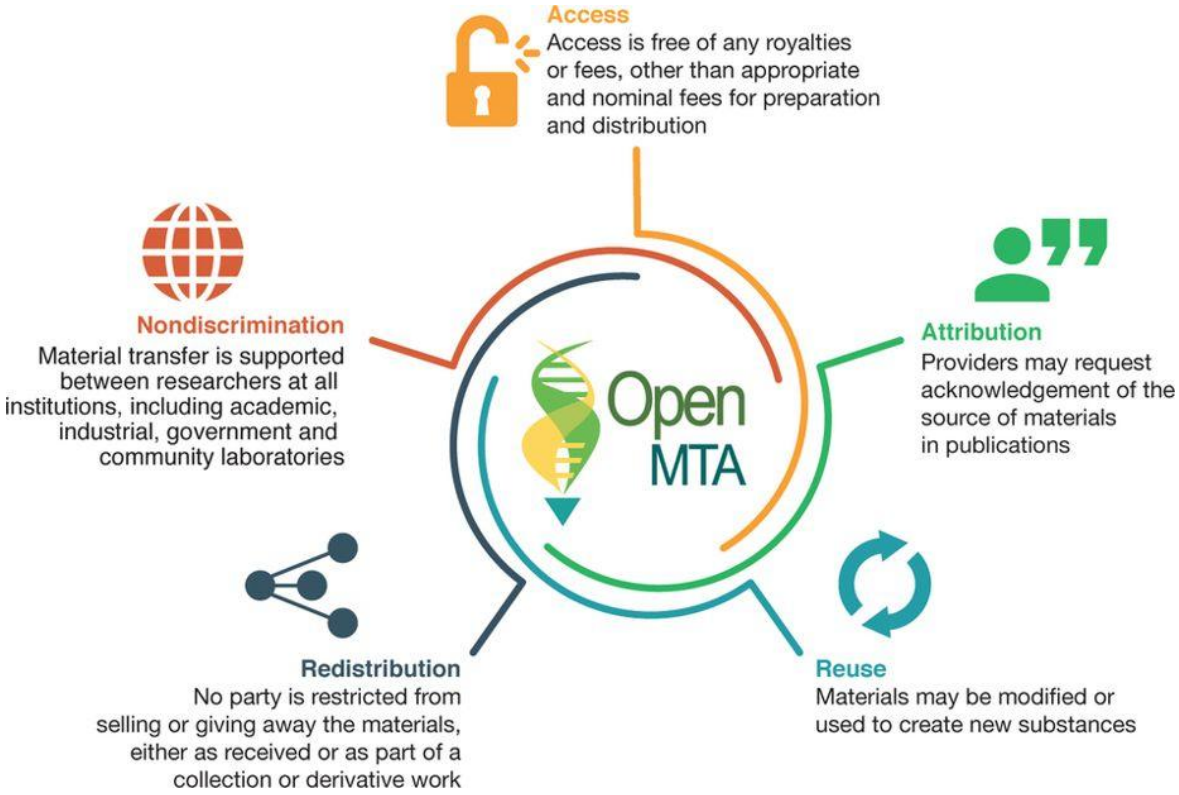
\- Current MTAs are highly restrictive! No redistribution of the material to collaborators without further permission, no commercial use.

Bubela, Tania, Jenilee Guebert, and Amrita Mishra. "Use and misuse of material transfer agreements: lessons in proportionality from research, repositories, and litigation." PLoS Biol 13.2 (2015): e1002060.

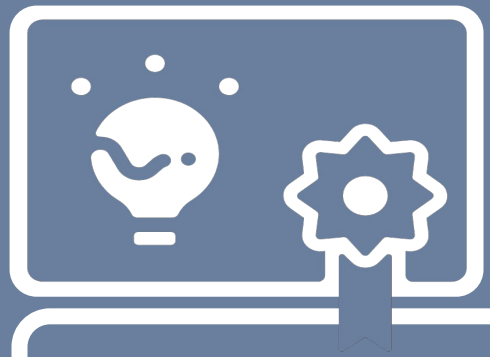


OpenMTA provides a simple, standardized legal tool that enables individuals and organizations to share their materials on an open basis.

http://openmta.org



Kahl, L., Molloy, J., Patron, N., Matthewman, C., Haseloff, J., Grewal, D., Johnson, R. and Endy, D., 2018. Opening options for material transfer.



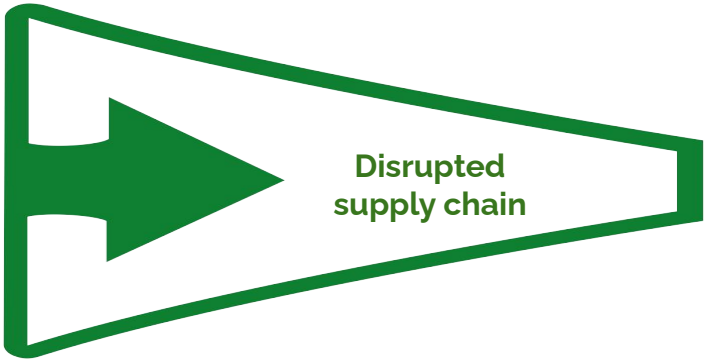
Intellectual Property

Part 4: Biological Tools

Building a sustainable bioeconomy requires access to biological research tools - maximising impact of a growing public domain

Open technologies

'Born open'
Off-patent
OpenMTA



Still limited access for low-resource settings



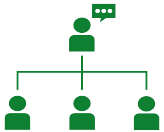
Expensive



Reliant on shipping from US/Europe



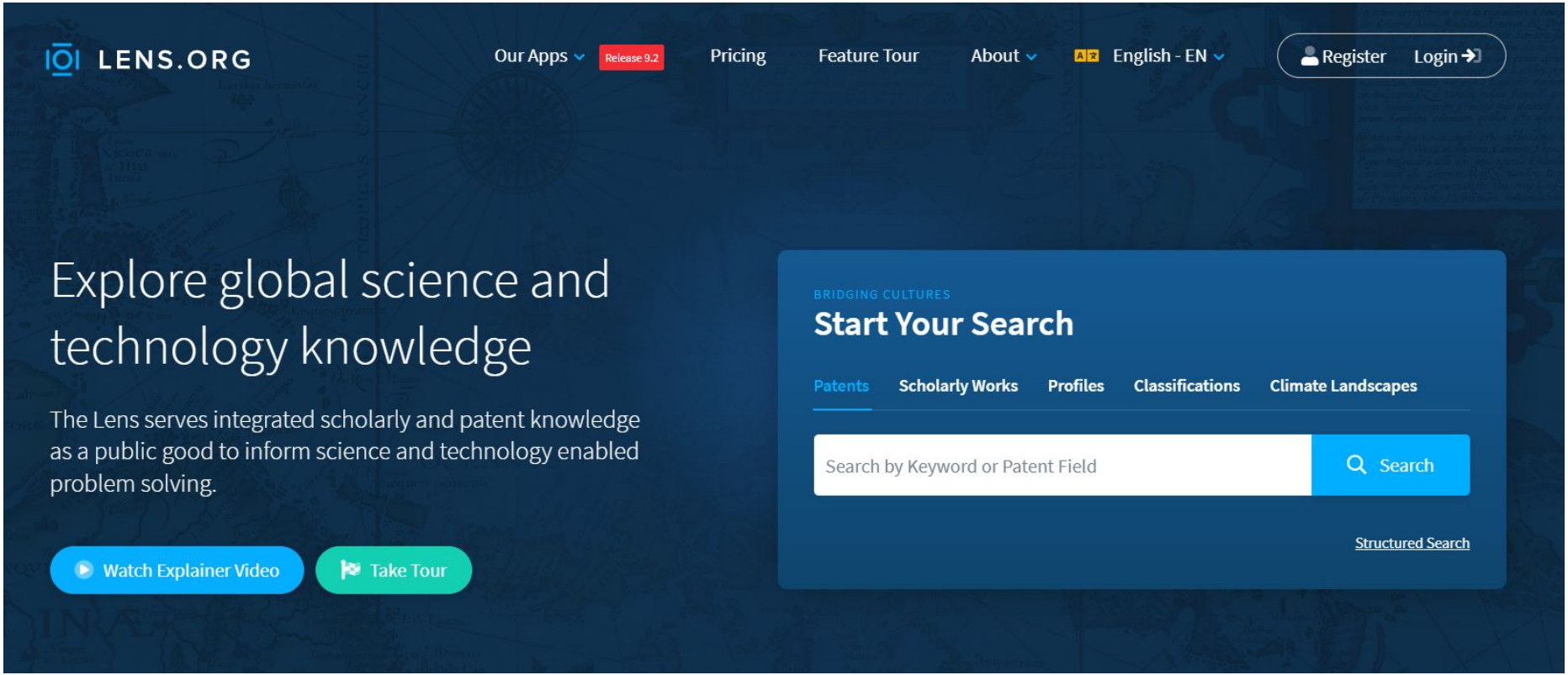
Cold chain problems



Lack of access to knowledge and training

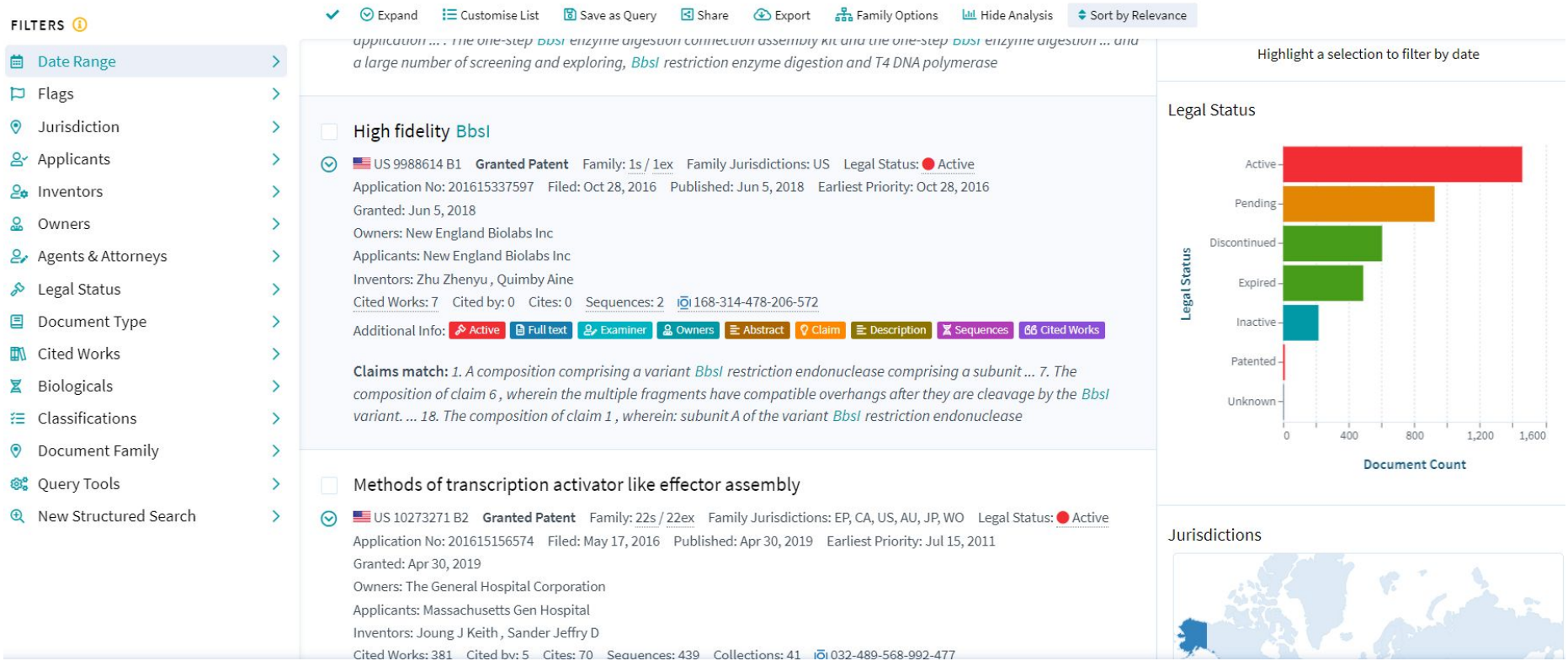
Making use of patents

- ➔ Open Access - no pay walls to the information
- ➔ Must contain enough detail to enable someone “skilled in the art” to practice the patent - not always true in practice but often more info that in a paper.
- ➔ lens.org is a fantastic resource with special features for biology, especially DNA and protein sequences
- ➔ Use patents as well as papers to inform your experiments and inventions



What is the sequence of BbsI restriction enzyme?

Not published in literature



What is the sequence of BbsI restriction enzyme?

Not published in literature

Abstract

A composition comprising a variant BbsI restriction endonuclease having reduced star activity is provided, as well as kits and methods employing the same.

Claims

1. A composition comprising a variant BbsI restriction endonuclease comprising a subunit A and a subunit B, wherein:
   the subunit A comprises an amino acid sequence that is at least 95% identical to SEQ ID NO:1, and
   the subunit B comprises an amino acid sequence that is at least 95% identical to SEQ ID NO:2, and wherein the amino acid at the position corresponding to amino acid 442 of SEQ ID NO:2 in the variant BbsI restriction endonuclease is not a Pro.
2. The composition of claim 1, wherein the amino acid at the position corresponding to amino acid 442 of SEQ ID NO:2 in the variant BbsI restriction endonuclease is an Ala.
3. The composition of claim 1, wherein the composition comprises a non-naturally occurring buffering agent.
4. The composition of claim 1, wherein the composition comprises glycerol.
5. The composition of claim 1, wherein the composition comprises a fragment of DNA comprising one or more recognition sequences for the variant BbsI restriction endonuclease.
6. The composition of claim 1, wherein the composition comprises multiple fragments of DNA that each comprises at least one recognition sequence for the variant BbsI restriction

...**Read All Claims**

EXAMPLES

[0032] Aspects of the present teachings can be further understood in light of the following examples, which should not be construed as limiting the scope of the present teachings in any way.

[0033] In order to identify a variant of BbsI that has reduced star activity, several variants of BbsI were made. The fidelity index (FI) for each variant and for wild type BbsI was determined using the method described in Wei et al (Nucl. Acids Res. 2008 36: e50). In this method, reactions containing the same amount of DNA and a serial dilution of each enzyme were performed using NEB buffers NEB1, NEB2, NEB3 and NEB4. The reaction products were run on a gel and quantified. In a typical gel, from left to right, each reaction contains the same amount of DNA that contains a recognition site for the enzyme, but the amount of enzyme is reduced as a 2-fold serial dilution across the gel. At the far right of the gel, there is very little enzyme, so little or no DNA is digested. As the amount increases toward the left, partially digested fragments start to appear, which eventually become fully digested when the amount of the enzyme reaches a critical point. This point corresponds to the lowest amount of enzyme needed for complete cleavage on cognate sites. At this point, all bands that can only be generated by this specific enzyme cleaving at its designated recognition sequence reach their highest intensities, and no other bands are present. This gives rise to the unique cleavage pattern that can be predicted based on the DNA sequence of the substrate and the recognition sequence of the enzyme. This pattern remains as the amount of the enzyme continues to increase until the star activity of the enzyme begins to appear. The amount of the restriction endonuclease for the lane that immediately precedes the initial star activity lane will be considered the highest amount showing no star activity. Once star activity appears, the normal cleavage band(s) is further cleaved into smaller fragments, visible as a weakening of the normal band(s) and the appearance of a new star activity band(s). The FI (fidelity index), which provides a measure of the amount of star activity for a restriction endonuclease, is defined as the ratio of the highest restriction endonuclease amount showing no star activity to the lowest restriction endonuclease amount needed for completed cleavage on cognate sites.

[0034] Exemplary results for a variant that comprises a P442A amino acid substitution are shown in **FIG. 1**.

[0035] The fidelity indices for the P442A variant are as follows (where the number in the brackets is the relative activity):

EXAMPLES

Aspects of the present teachings can be further understood in light of the following examples, which should not be construed as limiting the scope of the present teachings in any way.

In order to identify a variant of BbsI that has reduced star activity, several variants of BbsI were made. The fidelity index (FI) for each variant and for wild type BbsI was determined using the method described in Wei et al (Nucl. Acids Res. 2008 36: e50). In this method, reactions containing the same amount of DNA and a serial dilution of each enzyme were performed using NEB buffers NEB1, NEB2, NEB3 and NEB4. The reaction products were run on a gel and quantified. In a typical gel, from left to right, each reaction contains the same amount of DNA that contains a recognition site for the enzyme, but the amount of enzyme is reduced as a 2-fold serial dilution across the gel. At the far right of the gel, there is very little enzyme, so little or no DNA is digested. As the amount increases toward the left, partially digested fragments start to appear, which eventually become fully digested when the amount of the enzyme reaches a critical point. This point corresponds to the lowest amount of enzyme needed for complete cleavage on cognate sites. At this point, all bands that can only be generated by this specific enzyme cleaving at its designated recognition sequence reach their highest intensities, and no other bands are present. This gives rise to the unique cleavage pattern that can be predicted based on the DNA sequence of the substrate and the recognition sequence of the enzyme. This pattern remains as the amount of the enzyme continues to increase until the star activity of the enzyme begins to appear. The amount of the restriction endonuclease for the lane that immediately precedes the initial star activity lane will be considered the highest amount showing no star activity. Once star activity appears, the normal cleavage band(s) is further cleaved into smaller fragments, visible as a weakening of the normal band(s) and the appearance of a

What is the sequence of BbsI restriction enzyme?

Not published in literature

2 sequences found in this patent (in total)

Data obtained from: NCBI GenBank | USPTO Fulltext | EMBL-EBI Pat

Displaying 2 sequences

SEQ ID NO	Length	Type	Locations	Organisms	Occurrence	Tools
1	354	peptide	Claims, Detailed Description	**Declared organism:** *Brevibacillus laterosporus*		PatSeq Finder
2	572	peptide	Claims, Detailed Description, Summary	**Declared organism:** *Brevibacillus laterosporus*		PatSeq Finder

Filter Sequences

SEQ ID NO

SEQ ID NO (e.g. 10-12)

Type

Peptide (2)

Length

Peptides >300 aa (2)

Declared organism

Species Filter

Brevibacillus laterosporus (2)

Location in Document

Detailed Description (2) Summary (1)

Claims (2)

Clear Refine

What is the sequence of BbsI restriction enzyme?

Not published in literature

>US_9988614_B1_1

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EMIIGPLSLNDVDNNYRVMIDMIRKIRREKNNNKELADALNKLSESTKIKVNTLHNYTRFPLAALKYSGWVSSDKIKIYK
GRGTMLKLTDEGRKRAEWIKSSIDIGAEISEHESKEDLDKIIRISFFKMLERSYFDISSIREELASEFADIEEIYRNKDILLS
PYQTFRREKLESALGKYYKSEKNMIDEQAKKLPSDHLPSYEVEKQKVLKSTIVLKEIVSDKPKFSNGIALQIHEKKAVY
GEDIDNIVEQLIKEYETADKTVFYPLVANLFQLLGFPCENPRHGINYQRWDAIIVDDQYCIPIEIKSPSEEEFISVKAIRQA
LENKIVLLSRKVHPTNFESPSFVVGFNSPNERADVGRLISDIYDTFGIKIAVFDLRTLLILVVQKVLRGKTITMEQLRMLG
GIIDVQDI

What is the sequence of BbsI restriction enzyme?

Not published in literature

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