

Sample Patent Landscape Study

Exosomes for Drug Delivery

December 2020

Table of Contents

1. Intro	oduction	3
2. Obje	ective	5
3. Seal	rch Methodology	5
4. Sum	nmary	6
5. Tech	nical Analysis	6
5.1. B	ucketing of Relevant Patent Documents – Overall Technology	7
5.1.1.	Dissection of Patents/Applications Pertaining To 'Exosome - Sources'	8
5.1.2.	Dissection of Patents/Applications Pertaining To 'Exosomes - Isolation / Preparation'	
5.1.3.	Dissection of Patents/Applications Pertaining To 'Type of Cargo'	. 10
5.1.4.	Dissection of Patents/Applications Pertaining To 'Cargo Loading Method'	. 11
5.1.5.	Dissection of Patents/Applications Pertaining To 'Therapy Area'	. 12
5.2. L	eading Assignee Analysis	. 13
5.3. L	eading Assignee across Technology	. 14
5.3.1.	Dissection of Leading Assignees across 'Exosome - Sources'	. 14
5.3.2.	Dissection of Leading Assignees across 'Exosomes – Isolation / Preparation'	. 16
5.3.3.	Dissection of Leading Assignees across 'Type of Cargo'	. 17
5.3.4.	Dissection of Leading Assignees across 'Cargo Loading Method'	. 17
5.3.5.	Dissection of Leading Assignees across 'Therapy Area'	. 18
6. Non	-Technical Analysis	. 20
6.1.Trend	Analysis – Earliest Invention in Exosomes for Drug Delivery vs Geographies	. 20
6.2. T	rend Analysis – Legal Status Analysis	. 21
6.3. A	ssignee Based Trend Analysis	. 22
6.3.1.	Assignee Category	. 22
6.3.2.	Leading Assignees across Earliest Priority Years	. 22
6.3.3.	Leading Assignees across Earliest Priority Countries	. 23
6.4. P	atent Classification Based Trend	. 24
6.4.1.	Major IPCs - Main Class	. 25
6.4.2.	Major IPCs - Sub Class	. 25
6.4.3.	Leading Assignees across IPC - Main Classifications	. 26
6.4.4.	Leading Assignees across IPC – Sub Classifications	. 26
Appendix	A - References & Credits	. 28
Appendix	c B – Definitions Of IPC Classes	. 29
Disclaime	er	. 30
ABOUT II	PRD	. 30



1. Introduction

1.1. Exosome-based Therapeutics

Exosomes are extracellular vehicles produced by almost all of the cells and are present in diverse body fluids and normally comprise RNA and exclusive set of proteins. They play a vital part in intercellular communication by transferring molecules from one cell to another, potentially delivering the functional proteins, mRNA transcripts, and miRNAs to cells throughout the body. Due to their ability for superior passive targeting, owing to their small size, indigenous nature, and the ability to cross the biological barriers, the exosomes are found to be the most promising candidates for use as therapeutic drug delivery vehicles. Exosomes that are derived from cells such as dendritic and mesenchymal stem cells have potential therapeutic properties and are biocompatible and efficient agents against various disorders such as organ injury.

Further, exosomes are found to have potential for various therapeutic applications such as drug delivery systems for anti-cancer vaccines, proteins/peptides, small molecule drugs and nucleic acids, and therapies for diseases such as cancer and cardiovascular disease biomarkers. Also recent studies have proved that exosomes have immunotherapeutic applications and can act as a drug delivery system for targeted therapies with drugs and biomolecules, which can attribute to their ability to selectively express proteins.

In the recent times, a large number of government-funded research studies have been conducted, regarding the role of drug delivery using exosomes in several kinds of cancers, including melanoma, breast cancer, lung cancer, and pancreatic cancer, among others.

Although there is rapid advancement in the research related to exosome applications, there are numerous challenges associated with the development of exosome-based therapeutics, especially in the production of the exosome formulations due to their low productivity and heterogeneity accompanied by the barriers in storage, optimizing and isolation methods of exosome formulations, as well as efficient transfection strategies.

Further, stringent regulatory requirements for the approval and commercialization of exosome products pose as a major hurdle in the growth of the exosome-based therapeutic market that includes the exosome-based delivery vehicles.

1.2. Market Potential

Exosome market's growth is primarily steered by the ever-increasing funding for exosome research for various applications with a major focus on the targeted drug delivery for cancer ailments. The global exosome research products market is projected to reach USD 264 million by 2024 from USD 91 million in 2019, at a CAGR of 23.8% during the forecast period. The growth of this market is driven by factors such as the increasing funding for life sciences research, increasing prevalence of cancer, technological advancements in exosomes isolation and analytical procedures, and increasing advanced applications of exosomes.

The North American region holds one of the largest shares in the exosomes market, owing to



better healthcare infrastructure, effective government policies, a huge base of multinational companies, and high awareness among people about diagnostics and healthcare. Furthermore, many ventures relating to exosome research are very well supported by government funding. The growth of the biotechnology and pharmaceutical industries and growth in the number of cancer cases in the region are also supporting market growth.

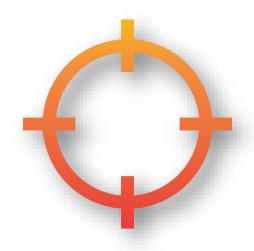
The Asia Pacific (APAC) market is anticipated to grow at a high CAGR in the next few years with maximum growth to be registered by countries *viz*. India, China, and Japan, driven by technological advancements, increase in research spending, and improvement in health care infrastructure in developing countries.

"Patent data shows 69% of the total references are pending applications. Higher percentages of applications point to a new or growing market"



2. Objective

- To perform detailed analysis of patenting activity pertaining to Exosomes and to understand underlying technologies.
- To generate useful insights about Exosomebased drug delivery technological field of study for the researchers at the industry.
- Graphical representation of trends from the mined data of relevant patents/applications.



3. Search Methodology



The first step is to create and define a patent set, which then serves as the basis of this study. Patent databases like Patseer have been used as our data sources. Search has been carried out in Abstract, Title and Claims fields of patent specifications by incorporation of Keywords and International Patent Classes.

4. Summary

Overview

This report analyses the global landscape of patents/applications filed in the technology area of exosomes for drug delivery

Patent Analysis

This report extensively analysed 700 patents/patent applications from the respective representative patent families, which resulted in the identification of 143 patents/patent applications relevant to the technology area of exosomes for drug delivery

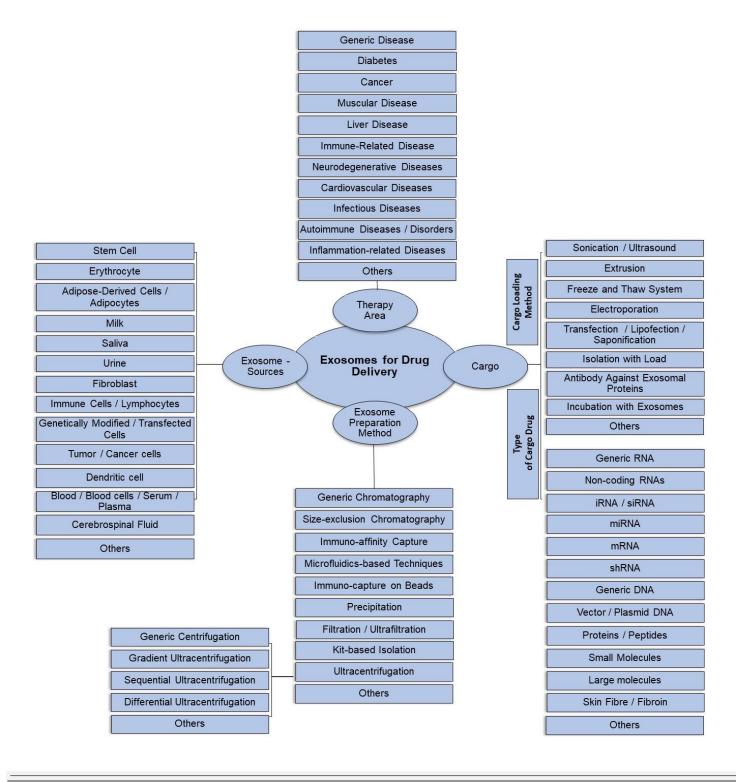
- USA tops the innovator geography with 60 priority applications.
- APAC countries China and Korea are majorly innovating in investigative technology, while EP region is yet to gain prominence in the technology area.
- Milk/colostrum from diverse sources is a significant source of exosomes, which offers the benefits of non-invasive collection methods and cheap availability.
- Stem cells have been mainly used because they are of paracrine origin of the exosome fraction that essentially contributes to the action of stem cells.
- Contemporary technologies like microfluidics-based, immune capture bead-based, or magnetic beads-based technologies for exosome isolation are yet to be explored by the leading assignees.
- Microfluidic devices including lab-on-a-chip devices, nanoplasmonenhanced scattering, membrane-mediated exosome separation are yet to be adopted to large-scale isolation systems.
- With the increasing number of cancer patients worldwide, inventions related to the delivery of small molecules, preferably anti-cancer drugs have garnered attention for using exosomes as targeted delivery vehicles.



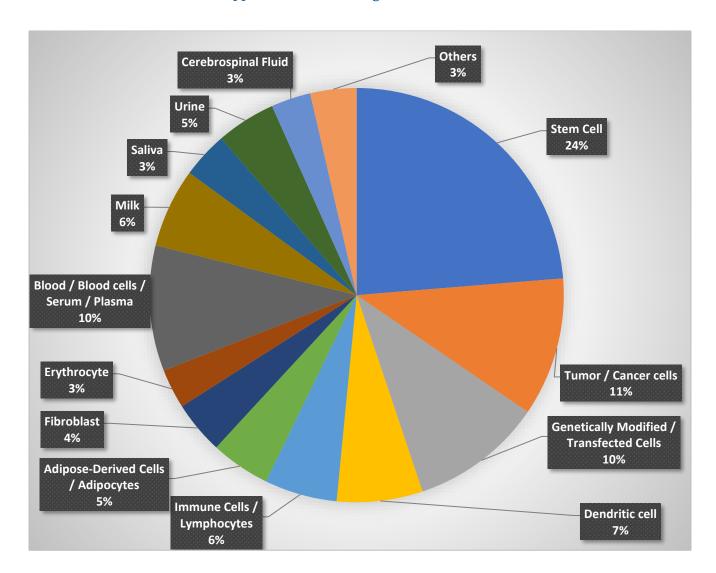
5. Technical Analysis

5.1. Bucketing of Relevant Patent Documents – Overall Technology

A set of 143 patent families were analyzed in depth to identify the focus areas of the patents related to exosome-based drug delivery systems.



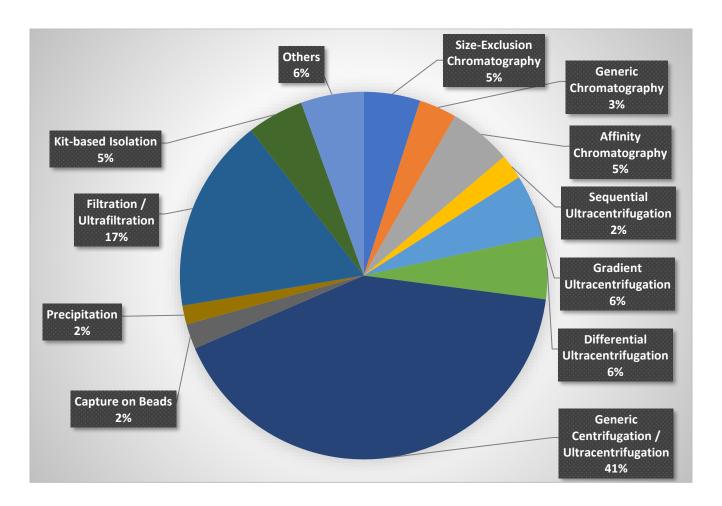
5.1.1. Dissection of Patents/Applications Pertaining To 'Exosome - Sources'





- Amongst the investigated cell types, stem cells are the most used and discussed source for exosomes, followed by tumor cells and genetically modified/transfected cells. Stem cells have been mainly used because of the paracrine origin of the exosome fraction that essentially contributes to the action of stem cells.
- ➤ It is to be noted that the milk/colostrum from diverse sources is a significant source of exosomes, which offers the benefits of non-invasive collection methods and cheap availability.

5.1.2. Dissection of Patents/Applications Pertaining To 'Exosomes – Isolation / Preparation'

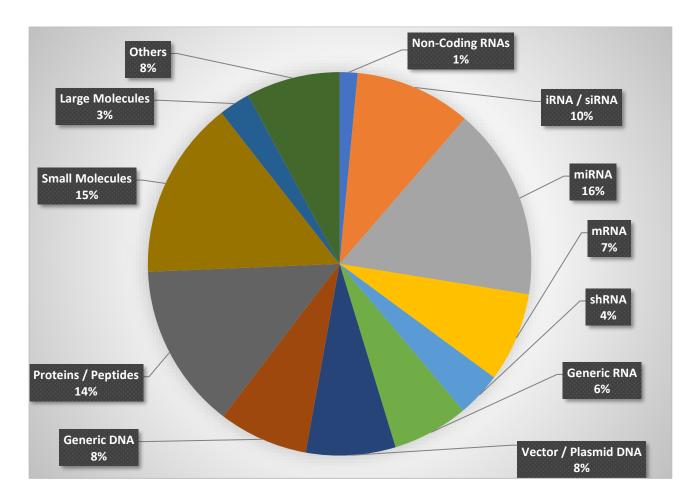




- ➤ Ultracentrifugation, including the differential, sequential, and density gradient centrifugations are the widely practiced conventional methods for extracting exosomes from various sources. However, the centrifugation methods are time consuming and tedious process, which opens the newer technologies like affinity capture. However, the said Technology is at a nascent stage of the development.
- ➤ Extraction kits, preferably Exoquick™, which is based on the compound polymerization precipitation are gaining popularity to extract exosomes from human samples. However, it can only be used for small volume samples and cannot be adopted for large scale separation.
- As evident from the patent data, microfluidic devices including lab-on-a-chip devices, nanoplasmon-enhanced scattering, membrane-mediated exosome separation are yet to gain popularity and have to cross many hindrances to be adopted to large-scale isolation systems.



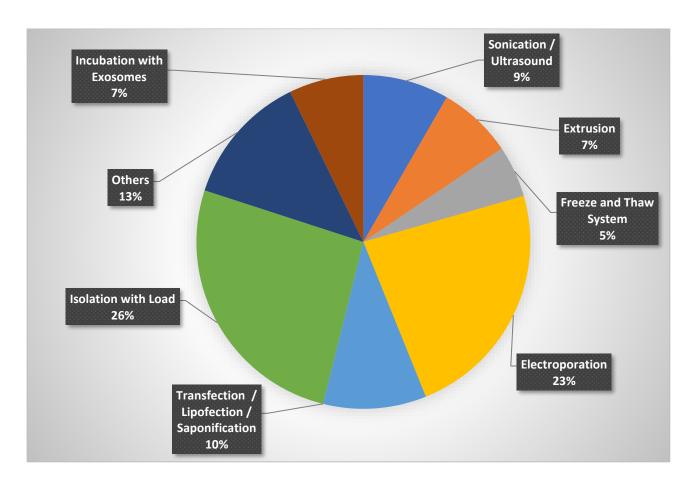
5.1.3. Dissection of Patents/Applications Pertaining To 'Type of Cargo'





- As expected, RNAs, especially miRNA and iRNA / siRNA are the preferred cargo types for exosome-based delivery, because they offer several advantages over differentiated cells, including the potential for autologous tissue and differentiation into multiple cell lines.
- > Small molecules, preferably cancer drugs have garnered attention for using exosomes as targeted delivery vehicles.
- ➤ Interestingly, exosomes that have the capacity to deliver RNAs, DNAs including plasmids/vectors are yet to gain popularity to deliver large molecules such as polysaccharides, polylactides, etc.

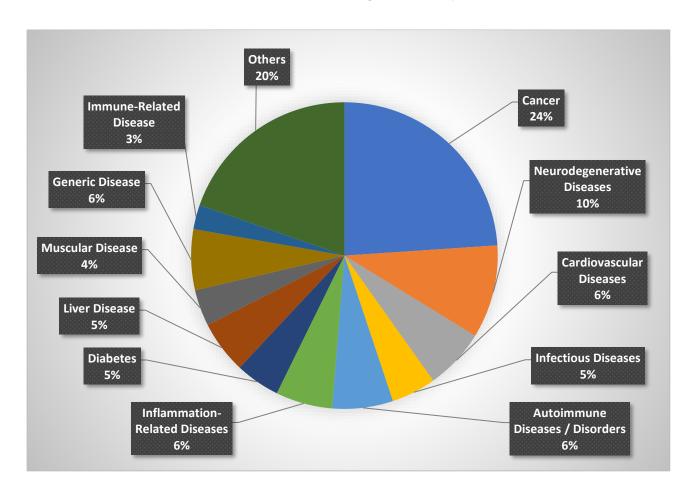
5.1.4. Dissection of Patents/Applications Pertaining To 'Cargo Loading Method'





- ➤ Electroporation proves to be the most sought-after method for loading small molecules as well as large molecules into the exosomes.
- For loading the nucleic acids and proteins, the methodology adopted is by loading the parental cells with the exogenous cargo, which is then released into exosomes. The said method offers the advantages of increased stability of the loaded cargo proteins, nucleic acids, due to the resemblance with that of the cellular environment.

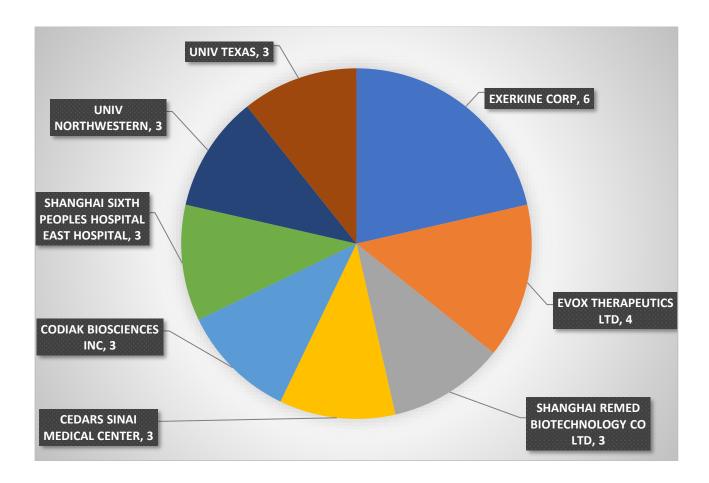
5.1.5. Dissection of Patents/Applications Pertaining To 'Therapy Area'

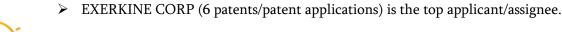




➤ Cancer is the main application therapy area by the targeted drug delivery using exosomes followed by neurological/neurodegenerative diseases, which is probably because of the anti-tumor immune response elicited by the tumor-derived immune cells.

5.2. Leading Assignee Analysis







- A sizeable number of applications are from the leading assignees originating from the APAC region, preferably from China and South Korea.
- ➤ Interesting to note that the EP region is yet to gain prominence compared to the USA and APAC region, in the investigative technology.
- ➤ EVOX THERAPEUTICS LTD (4 patents/patent applications) is the second most, leading innovator and it originates from the UK, which is significant since the EP region is lagging behind in the investigative technology.

5.3. Leading Assignee across Technology

	Type of Cargo Drug													
Leading Assignees				RI	NA				DI	NA.	Proteins			
Assignees	Non- coding RNAs	iRNA / siRNA	miRNA	mRNA	shRNA	Generic RNA	iRNA	Others	Vector / Plasmid DNA	Generic DNA	/ Peptides	Small Molecules	Large molecules	Others
EXERKINE CORP				4		3			1	4			1	
EVOX THERAPEUTICS LTD		1	2	2	2	1		2	1	1	3	1		3
SHANGHAI REMED BIOTECHNOLOGY CO LTD												3		
CEDARS SINAI MEDICAL CENTER			1	1		1						1		
CODIAK BIOSCIENCES INC		1	1		1	1				1	3	2	1	2
SHANGHAI SIXTH PEOPLES HOSPITAL EAST HOSPITAL												3		
UNIV NORTHWESTERN				1		1		1			1			
UNIV TEXAS		2	2	1	2				2	2		1		1

5.3.1. Dissection of Leading Assignees across 'Exosome - Sources'



- Leading assignees prefer the employment of exosomes isolated from stem cells, with maximum inventions recorded by EXERKINE CORP (5 patent/patent applications), followed by SHANGHAI REMED BIOTECHNOLOGY CO LTD (4 patent/patent applications) and SHANGHAI SIXTH PEOPLES HOSPITAL EAST HOSPITAL (4 patent/patent applications). Interestingly, the second leading assignee EVOX THERAPEUTICS LTD has not used specific cells for exosome isolation.
- ➤ EXERKINE CORP is the only company to investigate exosomes as delivery vehicles from most of the discussed sources including body fluids, with a maximum of 5 patents / patent applications relating to exosome isolation from Blood/Blood cells/ Serum/Plasma.



5.3.2. Dissection of Leading Assignees across 'Exosomes – Isolation / Preparation'

					Exosomes – Isolation / Preparation												
		Chromatography			Ultracentri	ugation (UC	F)							Others			
Leading Assignees	Size-Exclusion Chromatography	Generic Chromatography	Affinity Chromatography	Generic Centrifugation / UCF	Sequential UCF	Gradient UCF	Differential UCF	Others	Microfluidics- based Techniques	Capture on Beads	Precipitation	Filtration / Ultrafiltration	Kit-based Isolation				
EXERKINE CORP			3	4								3					
EVOX THERAPEUTICS LTD	3	1		1								3					
SHANGHAI REMED				3								3					
BIOTECHNOLOGY CO LTD				3								3					
CEDARS SINAI MEDICAL CENTER	1			1	1	1	1					2					
CODIAK BIOSCIENCES INC				1		1								1			
SHANGHAI SIXTH PEOPLES				3								3					
HOSPITAL EAST HOSPITAL				3								3					
UNIV NORTHWESTERN				1			1										
UNIV TEXAS				2	1	1						2					



- ➤ Conventional methods like chromatography-based techniques and filtration/ ultrafiltration techniques are the most preferred exosome isolation methodologies adopted by the leading assignees even though they are time consuming and costly, probably due to the scalability and proven methodologies.
- ➤ EXERKINE CORP (3 patent/patent applications) is the only company to adopt the recently developed technology, affinity based chromatographic separation of exosomes. However, none of the companies focused on the other contemporary technologies like microfluidics-based, immune capture bead-based, or magnetic beads-based technologies.

5.3.3. Dissection of Leading Assignees across 'Type of Cargo'

							Туре о	f Cargo Dr	ug						
				RI	NA				DI	NA					
Leading Assignees	Non- coding RNAs	iRNA / siRNA	miRNA	mRNA	shRNA	Generic RNA	iRNA	Others	Vector / Plasmid DNA	Generic	Proteins / Peptides	Small Molecules	Large molecules	Others	
EXERKINE CORP				4		3			1	4			1		
EVOX THERAPEUTICS LTD		1	2	2	2	1		2	1	1	3	1		3	
SHANGHAI REMED												3			
BIOTECHNOLOGY CO LTD												3			
CEDARS SINAI MEDICAL CENTER			1	1		1						1			
CODIAK BIOSCIENCES INC		1	1		1	1				1	3	2	1	2	
SHANGHAI SIXTH PEOPLES												3			
HOSPITAL EAST HOSPITAL												3			
UNIV NORTHWESTERN				1		1		1			1				
UNIV TEXAS		2	2	1	2				2	2		1		1	



- ➤ Leading assignees concentrated their research more on the delivery of RNAs, especially miRNA and iRNA/siRNA using exosome as delivery vehicles, with EXERKINE CORP (4 patent/patent applications) registering more inventions related to the delivery of mRNA and DNA than rest of the leading assignees.
- ➤ EVOX THERAPEUTICS LTD and CODIAK BIOSCIENCES INC have significant inventions related to the transport of proteins/peptides using exosomes (3 patent/patent applications each, respectively), while SHANGHAI REMED BIOTECHNOLOGY CO LTD and SHANGHAI SIXTH PEOPLES HOSPITAL EAST HOSPITAL (3 patent/patent applications each, respectively) have noteworthy inventions related to small molecules.

5.3.4. Dissection of Leading Assignees across 'Cargo Loading Method'

				Ca	argo Loading Me	thod			
Leading Assignees	Electrop oration	Sonication / Ultrasound	Extrusion	Freeze and Thaw System	Transfection / Lipofection / Saponification	Isolation with Load	Antibody against Exosomal Proteins	Incubation with Exosomes	Others
EXERKINE CORP	4				5				
EVOX THERAPEUTICS LTD						2			2
SHANGHAI REMED	3	3	3	3				3	
BIOTECHNOLOGY CO LTD	5	3	3	3				3	
CEDARS SINAI MEDICAL CENTER						2			
CODIAK BIOSCIENCES INC	1	1			1	2			1
SHANGHAI SIXTH PEOPLES	3	2	2	2				2	
HOSPITAL EAST HOSPITAL	3	Z	Z	Z				Z	
UNIV NORTHWESTERN						2			1
UNIV TEXAS	3				1				



- ➤ Electroporation proves to be the most sought-after method by the leading assignees for loading small molecules as well as the large molecules, with significantly higher inventions by EXERKINE CORP (4 patent/patent applications). Also, the company EXERKINE CORP registers maximum number of inventions (5 patent/patent applications) related to transfection/lipofection/saponification mode of loading cargo drugs.
- ➤ The leading assignees have registered significant inventions related to the loading of nucleic acids, through loading of the parental cells with the exogenous cargo, which is then released into exosomes.

5.3.5. Dissection of Leading Assignees across 'Therapy Area'

						Therapy area						
Leading Assignees	Cancer	Neurodege nerative Diseases	Cardiovascular Diseases	Infectious Diseases	Autoimmune Diseases / Disorders	Inflammation- related Diseases	Diabetes	Liver Disease	Muscular Disease	Generic Disease	Immune- related Disease	Others
EXERKINE CORP		2	1					2	2			3
EVOX THERAPEUTICS LTD	4	2	1	1	4	2	2	2	2	1		3
SHANGHAI REMED						1						3
BIOTECHNOLOGY CO LTD						1						3
CEDARS SINAI MEDICAL CENTER	1	1	2	1	1		1	1	2			1
CODIAK BIOSCIENCES INC		1								2		
SHANGHAI SIXTH PEOPLES		1				1					1	2
HOSPITAL EAST HOSPITAL		1				1					1	2
UNIV NORTHWESTERN	1									1		
UNIV TEXAS	3	1	1	1	1	1					·	1



As registered in the overall technology analysis, leading assignees too have concentrated more on cancer therapy by targeted drug delivery using exosomes followed by neurological/neurodegenerative diseases.

6. Non-Technical Analysis

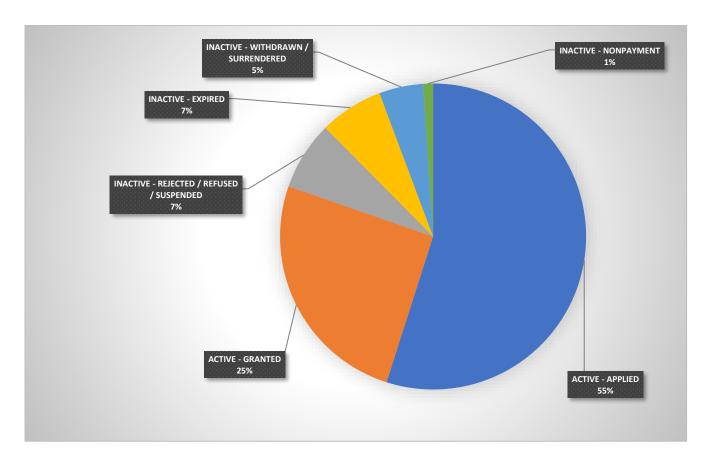
6.1. Trend Analysis – Earliest Invention in Exosomes for Drug Delivery vs Geographies

Earliest Priority	Earliest Priority Year													
Country	2003	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020
CA												1		
CN				2	1				1	4	3	19	19	3
EP												3		
FI												1		
FR			1											
GB			1		1					1	1	1		
JP			1	1		1						1		
KR									2	3	3	3	1	
SE							1							
TR											1	1		
TW										1				
US	1	1		2	2	1	2	4	10	10	13	14		



- ➤ Overall priority filing data infer that the exosomes for drug delivery technology had garnered much attention only recently in 2015 even though there were scattered research relating to the same as early as 2003.
- ➤ The investigative technology gained considerable popularity after 2015, with the maximum filings being recorded during the year 2018 (31% of the filings).
- ➤ The USA used to be a frontrunner in the investigative technology. However, in the current scenario, the APAC countries like China and Korea have been regularly innovating in the investigative technology.
- ➤ China and Korea are the only geographies to register inventions during the year 2019.
- ➤ In furtherance, China has registered the maximum inventions (13% of the filings) during the year 2019 and is the highest registered by any geography.

6.2. Trend Analysis – Legal Status Analysis

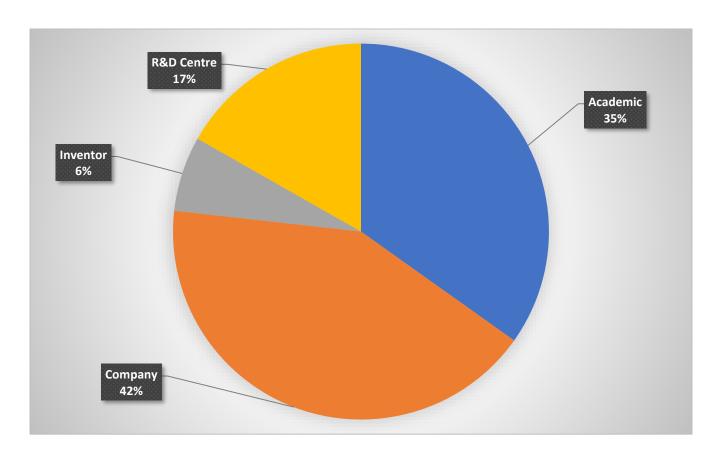




- ➤ 80% of active applications indicate the advancement in the investigative technology and the possibilities of path-breaking inventions in the days to come.
- ➤ It is also to be noted that the inactive patents (11%, that includes rejected/refused/suspended and withdrawn/surrendered patents) are way less than that of the active patents/ applications (80%), signifying the major researches are under-way in the investigative technology.

6.3. Assignee Based Trend Analysis

6.3.1. Assignee Category





52% of the patents/patent applications are filed by academics and research institutions, while 6% of the patents/patent applications are from the individual inventors. The contribution of these organizations/inventors in the investigative technology is substantial and is actively competing with the companies involved in this research.

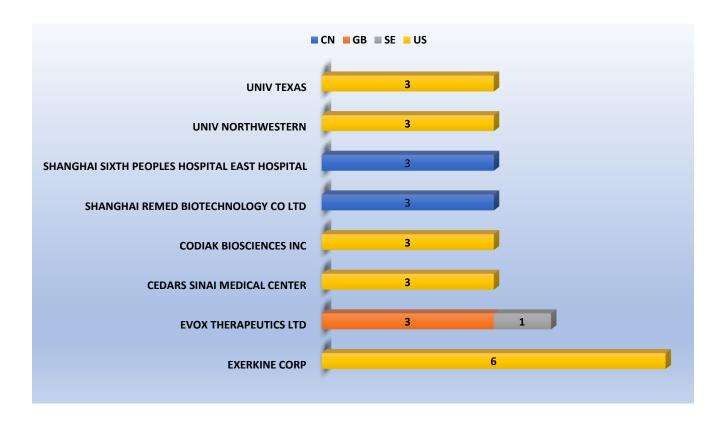
6.3.2. Leading Assignees across Earliest Priority Years





➤ The priority filing trend of the leading assignees indicates a gradual growth of the technology from 2014. The trend reflects the peak during 2018. It is evident that the USA has started generating increased revenue of USD 91 Million during 2019 and grows at approximately 24% CAGR annually, which is in line with the increased focus on the investigative technology from the year 2018.

6.3.3. Leading Assignees across Earliest Priority Countries

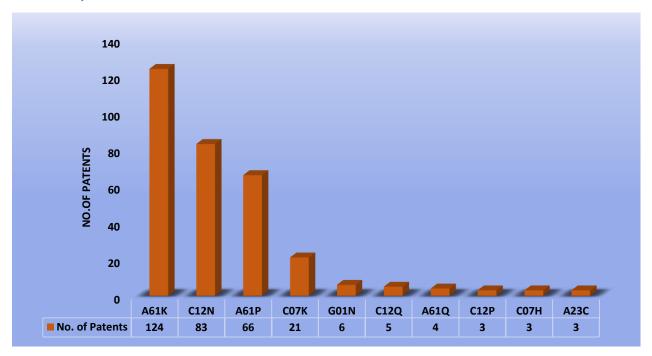




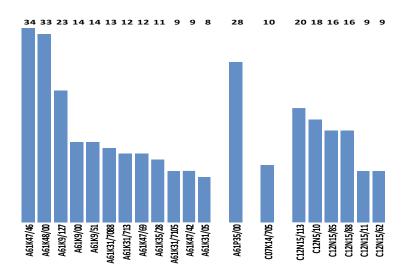
Of all the leading assignees, EXERKINE CORP is the only company which opted to file their patent applications in geographies other than their actual country of incorporation. EXERKINE CORP which has it headquarter in Canada, had filed all of its patent applications in the USA.

6.4. Patent Classification Based Trend

6.4.1. Major IPCs – Main Class



6.4.2. Major IPCs – Sub Class



The IPC sub-class definitions are provided in Appendix



6.4.3. Leading Assignees across IPC – Main Classifications

Loading Assignment	Main - IPCs							
Leading Assignees	A61K	A61P	С07К	C12N				
CEDARS SINAI MEDICAL CENTER	3							
CODIAK BIOSCIENCES INC	3							
EVOX THERAPEUTICS LTD	1		2	1				
EXERKINE CORP	1	4	1					
SHANGHAI REMED BIOTECHNOLOGY CO LTD	3							
SHANGHAI SIXTH PEOPLES HOSPITAL EAST HOSPITAL	3							
UNIV NORTHWESTERN	2		1					
UNIV TEXAS	3							

6.4.4. Leading Assignees across IPC – Sub Classifications

								PC -	Sub	Class	ifica	tions	5						
Leading Assignees	A61P3/00	C07K14/705	A61K35/545	A61K9/51	A61K9/127	A61K9/5176	A61P25/02	00/6TXL00	C12N15/88	A61K31/05	A61K35/34	A61K47/42	A61K9/10	A61K38/02	A61K38/17	A61K9/107	A61K48/00	A61K9/50	A61K9/00
CEDARS SINAI MEDICAL CENTER				1							1	1							
CODIAK BIOSCIENCES INC					1								1	1					
EVOX THERAPEUTICS LTD		1			1			1	1										
EXERKINE CORP	3	1				1	1												
SHANGHAI REMED BIOTECHNOLOGY CO LTD			2							1									
SHANGHAI SIXTH PEOPLES HOSPITAL EAST HOSPITAL			1	2						·	·							·	
UNIV NORTHWESTERN		1													1	1			
UNIV TEXAS			·										·				1	1	1

Key Patents/Patent Applications

Patent/Publication No.	Summary of Invention
CN110448696A UNIV HENAN SCIENCE & TECH	The invention relates to a plant-based exosomal vesicle (i.e. Algae <i>Dunaliella salina</i>) used in the targeted delivery of gene constructs or drugs. The said delivery system is found to have effective delivery rates and are easily accepted by the human body.
<u>CN111035769A</u> RAO LEI	The invention provides an exosome nano drug loading system modified by superparamagnetic nano-iron comprising comprises an exosome for loading an insulin secretion-promoting drug and superparamagnetic nano-iron. The said carrier system can be targeted to the target cells via an external magnetic field.
CN108753806A FOURTH MILITARY MEDICAL UNIV PLA	The invention discloses an expression vector of a fusion protein for enhancing target RNA loading into an exosome, wherein the said protein comprises target RNA binding protein sequence and an exosome membrane targeting protein sequence. The exosome membrane targeting protein sequence can be localized in the exosome, which increases the loading of target RNA sequence.
CN109432427A SHANGHAI NAT ENGINEERING RES CENTER NANOTECHNOLOGY	The invention provides a preparation method of a tumor targeting heat therapy material taking exosome as a carrier, wherein the heat therapy material is a synthesized gold nano-rod, which has a photo-thermal curative effect and has a targeting ability to lung cancer to accelerate the death of lung tumor cells.
WO2016187717A1 EXERKINE CORP	The present invention relates to exosomes, and more particularly, to the use of exosomes for genome editing. The said exosomes are genetically modified to incorporate or express a nuclease genome editing system.
<u>WO2011062244A1</u> NA	The present invention discloses a highly stable membrane vesicle, preferably exosomes for targeted delivery of siRNA or miRNA, wherein the loading of the said nucleic acid into the exosomes happens by the introduction of drugs into the exosome-producing cells, which in turn excretes the exosome-loaded drugs.
<u>US10538570B2</u> UNIV NORTHWESTERN	The present invention relates to a packaging protein and a cargo RNA in which the packaging protein, wherein the said packaging protein is a fusion protein that includes an RNA-binding domain and an exosome-targeting domain. The said fusion protein binds specifically such that the cargo RNA is packaged in the lumen of the exosomes.
CN110079555A HUNAN YEARTH BIOTECHNOLOGY CO LTD	The invention relates to a method for transfecting stem cells by utilizing exosome, wherein the said method comprises delivery of genetic matter to the exosome via gene engineering technology and is delivered to the interiors of the stem cells.



Appendix A - References & Credits

- 1. https://www.pharmiweb.com/press-release/2020-10-12/exosome-therapeutic-marketglobal-industry-research-by-share-growth-trends-size-revenue-top-lea
- 2. https://www.transparencymarketresearch.com/exosome-technologies-market.html
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Appendix B – Definitions Of IPC Classes

Definition
HUMAN NECESSITIES; MEDICAL OR VETERINARY SCIENCE; HYGIENE; PREPARATIONS FOR MEDICAL, DENTAL, OR TOILET PURPOSES
Phenols;
Compounds having three or more nucleosides or nucleotides ;
Natural ribonucleic acids, i.e. containing only riboses attached to adenine, guanine, cytosine or uracil and having 3'-5' phosphodiester links;
Double-stranded nucleic acids or oligonucleotides ;
Bone marrow; Haematopoietic stem cells; Mesenchymal stem cells of any origin, e.g. adipose-derived stem cells;
Proteins ; Polypeptides ; Degradation products thereof ; Derivatives thereof, e.g. albumin, gelatin or zein ;
Ingredients of undetermined constitution or reaction products thereof, e.g. skin, bone, milk, cotton fibre, eggshell, oxgall or plant extracts;
the conjugate being characterised by physical or galenical forms, e.g. emulsion, particle, inclusion complex, stent or kit;
Medicinal preparations containing genetic material which is inserted into cells of the living body to treat genetic diseases; Gene therapy;
Medicinal preparations characterised by special physical form ;
Liposomes ;
Nanocapsules ;
Phenols;
HUMAN NECESSITIES; MEDICAL OR VETERINARY SCIENCE; HYGIENE; SPECIFIC THERAPEUTIC ACTIVITY OF CHEMICAL COMPOUNDS OR MEDICINAL PREPARATIONS
Antineoplastic agents ;



С07К	CHEMISTRY; METALLURGY; ORGANIC CHEMISTRY; PEPTIDES
C07K14/705	Receptors ; Cell surface antigens ; Cell surface determinants ;
B29C	CHEMISTRY; METALLURGY; BIOCHEMISTRY; BEER; SPIRITS; WINE; VINEGAR; MICROBIOLOGY; ENZYMOLOGY; MUTATION OR GENETIC ENGINEERING; MICROORGANISMS OR ENZYMES; COMPOSITIONS THEREOF; PROPAGATING, PRESERVING, OR MAINTAINING MICROORGANISMS; MUTATION OR GENETIC ENGINEERING; CULTURE MEDIA
C12N15/11	DNA or RNA fragments ; Modified forms thereof ;
C12N15/113	Non-coding nucleic acids modulating the expression of genes, e.g. antisense oligonucleotides;
C12N15/62	DNA sequences coding for fusion proteins ;
C12N15/85	for animal cells ;
C12N15/88	using microencapsulation, e.g. using liposome vesicle;
C12N5/10	Cells modified by introduction of foreign genetic material, e.g. virus-transformed cells ;

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