Genome Editing Inventive Energy

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GENOME EDITING INVENTIVE ENERGY 2018

INTERNATIONAL PATENT CLASSES (IPC): Genome Editing

IPC Domain	Description
A61K9/5031	Organic macromolecular compounds obtained otherwise than by reactions only involving carbon-to-carbon unsaturated bonds, e.g. polyethylene glycol, poly(lactide-co-
C12N5/0635	B lymphocytes
C12N5/0696	Artificially induced pluripotent stem cells, e.g. iPS
C12N15/09	Recombinant DNA-technology
C12N15/11	DNA or RNA fragments; Modified forms thereof; Non-coding nucleic acids having a biological activity
C12N15/85	Vectors or expression systems specially adapted for eukaryotic hosts for animal cells
C12N15/87	Introduction of foreign genetic material using processes not otherwise provided for, e.g. co-transformation
C12N15/102	Mutagenizing nucleic acids
C12N15/907	Stable introduction of foreign DNA into chromosome using homologous recombination in mammalian cells
G01N33/5002	Partitioning blood components

Genome editing is a type of genetic engineering in which DNA is inserted, deleted, modified or replaced in the genome of a living organism. The cloning techniques which are in use for a significant time now are the direct result of the advancement in the genome editing domain.

These cloning techniques are being exploited for a wide array of medical, agricultural, industrial and research applications for past several decades. The genome editing domain has experienced rapid growth in the last few years, primarily due to the CRISPR revolution.

When compared to the older gene editing technologies, CRISPR has the greatest number of patent filings and publications in recent years, as well as the most collaborations and licensing deals.

We identified following top 10 International Patent Classification (IPC) in the Genome editing domain through the study of key patents. The overall number of Applications published in the United States Patent and Trademark Office (USPTO) and Patents granted by USPTO are given in the table below (from the year 2010 till 2017. These are total numbers granted and published by the world at large at USPTO in that specific year.

S.No	IPC Domain	Year							
1	**B60W10/06**	2010	2011	2012	2013	2014	2015	2016	2017
	Application	1	1	1	1	1	1	1	1
	Granted	1	1	1	1	1	1	1	1
2	**B60W10/10**	2010	2011	2012	2013	2014	2015	2016	2017
	Application	1	1	1	1	1	1	1	1
	Granted	1	1	1	1	1	1	1	1
3	**B60W10/18**	2010	2011	2012	2013	2014	2015	2016	2017
	Application	1	1	1	1	1	1	1	1
	Granted	1	1	1	1	1	1	1	1
4	**B60W10/20**	2010	2011	2012	2013	2014	2015	2016	2017
	Application	59	25	15	2	1	1	1	40
	Granted	1	121	118	93	87	89	67	68
5	**B62D15/02**	2010	2011	2012	2013	2014	2015	2016	2017
	Application	187	41	123	56	36	49	42	151
	Granted	75	121	151	213	240	299	324	421
6	**B60R11/04**	2010	2011	2012	2013	2014	2015	2016	2017
	Application	91	247	350	256	231	188	186	218
	Granted	1	1	47	1	1	86	176	256
7	**G05D1/02**	2010	2011	2012	2013	2014	2015	2016	2017
	Application	1	126	53	53	21	15	21	36
	Granted	1	66	6	51	98	106	87	99
8	**G05D1/10**	2010	2011	2012	2013	2014	2015	2016	2017
	Application	1	1	1	1	1	1	1	1
	Granted	1	1	1	1	1	1	1	1
9	**G08G1/09**	2010	2011	2012	2013	2014	2015	2016	2017
	Application	1	1	1	1	1	1	1	1
	Granted	1	1	1	1	1	1	1	1
10	**G06K9/62**	2010	2011	2012	2013	2014	2015	2016	2017
	Application	1	1	1	1	1	1	1	1
	Granted	1	1	1	1	1	1	1	1

STATE OF ART OF ANY TECHNOLOGY USING CRAFITTI's INVENTIVE ENERGY

Inventive Energy (IE) is a yearly metric of the trend of last five years of invention activity in the specific technological domain such as the Genome editing calculated based on a number of patent applications published and a number of patents granted in the respective technological domain. **Inventive energy is a composite metric of two indices – Patent Intensity Index and Patent Activity Index.**

> CRAFITTI's **INVENTIVE ENERGY** measures the pace and intensity of **inventive activity** in a particular technological field. Inventive Energy provides a true picture of the state of the art of technology as it is a **composite metric** of Patents Granted and Patent Applications published in specific technology domains annually for a period of five years.
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> ***Inventive Energy*** *in specific technology domains can be utilized by existing technology players, start-ups, new players, investors, VCs, Research and Development teams and technology and Product Strategy Teams to design more informed future.*

Patent Intensity Index of a year is measured in terms of the yearly average of a number of total patents granted and patent applications published in last 5 years. *As an analogy, the Patent Intensity Index is denoted as the Mass which is reflected as a number of Patents and Applications granted and published respectively in the preceding 5 years.*

Patent Activity Index is measured in terms of the yearly average of *relative* pace of patent applications and granted patents in the IPC domain. *As an analogy, the Patent Activity Index denotes the Velocity or relative pace of Patents and Applications, granted and published respectively in the preceding 5 years, with higher weightage assigned to recent years.*

For any year, the two indices include a measure of yearly averages of last five years of a number of applications published and patents granted. For example, for 2017, these indices use data from years 2013-2017.

Patent Activity Index of top 10 Genome editingIPC classes for years 2014-2017

A value of **Patent Activity Index** *is less than 1.0 indicates that relative average number of applications filing is reducing compared to a number of patents being granted.* **The index also gives a red, amber and green signal.** Red indicates the value of the index is less than 1.0. **Amber** indicates it is between 1.0 and 2.0 and green indicates it is above 2.0, i.e., *the number of applications being published every year on an average is more than 2 times the number of patents being granted on an average*. A higher value of patent activity index is an indication of more recent inventive activity in the domain or the specific IPC class. In turn, a higher activity index will signify a higher Inventive Energy. *Activity Index is analogous to*

the velocity of the particle. The PAI (Patent Activity Index) of top 10 Genome editing IPCs for years 2014-2017 are given below.

IPC Domain	Description	BM-PAI 2014	BM-PAI 2015	BM-PAI 2016	BM-PAI 2017
A61K9/5031	Organic macromolecular compounds obtained otherwise than by reactions only involving carbon-to-carbon unsaturated bonds, e.g. polyethylene glycol, poly(lactide-co-	1.00	1.00	1.00	1.00
C12N5/0635	B lymphocytes	1.00	1.00	1.00	1.00
C12N5/0696	Artificially induced pluripotent stem cells, e.g. iPS	1.00	1.00	1.00	1.00
C12N15/09	Recombinant DNA-technology	5.22	0.04	0.02	0.27
C12N15/11	DNA or RNA fragments; Modified forms thereof; Non-coding nucleic acids having a biological activity	0.50	0.26	0.21	0.25
C12N15/85	Vectors or expression systems specially adapted for eukaryotic hosts for animal cells	193.33	111.36	63.35	48.64
C12N15/87	Introduction of foreign genetic material using processes not otherwise provided for, e.g. co-transformation	1.91	1.39	1.06	0.35
C12N15/102	Mutagenizing nucleic acids	1.00	1.00	1.00	1.00
C12N15/907	Stable introduction of foreign DNA into chromosome using homologous recombination in mammalian cells	1.00	1.00	1.00	1.00
G01N33/5002	Partitioning blood components	1.00	1.00	1.00	1.00

*BM-PAI – *Bhushan Mishra Patent Activity Index* – named after its creators

As can be seen in the above table, the PAI for IPC classes C12N15/85 Vectors or expression systems specially adapted for eukaryotic hosts for animal cells are above 2.0 for years 2014, 2015, 2016 and 2017, indicated in green. The PAI for C12N15/09 Recombinant DNA-technology is above 2.0 for years 2014, indicated in green, and below 1.0 for the year 2017, indicated in red.

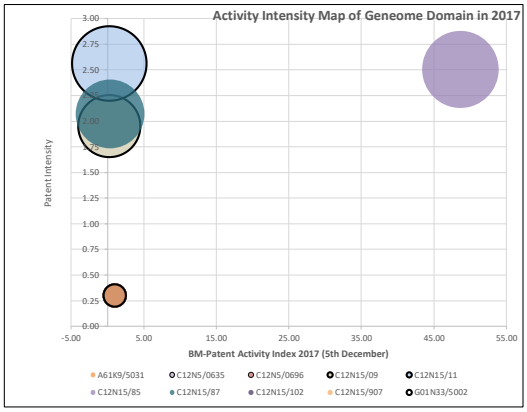
Similarly, for the IPC class A61K9/5031 (Organic macromolecular compounds obtained otherwise than by reactions only involving carbon-to-carbon unsaturated bonds, e.g. polyethylene glycol, polylactide-co-glycolide); C12N5/0635 (B lymphocytes, they function in the humoral immunity component of the adaptive immune system by secreting antibodies); C12N5/0696 (Artificially induced pluripotent stem cells, e.g. iPS); C12N15/102 Mutagenizing nucleic acids); C12N15/907 (Stable introduction of foreign DNA into chromosome using homologous recombination in mammalian cells); and G01N33/5002 (Partitioning blood components), the PAI is below 1.0 for years 2014, 2015, 2016 and 2017, indicated by amber.

The PAI for C12N15/87 (Introduction of foreign genetic material using processes not otherwise provided for, e.g. co-transformation) is below 1.0 for years 2014, 2015, and 2016 and below 1.0 for the year 2017, indicated in red. Further, the PAI for C12N15/11 (DNA or RNA fragments; Modified forms thereof; Non-coding nucleic acids having a biological) activity is red (below 1.0) for the years 2014-2017. This implies that the number of Patent Applications being published in the preceding 5 years (inclusive of current year) *remains less* than the number of Patents being granted. This indicates a reducing Invention activity in the specific domain. Thus, it can be concluded that IPC domains C12N15/09, and C12N15/11 are seeing reducing Invention Activity and has low invention velocity from 2010 to 2017.

*C12N15/85 is the only prominent IPC classifications in the Genome editing which talks about **vectors or expression systems specially adapted for eukaryotic hosts for animal cells**. The inventive activity in C12N15/09 was higher in the year 2014, since then the patent activity has been reducing as the number*

of Patents being granted has started increasing. Further, there are less movement of the inventive activity in A61K9/5031, C12N5/0635, C12N5/0696, C12N15/102, C12N15/907, and G01N33/5002 IPC classes.

Activity Intensity Maps of Top 10 Genome editing IPC classes in the year 2014 and 2017



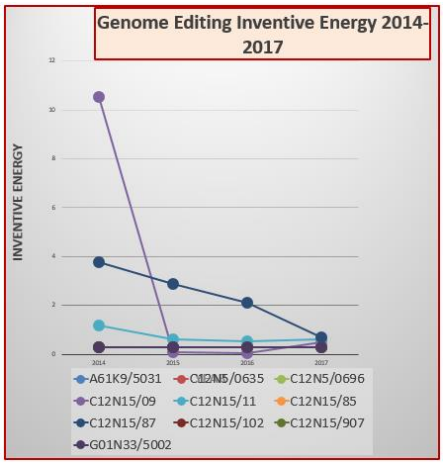
Activity Intensity Map (**AIM**) of a set of IPC classes is a Crafitti proprietary visualization of intensity in terms of a number of patents granted and patent applications published, and inventive activity in terms of relative pace of patent applications and granted patents in any IPC domain. For any year say 2014, these indices include a measure of yearly averages of last five years of a number of applications published and patents granted. For example, for 2014, these indices use data from years 2010, 2011, 2012, 2013 and 2014.

Genome editing Inventive Energy of Top 10 IPC classes

Inventive Energy for the year 2014 for IPC class A61K9/5031 is simply a product of Patent Activity Index

IPC Domain	Patent Activity Index				Patent Intensity				INVENTIVE ENERGY			
IPC	BM-PAI 2014	BM-PAI 2015	BM-PAI 2016	BM-PAI 2017	2014	2015	2016	2017	2014	2015	2016	2017
A61K9/5031	1.00	1.00	1.00	1.00	0.30	0.30	0.30	0.30	0.30	0.30	0.30	0.30
C12N5/0635	1.00	1.00	1.00	1.00	0.30	0.30	0.30	0.30	0.30	0.30	0.30	0.30
C12N5/0696	1.00	1.00	1.00	1.00	0.30	0.30	0.30	0.30	0.30	0.30	0.30	0.30
C12N15/09	5.22	0.04	0.02	0.27	2.02	2.04	1.98	1.95	10.54	0.09	0.05	0.52
C12N15/11	0.50	0.26	0.21	0.25	2.40	2.42	2.49	2.56	1.19	0.63	0.53	0.64
C12N15/85	193.33	111.36	63.35	48.64	2.39	2.45	2.48	2.50	461.96	272.80	157.32	121.83
C12N15/87	1.91	1.39	1.06	0.35	1.98	2.08	2.01	2.07	3.77	2.90	2.12	0.72
C12N15/102	1.00	1.00	1.00	1.00	0.30	0.30	0.30	0.30	0.30	0.30	0.30	0.30
C12N15/907	1.00	1.00	1.00	1.00	0.30	0.30	0.30	0.30	0.30	0.30	0.30	0.30
G01N33/5002	1.00	1.00	1.00	1.00	0.30	0.30	0.30	0.30	0.30	0.30	0.30	0.30

for the year 2014 (in this case a value of 1.00) and Patent Intensity for the year 2014 (in this case a value of 0.30). The Inventive Energy for the year 2014 for IPC domain A61K9/5031 comes out to be 1.00 x 0.30 = 0.30, as shown in the Table. In general, the Inventive Energy of IPC class C12N15/85 vectors or expression systems specially adapted for eukaryotic hosts for animal cells is highest among these top 10 IPC classes.



Key Findings

Due to its inherent simplicity and utilization of substantial information on published and granted patents, the present study on the inventive energy provides a de facto standard for enterprises active in the Genome editing to evaluate the front edge of technology in various applications of the genome editing.

IPC class on the vectors or expression systems specially adapted for eukaryotic hosts for animal cells (C12N15/85) has seen the tremendous inventive energy in the 2014-2017 Index. Other two prominent IPC classes on Introduction of foreign genetic material using processes not otherwise provided for, e.g. co-transformation (C12N15/87), and recombinant DNA-technology (C12N15/09) have also been quite active among the gene editing enthusiasts and R&D teams.

One of the findings from the present inventive energy study is that the patenting activity was higher in the gene editing domain in the year 2014. Further, there is a decrease in the patent activity in the DNA or RNA fragments; Modified forms thereof; Non-coding nucleic acids having a biological activity (C12N15/11) which were higher in the year 2014. However, despite all the development and progress in the gene editing domain there is a dire need for more advanced gene editing techniques that are precise and accurate. The use of programmable nucleases for genetic modifications has increased in past decade for its potential to treat various inheritable diseases and cancer. In past decade three major classes of programmable nucleases have come to light– the zinc finger nucleases (ZFNs), transcription activator-like effector nucleases (TALENs) and the clustered regularly interspaced short palindromic repeats (CRISPR)–associated Cas9 (CRISPR/Cas9).

IPC classes with high Inventive Energy typically will have higher business potential and growth in the Genome editing. The Inventive Energy can be utilized to create the Genome editing Inventive Strategy to find problems in high inventive energy IPC classes. This can be a leading indicator for not only any startup or disruptor but also to existing patent owners to expand and strengthen their portfolio through this guidance rather than letting serendipity and opinion about future guide their inventive effort.

As the patent examiner not only evaluate the patentability of the corresponding technology but also assess the legal aspects of the filed patent application at various levels of scrutiny before granting the patent, therefore, patent grant trends identified by the present inventive energy study in the Genome editing will enable the decision maker with the due-diligence aspects of the Genome editing.

Any organization willing to invest in the Genome editing can utilize invention energy metric in general and this study, as it automatically takes care of three major inputs required to understand the state of the art of Genome editing – Patent Applications, Granted Patents and Specific IPC classes relevant to Genome editing in a composite metric.

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