

Scoping Report on Potential Implications of New Synthetic Biology and Genomic Research Trajectories on the ITPGRFA: Legal Dimensions

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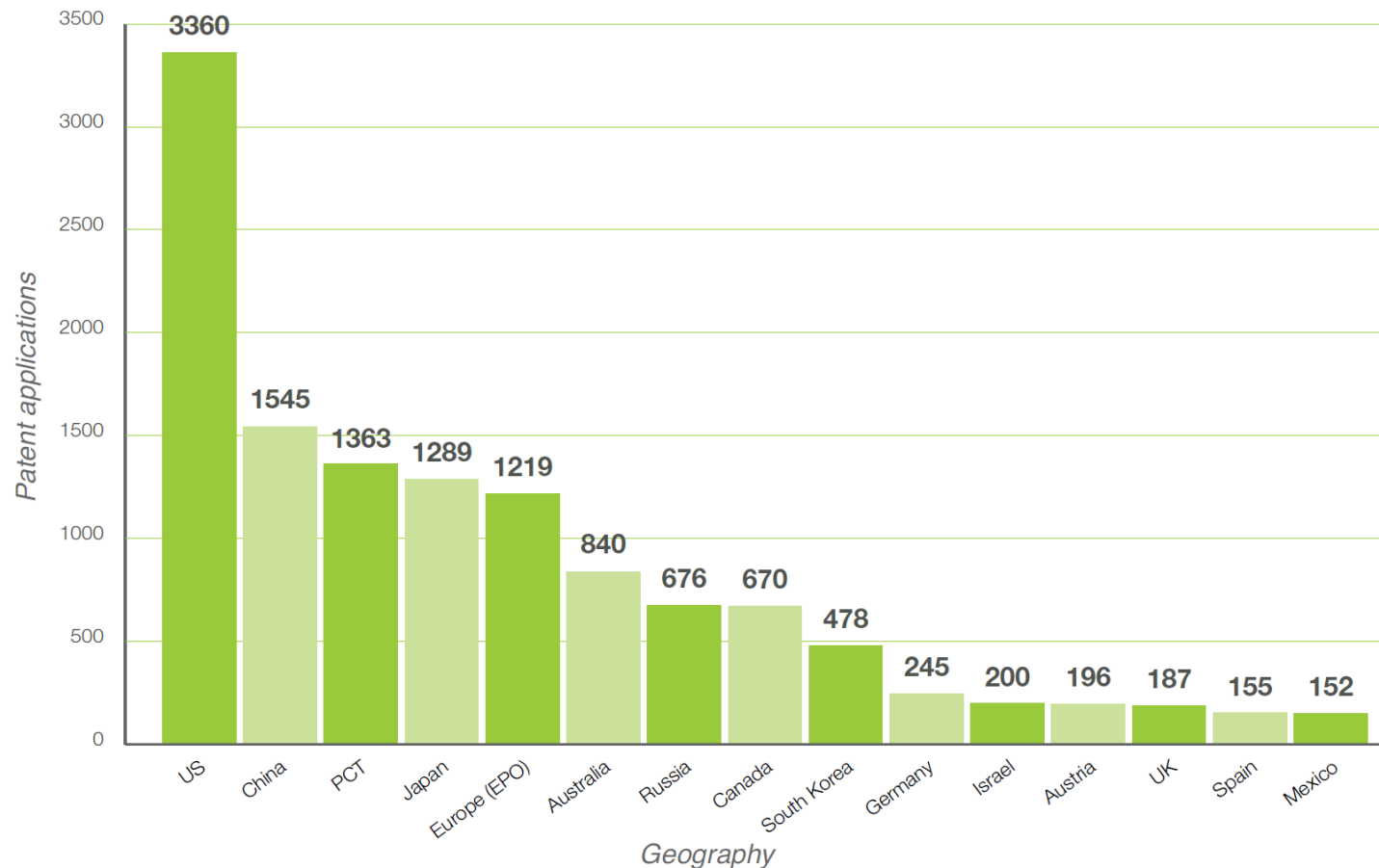
Overview

IP and Digital Sequence Information (DSI)

- Patents
 - Openness initiatives
- Trade secret
- Copyright
- IP protection relevant to, *inter alia*, benefit-sharing, value generation, and accessibility goals of the Treaty

Researchers publish, but many also seek patents on synthetic biology inventions

Fig. 16: Total patent applications since 2003 by geography for synthetic biology inventions



Recent patents in synthetic biology

| Patent number | Description | Assignee | Inventor | Date |
|---------------|--|--|--|-----------|
| US 9,388,417 | A novel customized small RNA (sRNA) that reduces gene expression in prokaryotic cells, a preparation method thereof, and the use thereof, and more particularly to a synthetic sRNA comprising an Hfq binding site, derived from the sRNA of any one of MicC, SgrS and MicF, and a region that base-pairs with the target gene mRNA, and to a preparation method thereof and the use thereof. The synthetic sRNA can be used to construct recombinant strains for efficient production of various metabolites and to establish efficient methods for production of various metabolites. | Korea Advanced Institute of Science and Technology (Daejeon, S. Korea) | Lee SY, Na D, Yoo SM | 7/12/2016 |
| US 9,382,537 | Methods and compositions for introducing microRNA (miRNA) activity or function into cells using synthetic nucleic acid molecules. Also, methods and compositions for identifying miRNAs with specific cellular functions that are relevant to therapeutic, diagnostic and prognostic applications wherein synthetic miRNAs and/or miRNA inhibitors are used in library screening assays. | Asuragen (Austin, TX, USA) | Brown D, Ford L, Cheng A, Jarvis R, Byrom M, Ovcharenko D, Devroe E, Kelnar K | 7/5/2016 |
| US 9,382,366 | Synthetic mimics of cell-penetrating peptides, especially certain novel monomers, oligomers and polymers (for example, co-polymers) that are useful for the preparation of synthetic mimics of cell penetrating peptides, their compositions, preparations and use. | University of Massachusetts (Boston) | Tew GN, Gabriel GJ, Som A, Tezgel AO | 7/5/2016 |
| US 9,376,681 | Synthetic oligonucleotide mimetics of miRNAs, in particular double-stranded, chemically modified oligonucleotide mimetics of miR-29. Also, pharmaceutical compositions comprising the mimetics and their use in treating or preventing conditions associated with dysregulation of extracellular matrix genes, such as tissue fibrotic conditions. | miRagen Therapeutics (Boulder, CO, USA) | Montgomery RL, Dalby CM, Van Rooij E, Gallant-Behm C | 6/28/2016 |
| US 9,376,669 | Nucleic acids encoding proteins, therapeutics comprising nucleic acids encoding proteins, methods for inducing cells to express proteins using nucleic acids, methods, kits and devices for transfecting, gene editing and reprogramming cells, and cells, organisms and therapeutics produced using these methods, kits and devices. Also, methods and products for altering the DNA sequence of a cell, methods and products for inducing cells to express proteins using synthetic RNA molecules, and therapeutics comprising nucleic acids encoding gene-editing proteins. | Factor Bioscience (Cambridge, MA, USA) | Angel M, Rohde C | 6/28/2016 |
| US 9,370,606 | A synthetic tissue or complex that can be produced by culture and has a high level of differentiation ability. Also, a therapy and medication for repairing and/or regenerating tissue using replacement and covering, and a method for producing an implantable synthetic tissue that does not require a plurality of monolayer cell sheets assembled to form a three-dimensionally structured synthetic tissue. | Two Cells Co. (Hiroshima, Japan) | Nakamura N, Yoshikawa H, Ando W | 6/21/2016 |
| US 9,365,618 | A TNFR2 expression-inducing composition including as an active ingredient a peptide having TNFR2 expression-inducing activity, and a method for producing cells that express TNFR2 selectively by use of the composition, including culturing at least one species of cells capable of expressing TNF receptor 2, and supplying the cells with a synthetic peptide consisting of a nuclear localization signal sequence (NLS) or a nucleolar localization signal sequence (NoLS) to enhance TNFR2 expression in the cells. | Toagosei Co. (Tokyo) | Kobayashi N, Yoshida T, Niwa M | 6/14/2016 |
| US 9,365,603 | Strengthening inositol monophosphatase activity in a transformant by introducing a myo-inositol biosynthesis pathway into a host microorganism that does not possess an endogenous myo-inositol biosynthesis pathway, such as <i>Escherichia coli</i> ; useful for recombinant DNA techniques and synthetic biology methods. | Asahi Kasei Chemicals (Tokyo) | Konishi K, Imazu S, Sato M | 6/14/2016 |
| US 9,359,399 | Synthetic peptide amide ligands of the κ -opioid receptor and particularly to agonists of the κ -opioid receptor that exhibit low P450 CYP inhibition and low penetration into the brain. Pharmaceutical compositions containing these synthetic peptide amides are useful in the prophylaxis and treatment of pain and inflammation associated with a variety of diseases and conditions, including visceral pain, neuropathic pain, hyperalgesia, inflammation associated with conditions such as irritable bowel disease and irritable bowel syndrome, ocular and otic inflammation, other disorders and conditions such as pruritis, edema, hyponatremia, hypokalemia, ileus, tussis and glaucoma. | Cara Therapeutics (Shelton, CT, USA) | Schteingart CD, Menzaghi F, Jiang G, Alexander RV, Sueiras-Diaz J, Spencer RH, Chalmers DT, Luo RZ | 6/7/2016 |

Source: US Patent and Trademark Office (<http://www.uspto.gov>); European Patent Office (<http://www.epo.org>).

Interest in Agricultural Synthetic Biology: UC Berkeley/UC San Francisco CRISPR Research Institute Expands into Agriculture

CRISPR/Cas 9 gene editing tool allows for precise deletions and insertions of DNA sequences

Plan to invest \$125 million over 5 years to develop “higher-yield, more pest-resistant crops that a large proportion of the world’s population depend on” potentially including wheat, corn, rice, cassava, and cacao



<http://news.berkeley.edu/2017/01/24/crispr-research-institute-expands-into-agriculture-microbiology/>

Patent Infringement Concerns

Patents may be obtained on mutations that eventually occur naturally, subjecting farmers/breeders to infringement liability

Researchers using non-CRISPR-Cas gene editing technologies may have to establish lack of infringement of CRISPR-Cas patents due to process patent infringement presumption

Patents and DSI

Patents: Primary form of IP protection for synthetic biology inventions

Patent rights are territorial, laws differ by country

Some synthetic biology inventions that merely copy existing sequences/compounds may not be patent-eligible in U.S., Australia (*Myriad Genetics* cases), but most synthetic DSI inventions should be patent eligible in major patenting jurisdictions (Europe, US, Japan, Australia, etc.) if they differ appreciably in form and/or function from nature.

Patents and DSI

However, the development and use of DSI in synthetic biology projects may pose a challenge to the ABS structure of the Treaty.

Article 12.3(a) of the Treaty: access to material under the MLS is solely for purposes of “utilization and conservation for research, breeding and training for food and agriculture”, and excludes “chemical, pharmaceutical and/or other non-food/feed industrial uses.”

Researchers can effectively use and **patent** DSI from MLS material (e.g. obtained through DSI in publicly accessible databases) in any kind of research, including chemical and/or pharmaceutical, without such usage being easily monitored for benefit sharing obligations.

Registries of “standard” biological parts



Standard European Vector Architecture



biofab



BioBricks Draft Open MTA

Goal: Facilitate low transaction cost access to genetic material/information for scientific progress

Problems: Does not appear to recognize

- Benefit sharing obligations of users of material from the MLS
- Rights of sovereigns in non-Treaty genetic material/information



Public Domain Chronicle (PDC)



PDC combines aspects of a few existing platforms and institutions, with a few new elements.

| | | Defensive Publication Service | Traditional Journal | Open Access Journal | Preprint Server | Patent Application | Weblog |
|----------------------|---------|-------------------------------------|------------------------|---------------------------|--------------------|-----------------------|---------|
| Speed | Instant | Fair | Fair | Fair | Instant | Slow | Instant |
| Search | Good | Fair | Good | Good | Good | Fair | Good |
| Metadata | Rich | Minimal | Rich | Rich | Rich | Rich | Medium |
| Preparation | Low | Low | Fair | Fair | Fair | High | Fair |
| Accessibility | High | Low | Low | High | High | High | High |
| Review | None | None | Long | Long | Cursory | Long | None |
| Cost | Free | Medium | Medium | Medium | Free | Expensive | Free |

Defensive Publication Bulletin

At a high level, PDC is probably closest to a “defensive publication” journal or bulletin, such as [Research Disclosure](#). Like a defensive publication bulletin, PDC accepts and publishes terse descriptions of new inventions. These descriptions qualify as prior art, preventing later patent applications. Unlike a defensive publication bulletin, PDC is free to use, free to access, and preserves richer metadata, making it easier to build effective search tools to find relevant records.

Trade Secrets and DSI

Alternative or supplement to patent protection

- Researchers may choose not to publish or patent (time cost, concerns of being scooped)
- Commercial DNA synthesis providers may develop secret databases and maintain secrecy of designer sequences developed for clients
- Use of trade secrecy likely to negatively impact tracking of MLS material or information

Copyrights and DSI

Copyright: Some advocate for copyright protection for synthetic DNA sequences to allow open source (“copyleft”) licensing (copyright owners control derivative works), also less expensive, faster than patent protection

- **India:** Delhi High Court, no copyright protection for hybrid seed DNA sequences (Emergent Genetics India Pvt. Ltd. v. Shailendra Shivam and Ors. 2011)
- **United States:** Copyright Office has rejected DNA sequence registration so far (sequences dictated by function, not considered expressive works, view may change over time (e.g. software))

If copyright protection extended to DSI, could provide additional benefit-sharing revenue for DSI from Treaty material

Areas for Further Study

(1) the extent to which the use of Treaty crops in DSI patents can be identified and whether it is even feasible to attempt to do so, as opposed to exploring creative ways to guarantee benefit sharing while maintaining open access to DSI from Treaty crops

Areas for Further Study cont.

(2) The impact of gene editing licensing barriers on Treaty crop improvements and Treaty benefit sharing.

- -include an assessment of the robustness of the CRISPR patent pool and whether other interventions may be necessary to enable beneficial crop improvements to be brought to market, especially in low and middle income countries across the globe.

Areas for Further Study

(3) How differences in regulation for synthetic biology technologies may affect and promote their adoption which could then tangentially impact the Treaty benefit-sharing system.

Thank you

