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Patenting trends in diagnostic and treatment strategies of autism spectrum disorders

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ABSTRACT

Autism is a spectrum of developmental disorders characterized by impairments in social interaction, communication, often accompanied by stereotypical behaviors. The high prevalence of this disorder has raised the need to understand the underlying molecular mechanisms that would help in both diagnosis and treatment of the disorder. This review talks about a variety of diagnostic and treatment strategies and therapeutic targets of patent documents from various companies, universities, hospitals, research and developing organizations. We have identified and reported the leading assignees and their patenting activities over the time period, trends, geographical distributions, international patent classification analysis and the like.

Contents

1. Introduction

Neurodegenerative disorders without proper diagnostic markers have become a menace to clinical world. Autism spectrum

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of lifelong disabling neurological disorders collectively referred to as autism spectrum disorders is characterized by deficits in social interaction, verbal and nonverbal communication. Autism spectrum disorders are often accompanied with repetitive and stereotyped patterns of behavior [1–3]. Availability of rich means of data in the last decades indicate the higher prevalence and universality of the disorder than previously thought [4]. However the diagnostic and treatment methods for autism spectrum disorders (ASD) are still at elementary level and are based on behavioral history and assessments [5]. There are no detailed community–linked studies on prevalence of ASD in India. The rise in the prevalence [6–9] has intensified the need for exploring the latest technologies with focus on diagnostic markers and treatment strategies, for a comprehensive overview of the disorder. Patent documents contain important research outcomes with rich technical terminology that demands a lot of human efforts for analyses. But thanks to the enduring text mining approaches facilitating the screening of relevant patents. Integrating science and innovation strategy to meet the increasing prevalence rate engages greater reliance on landscape studies to track trends and support the coordination of activities. More than ever before, industry, policy makers, researchers, governments and academia rely on 'landscapes' to map scientific and technological trends so as to provide information on the association between multiple sets of indicators measured against temporal, technical or spatial dimensions [10]. Designing analytical strategies based on interest of various audiences and addressing issues specifically increases scope of in-depth analysis of a narrow range of patents for researchers, to entire technological fields for industries that can enable a high level of understanding for strategic planning especially across jurisdictions [11]. The present landscaping studies were commenced to gather the patent information on autism with an aim to understand various diagnostic and treatment approaches, so as to identify the technology for future research [12]. The current work endeavors to provide unique glimpse at technology trends and shifting paradigms in autistic research.

2. Methodology

The present study is based on patent filings from 1989 to 2014. The methodology followed in the present study is illustrated in Fig. 1.

2.1. Data mining

Class codes and keywords were obtained from relevant patents, databases & thesauri. Key concepts as well as synonyms for autism, and the associated spectrum disorders were identified after careful observation. In addition to experimental searches with various free databases (Espacenet, USPTO. Patentscope), Thomson Innovation database was selected for patent retrieval for its worldwide content coverage and outstanding patent family registration. A broad search was carried out using the suitable keywords and class-codes so as to assemble patents into technological categories. For ease of retrieval and tracking, patent filings are usually categorized under suitable classification codes based on type of invention. IPC codes A61P25/00 which covers drugs for disorders of nervous system, C12Q0001/68 covering a variety of compositions and measuring processes involving enzymes or microbes specifically nucleic acids. Likewise A61P 25/18 is related to antipsychotics, i.e. neuroleptics; drugs for mania and patents for treating neurodegenerative disorders of the central nervous system, e.g. nootropic agents, cognition enhancers fall under A61P 25/28 and such others were considered for search (Table 1).

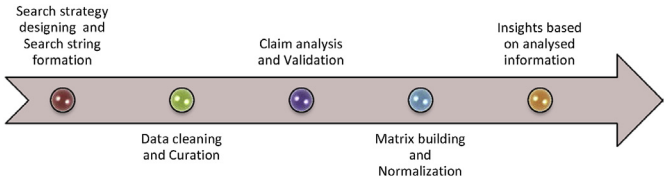

Fig. 1. Iterative process of patent searching.

2.2. Generation of search strings

Patents related to diagnostic and treatment strategies of ASD were extensively searched in Thompson innovation. Search terms considered for this study included *Autism*, *Autism spectrum disorder*, *Diagnostic markers* and the terms related to molecular genetic diagnosis included *single nucleotide polymorphisms*, *mutations*, *genomic aberrations, comparative genome hybridisation*, *copy number variations, cytogenetic abnormalities.* The terms related to the biomarkers included *hormones, peptides, metabolites, immunological markers, toxicologic markers, gastrointestinal markers, neurologic markers.* Treatment methods included *drugs, compositions, formulations, natural extracts, dietary supplements, vitamins, alternate treatment, ayurvedic formulation, homeopathic preparations, and traditional treatment*.

Appropriate truncations were used to cover all forms of search terms. Many of these keywords were retrieved using the search field of “Title, Abstract and Claims”; Whereas, searches under the field of “Description” or “Specification” were excluded. It was useful to limit each search using the specific terms under the search field of “Claims”. Other limits on searches were organized by assignees, or other definitional fields that provide an extensive coverage for almost all the patents that were filed. A careful and systematic search has given an outcome of more than 2950 patents till June 10, 2014. The total obtained patents were run through a family filter to remove the duplicates which resulted in 900 patents.

2.3. Data cleaning and curation

The next step after the collection of patent documents is the removal of major off-topic areas. Cleaning involves reassessing the documents in the data and leaving any that are not falling in the intended scope of the analysis. In order to maintain the accuracy and integrity of the data, filters were used at all the stages of data analysis to categorize the relevant and irrelevant data patents possessing the words ‘autism’ or ‘autism spectrum disorders’ in its title dealing with diagnostic and treatment strategies of said disorders were considered primarily. Patents having usage of ASDs in the abstract or the claims without autism in their title were considered at the next level. Furthermore, the patents related to central nervous system disorders other than autism and patents related to more than 10 central nervous system disorders claiming along with autism were removed and the final relevant patents comprising 444 records related to diagnostic and treatment methods of ASD. Data curation was carried out by arranging data sets in to consistently formatted and structured pattern manually for periodic future updates.

2.4. Claim analysis & expert validation

After cross-deduplication, patents often need further review for determination of their specificity on the area of interest. Claims of individual patents were thus closely scrutinized manually and validated. The collection contained inventions that are very specific to ASD and covered diagnosis, treatment

Table 1
IPC.

IPC Code	Count	Description
A61P 25/00	30%	Drugs for disorders of the nervous system
C12Q 1/68	21%	Involving nucleic acids
A61P 25/18	11%	Antipsychotics, i.e. neuroleptics; Drugs for mania or schizophrenia
A61P 25/28	7%	For treating neurodegenerative disorders of the central nervous system, e.g. nootropic agents, cognition enhancers, drugs for treating Alzheimer's disease or other forms of dementia
A61P 25/24	6%	For treating neurodegenerative disorders of the central nervous system, e.g. nootropic agents, cognition enhancers, drugs for treating Alzheimer's disease or other forms of dementia
A61K 31/519	5%	Ortho- or peri-condensed with heterocyclic rings
G01N 33/53	5%	Immunoassay; Biospecific binding assay; Materials therefor
G01N 33/68	5%	Involving proteins, peptides or amino acids
A61K 31/00	5%	Medicinal preparations containing organic active ingredients
A61K 31/496	5%	Non-condensed piperazines containing further heterocyclic rings, e.g. rifampin, thiothixene

method, composition, drug discovery or screening, product, process and special conditions if any like mode of administration, sample used for diagnosis, disease claimed for diagnosis or treatment, novel drugs if any based on patent type etc. to assess present status and trends in technology development, to classify and map the technology to relevant application areas for strategic planning and to develop a commercially successful patent management strategy. Expert validation reduces the percentage of irrelevant patents and ensures that important branches or key technologies within a field are not omitted.

2.5. Matrix building and normalisation

For the analysis of the data pertaining to bibliographic information comprising of patent number, title, inventor name, assignee name, priority country, priority date, publication date and IPC, the matrix representing the overall information was generated. The technical taxonomy comprised claims and normalisation was carried out based on standard procedures.

3. Results and discussion

Bibliometric analysis & autism research insights from past 25 years.

3.1. Patent trend line

The application date in patent documents reveals timing of invention, process and strategy pursued by the applicant. In the present study, two indicators, namely priority year and publication year, were used to determine trends in inventive activities over a span of years (Fig. 2). Unlike publication year that reflects the time the patent information is released to the public from statutory offices, priority date/year is much preferred as it indicates first date of filing of patent application anywhere in the world and is considered closest to the invention date. Our analyses have revealed that the patenting activity which is generally evaluated through priority year and publication year has slower growth in first decade (1989–1998) with a steep increase in 1999–2008. A huge surge in the new patent applications for autism is noticed in 2008. Moreover, consistent additions in

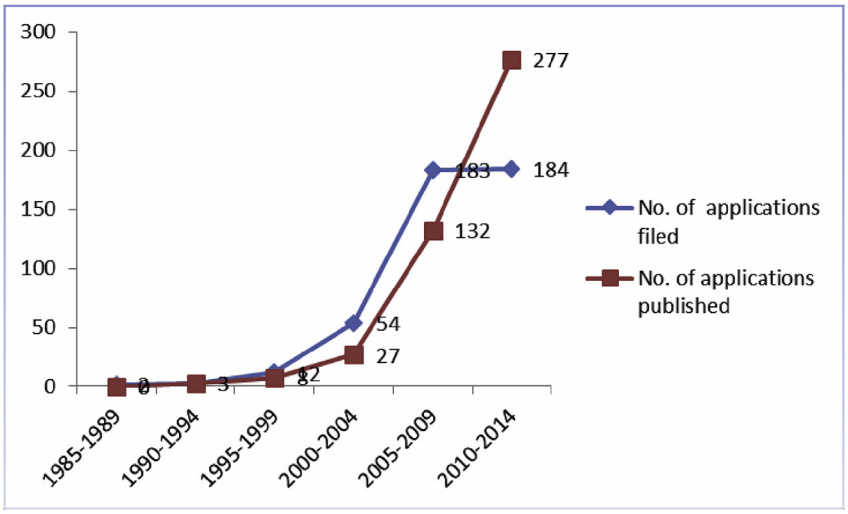

Fig. 2. Presentation of the patent application trends.

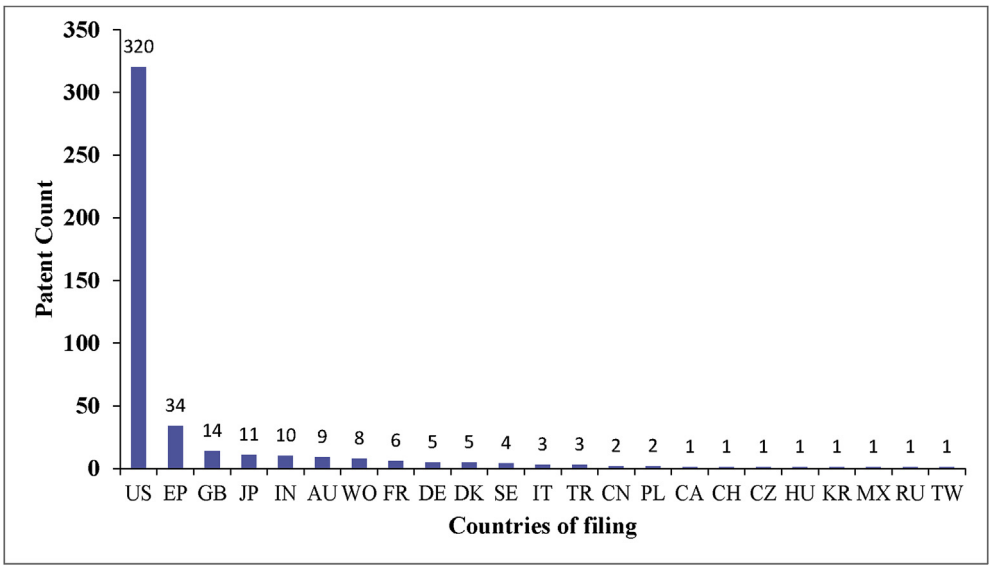

Fig. 3. Geographical distribution of priority countries and the proportion of patents filed.

patent families implicates that more inventions filed for autism since 2009 and continued till date. The similar vogue was observed in publication year, though not coinciding with priority year. This variation is due to difference in timelines at national patent offices during examinations. Also, a spike in a patent publication trend line was observed for the publication of family members of these new inventions in the corresponding years. The increase in prevalence rate have alarmed the innovative world as suggested by the patent trend line which showed a sharp increase in last five years more notably than ever before. There is a gradual increase in the trend until 2008, followed by steep rise until 2013. Fig. 2 explains the patent publication trends, where there is a gradual increase in the trend until 2003, followed by steep rise until 2014.

3.2. Geographical distribution of priority country

Since patent based statistics serve as indicators for inventive activity, geographical distribution of patents across the world is seen to asses which country is the master player in patenting innovative methods related to autism and the market trends in different countries. Determining the priority country (country of first filing) is the easiest way to get an idea of where inventions were made, and typically corresponds to a company location. Global companies may file in multiple countries if they have R&D facilities in each place. Most of the inventions in this collection were filed first in the US, with almost 72% of the patents filed suggesting that majority of companies filing patents are either US based or the major market for the therapies is US. While EPO has second place with 8% of total filed patents observations, the

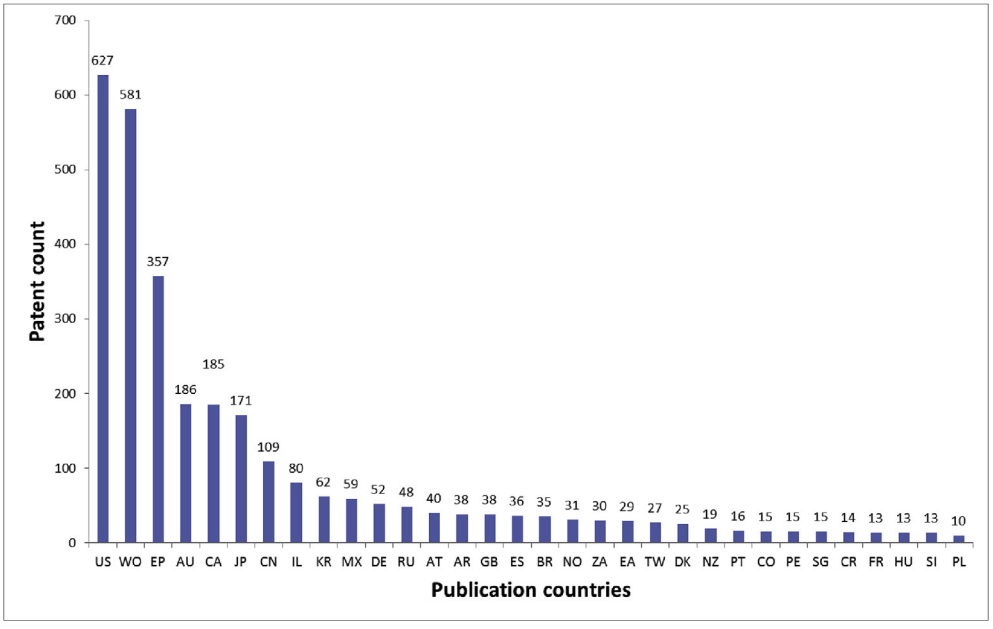

Fig. 4. Histogram representing the geographical distribution of Family members and the proportion of patents filed.

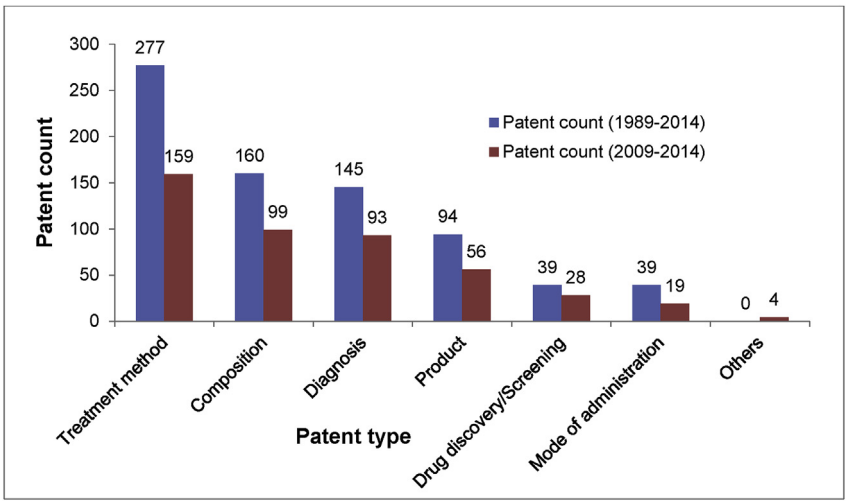

Fig. 5. Comparative patent publication trends.

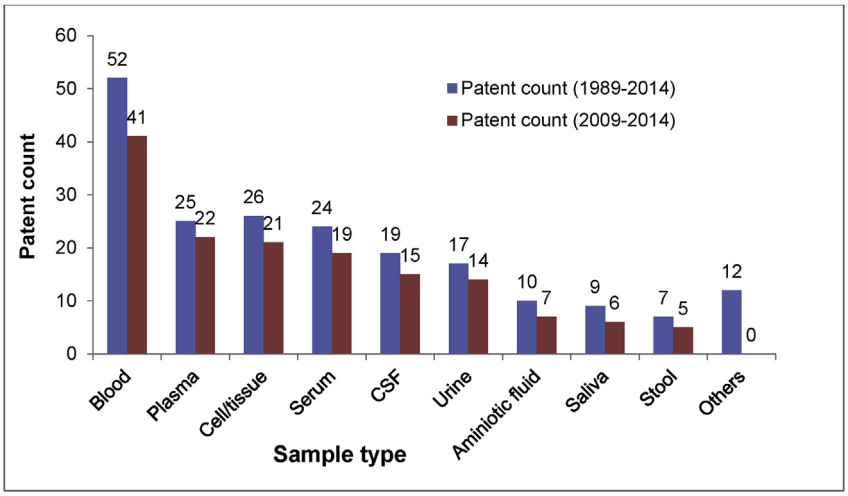

Fig. 6. Comparison of different sample types used for diagnosing autism.

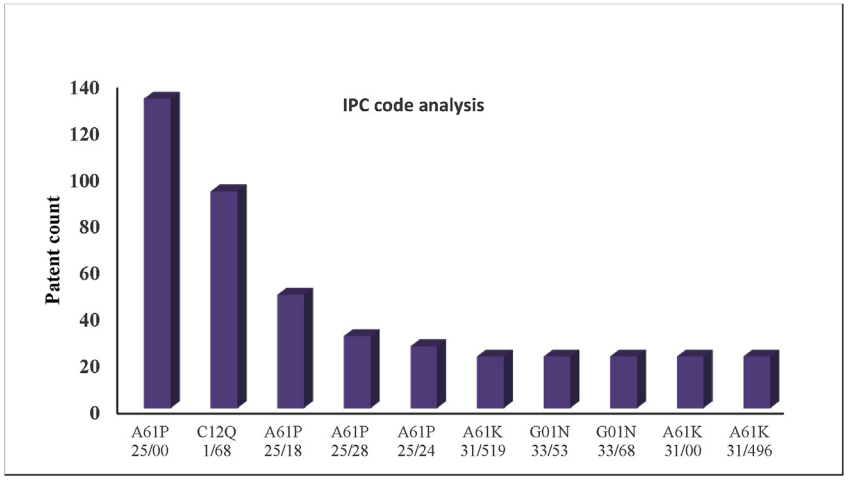

Fig. 7. Histogram showing IPC code analysis.

Table 2
Pharmaceutical companies working on autism.

Company	No. of Patents	Compounds	Research Focus
Pfizer	11 (2.53%)	Heteroaromatic compounds, pyridyloxymethyl, benzisoxazole azabicyclic derivatives	Serotonin and dopamine receptors as targets for treatment
Afraxis	6 (1.38%)	8(Heteroarylmethyl)Pyrido[2,3-D]Pyrimidin-7(8h)-Ones, 8-(Sulfonylbenzyl)pyrido [2,3-d]pyrimidin-7(8H)-ones	p21 -activated kinase (PAk) inhibitors
Solvay Pharmaceuticals B.V	6 (1.38%)	Aryloxyethylamine derivatives, N-Oxides of pyridylmethylpiperazine and -piperidine derivatives, Benzdioxane piperazine derivatives	Treatment by serotonin reuptake inhibition and affinity for dopamine-D2 receptors with novel pharmaceutical preparations
Forest Laboratories Holdings	4 (0.92%)	Memantine formulations and dextromethorphan derivatives	Treatment using memantine and its formulations
Edison Pharmaceuticals	4 (0.92%)	2-substituted-p-quinone derivatives, tocotrienols or tocotrienol enriched extracts, Catechol derivatives	Treatment of oxidative stress in ASD
Neuro Search A/S	4 (0.92%)	Diazabicyclo derivatives, piperidine-4-carboxylic acid phenyl-alkyl-amide derivatives	Treatment targeting Monoamine oxidase (MAO) Inhibitors
Janssen Pharmaceuticals	3 (0.69)	Risperidone pamoate, carbamate compounds.	Treatment with Risperidone
Others	53 (12.23%)	D1/D5 antagonists tazarotene tamoxifen	Neurotransmitters increased eye contact restoration of steroid hormone signaling

contribution made by UK-based companies was relatively less (3%). Fig. 3 depicts the geographical distribution of priority countries and the proportion of patents filed.

3.3. Geographical distribution of family members

Looking at patent applications in another way, it is easy to see that the companies file for protection not only locally (priority country), but also in other regions where they expect to require protection for their product, or for manufacturing of their product. In order to identify the percentage of patents filed at different countries portraying relevant information through one or several common aspects, geographical distribution of patent family members were analyzed. This analysis has revealed a total of 2989 applications stating that the United States clearly dominates, patenting activity in diagnosis and treatment strategies pertaining to ASDs. Majority of the patents are first filed in US. Apart from the first filings in US patents have then been filed in EP, Australia, Canada, Japan and China (Figs. 3 and 4).

3.4. Comparative patent publication trends & autism research insights from past 5 years

To investigate whether and to which end does the autism research is focused all the patents were categorized by the patent type (treatment based, diagnostic based, sample based) more research focus was towards developing a novel treatment method to cure the disorder. A total of 277 were collected, out of which 159 were published in last five years. In accordance with patents related to mode of administration out of 39 patents in 25 years, 19 were

Table 3
Bio-pharma companies working on autism.

Company	No. of Patents	Compounds/Genes	Diagnosis & treatment targets
Roche Holding AG	19 (4.22%)	MGlu2/3 Antagonists, Imidazole derivatives, Ethynyl derivatives, Benzimidazoles	Compounds and compositions targeting mGlu2/3, mGluR-5 receptor activity
IntegraGen	12 (2.66%)	SLC6A7, PITX1, PRKCB 1, OTOA, ATP2B2, EN2, CDH9, MARKL, ITGB3, CNTNAP2, AND HOXAL, JARID2, HTR5A and many more	Genotyping Test ARISk® having over 1700 genetic markers for assessing risk of autism
Lexicon Pharmaceuticals	5 (1.11%)	Amine-linked multicyclic compounds, (3'-chlorobiphenyl-4-yl)(1-(pyrimidin-2-yl) piperidin-4-yl)methanone, (S)-Phenyl(heterocycle)methanol-based compounds	Proline transporter inhibitors
Intra-cellular therapies	4 (0.88%)	Novel 2-(optionally hetero) arylmethyl-3- (optionally hetero) arylamino-[2H]-pyrazolo [3, 4-d] pyrimidine-4,6 (5H, 7H)-dione compounds.	Phosphodiesterase 1 inhibitors, CNSProfile™
Auspex Pharmaceuticals	4 (0.88%)	Arylpiperazine, Benzisoxazole	Carboxylic acid inhibitors of histone deacetylase, gaba transaminase and serotonin dopamine receptors as targets for treatment.
Repligen Corp	4 (0.88%)	Secretin, Methylxanthines, Uridine, CTLA4 compositions	Biological drugs
Curemark Lic	3 (0.66%)	Lactulose,, digestive enzymes and their delivery systems for autism treatment	Pancreatic enzymes compositions and their delivery systems for autism treatment using lipid technology.
Eli lilly & company	3(0.66%)	Olanzapine, atomoxetine hydrochloride.	Treatment using nor epinephrine reuptake inhibitor.
SynapDx Corporation	3 (0.66%)	Gene expression profiling for marker identification, C20orfl73, TRPM5, TPM2, CCNE2, CKAP2L, CAND2, MTR R2L3, LDLRAP1, ASPM, ZDHHC15, RASL10B and many more	Blood-based test development for detection of ASD
Others	57 (12.66%)	Markers: levels of neurotensin, interleukin-6, IL-33, PAF, tryptase, VEGF in serum Treatment: flavonoids, olive kernel extract complement factor I decreased tryptophan metabolism baclofen	Serum markers & treatment GABA(B) agonist

Table 4
Universities & research institutes working on autism.

Name	No. of Patents	Compounds/Genes	Diagnosis/Treatment Focus
Massachusetts Institute of Technology	11 (2.51%)	Compound is a Group III mGluR agonist, endocannabinoid antagonist	Treatment focused on cell signalling
		IGFl, IFN [gamma], statin	Parvalbumin activity inhibition.
		Composition comprising BMS-387032, SNS-032, CHI4- 258, TKI-258, EKB-569, JNJ-7706621, PKC-412, staurosporine, SU-14813, sunitinib, VX-680, or MK-0457	PAK inhibitors
		Mutations in serotonin transporter (Slc6A4), Pten genes	Treatment of ASD characterized by increased head size (circumference) and deficits in social behavior
		CI-994	HDAC inhibitor treatment
University of California (complementary and alternative medical (CAM) therapies with dietary supplements for treatment)	10 (2.28%)	Cysteamine	Antioxidant treatment
		Decreased apolipoprotein B, increased transferrin, increased TNF-alpha converting enzyme, decreased dedicator of cytokinesis protein 1 (DOCK 180) and increased complement factor H-related protein (FHRl).	Polypeptide markers
		Increased numbers of B cells and increased numbers of natural killer (NK) cells	Immune cell markers
		Hormone, vitamin, neurotransmitter, phospholipid.	Metabolite markers
Vanderbilt University	9 (2.05%)	SLC6A4 gene, serotonin transporter (SERT) protein, IB-MECA, CF101, AB-MECA or N6-2-(4-Aminophenyl) ethyladenosine, heteroarylamine carboxamide analogs, Bicyclic oxazole lactams	Diagnosis of allelic variations in SERT and Modulation of Neurotransmitters.
John Hopkins University	8 (1.83%)	Chromosome 11q12-13, JARID2 gene, Cholesterol, AT-1 inhibitor, β- chimaerin modulators.	Identifying therapies, genetic markers neuroimmune factors, pathways and modulators linked to autism
George Washington University	5 (1.14%)	ASS, ALOX5AP (FLAP), DAPK1, and IL6ST, RORA, BCL-2 genes.	Gene expression profiling, DNA methylation, microRNA profiling with DNA microarray technology.
Columbia University	5 (1.14%)	VIPR2 gene copy number variations, 7_q36 region of human chromosome 7, carbohydrate transporter GC globulin biomarker molecules: GLUT2 or SGLT1	Gene expression, GC globulin biomarker
Emory University	4 (0.91%)	FMR1 gene, detecting phosphatidylinositol 3-phosphate	Fragile X mental retardation protein 1 modulator, phosphoinositide 3-kinase inhibitor
Mount Sinai School of Medicine	3 (0.68%)	Namenda, mGluR antagonists	Memantine to treat autism, SHANK3 deletion assay and treatment
Hamamatsu University	3 (0.68%)	Levels of very low-density lipoprotein, cholesterol, triglyceride, FABP3, FABP4, FABP5, and FABP7.	Determining risk of autism
INSERM	3 (0.68%)	Epothilones	Treatment of neuronal connectivity defects
		HERV-H	Molecular marker
		Bumetanide	Inhibits the importation of chloride into neurons and improve its out flow
Others	92 (21.04%)	Detection of Epigenetic genes/markers, decreased metabolism of tryptophan, CNTNAP2 gene, novel region on chromosome 5pl4.1	Epigenetics, cell culture, Chromosome abnormality

published in last five years and they were mostly claimed on administering the drug orally and transdermally (Fig. 5). These novel and best suited modes of administration attain significance among all invasive methods to children with autism because of their minimal invasion.

Notably the focus on inventing new diagnostic methods has increased from past five years. Many patents in the last five years have focused on diagnosing the ASD as compared to last 25 years. Out of 145 patents for diagnosis, 99 are published in last 5 years. Identification of genetic and biochemical marker for ASD can potentially improve the validity and efficiency of existing diagnostic methods that rely on traditional methods of diagnosis using behavioral assessments. The hope of developing target based treatment approaches can only be fulfilled by identifying specific markers as competent sources of diagnosis. In the past 25 years apart from SNPs, copy number variations and genetic markers Neurotransmitters and their receptors like serotonin, SLC genes, dopamine metabolites, GABA and genes related to glutamatergic pathways have been detected as potential markers for diagnosis of ASD. Glutamatergic pathways and Neurotransmitters appear to be thing of past, not many patents filed for these categories in the last 5 years. The number of patents filed for metabolites and biomarkers has largely increased in the recent years. A great majority of ASD research has concentrated in exploring neurotransmitter/receptors as targets to treat ASD. Among the neurotransmitters novel drugs, serotonin uptake inhibitors, agonists/antagonists, had 46 patents followed by glutamate receptor 5 antagonists (36), dopamine (34), NMDA (20), GABA (17), acetyl choline (11), monoamine oxidase (6), AMPA receptor (4), cannabinoid (4), norepinephrine (4), adenosine(2), melanocortin (1), melatonin receptor (1). Besides this novel drugs like quinazoline and quinolinone derivatives were heavily featured followed by probiotics, vitamins, S-adenosylmethionine. Neurotransmitters continue as main treatment approaches L-glutamate overtook serotonin during last 5 years, apart from that the profile of neurotransmitters remained the same. Novel drugs seem to have evolved a lot in last 5 years (26 patents in this period as against 38 in all years). Patent activity for antibodies has seized in the last 5 years.

Different samples used for diagnosing autism ranges from blood, cell/tissue, plasma, serum, cerebro spinal fluid, urine, amniotic fluid, saliva and stool etc. Blood is major sample used for autism diagnosis where 52 patents were filed in last 25 years. In which 41 were published in the past 5 years showing the importance of blood based diagnosis. All the samples used for autism diagnosis was compared and depicted in Fig. 6.

Table 5
Hospitals working on autism.

Name	No. of Patents	CNV in Chromosomes/Genes	Research Focus
Children's Hospital of Philadelphia	5 (1.07%)	Copy Number Variations in chromosomes duplication:Chr2, Chr3, Chr4, Chr6, Chr7, Chr8, Chr9, Chr14, Chr15, Chr17, Chr19, Chr20, Chr22 Genes: GABRA5, GABRA3, GABRB3	Detecting genetic alterations using microarray and developing target based treatment
Hospital for Sick Children	4 (0.85%)	CNV in SHANK1 gene, mutations in PTCHD1AS1, PTCHD1AS2, PTCHD1AS3 containing disruption of a promoter sequence in ChrX, SHANK3, NFIA, DPP6, DYPD, DPPlO, GPR98, PQBPl, ZNF41 and FTSJl	Detecting genetic markers for autism risk assessment
Murdoch Children's Research Institute	4 (0.85%)	Fragile X Mental Retardation (FMR) genetic locus-FREE3, intron 2	Diagnosis and treatment of epigenetic disorders
Children's Medical Center Corporation	3 (0.64%)	HIST3H3, AMT, GLDC PEX7 genes and genes related to KEGG pathways	Novel mutations identification for novel treatment approaches
Others	12 (2.57%)		

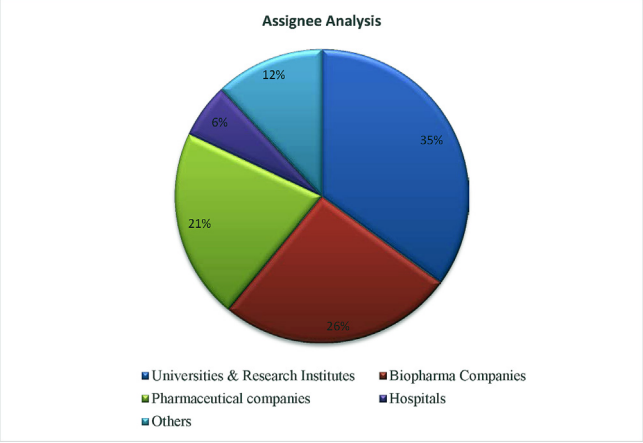

Fig. 8. Pie chart representing Assignee Analysis.

3.5. IPC code analysis

A more thorough assessment of patents was made by analyzing the distribution pattern of the patents in a range of categories under International Patent Classification and found about 10 IPC classes covering a huge area of segments. It was found that maximum numbers of patent records (30%) were categorized in IPC code A61P25/00 which covers drugs for disorders of nervous system (Fig. 7).

3.6. Assignee vs diagnosis and treatment

In order to understand the contribution of pharmaceutical companies (Table 2), biopharma companies (Table 3), universities & research institutes (Table 4), hospitals (Table 5) the patents filed by the same were tabulated each illustrating the research focus. Assignee groups having low patent activity (>3) were placed in others in their respective groups. The pie chart Fig. 8 illustrates the count and percentage contribution of various assignees indicating that universities & research institutes were acting as major players in autism research covering around (35%) of total patent filings that appear to have focused their research towards identifying novel diagnostic markers and treatment targets, followed by (26%) of biopharma companies with their research directed towards producing diagnostic kits for detecting blood based markers, biological drugs that can be used for target based treatments. While (21%) of Pharmaceutical companies developing compounds targeting neurotransmitter receptors, and oxidative stress (6%) of hospital research revolves around detecting genetic alterations for risk assessment. Patent applications that do not fall in any of the above categories were placed in others (12%) Significant drugs which are in pipeline of various pharma/Biopharma companies along with different stages of clinical trials were showed in Table 6.

4. Conclusion

Although the world of autism research is expanding, the complexities that make autism hard to understand are still to be unraveled to facilitate diagnosis and monitoring of progression of neurological conditions and treatment response and to identify targets for therapeutic intervention. As the safe and effective treatments for ASD remain limited, there is great interest in identifying and treating infants at risk for autism prior to onset of overt symptoms. Early intervention leads to enhanced treatment outcome. Risk assessment based on testing for genetic and epigenetic factors, biomarkers, associated with autism could allow interventions to begin during the infant period and thereby reduce or prevent the development of the full blown syndrome In the post globalized world of science and technology one of the most remarkable features is the growing consciousness among people regarding IPR's and their role on society. Assessing the link between autism and various factors affecting brain development is main focus for research and development. Therapies ranging from psychoanalysis to psychopharmacology have been employed in the treatment of autism. Many of the treatments, however, address the symptoms of the disease, rather than the causes. Although some clinical symptoms may be lessened by these treatments, modest improvement, at best, has been demonstrated in a minor fraction of the cases hence there is no evidence that these medications can improve core features (e.g., social responsiveness), in all No single treatment is personalized to the child's needs. Finding new ways to observe and test for the condition gives new insights for best targeted treatment approaches in future with research focusing on stem cell lines, vaccines, gene therapy, nano formulations and so forth. In brief, gastrointestinal abnormalities, immune dysfunctions, detoxification, and/or nutritional deficiencies or imbalances have all been suggested as potential biomedical “triggers” for ASD and it is hard to determine which scenario comes first. Mechanism-based strategy that targets the intrinsic cellular stress response, including mitochondrial biogenesis, peroxisome proliferation, activation of the stress proteome, transcription and/or translation of genes and proteins encoded by genes comprising heat shock and unfolded protein, genes for autophagic responses, genes for antioxidant responses, and modulates the metabolic defects that contribute to the symptomatology of autism spectrum disorders.

Table 6
Significant drugs of pharma/biopharma companies in pipeline.

Name of the Company	Drug/Drug candidate	Drug Target	ClinicalTrials.gov Identifier	Clinical trials
Pfizer	Quillivant XR (liquid methylphenidate)	Central nervous system stimulant	NCT02255565	Phase 4
Eli lilly & company	Atomoxetine (brand name: Strattera) Atomoxetine Hydrochloride	Norepinephrine (noradrenaline) reuptake inhibitor (NRI)	NCT00380692 NCT00485849	Phase 4 Phase 4
Janssen Pharmaceuticals	Risperidone (R064766) Paliperidone ER	Reducing aggression, self-injury, and irritability	NCT01624675 NCT00549562	Phase 3 Phase 3
Repligen Corp	RG1068	Synthetic human secretin	NCT00036244	Phase 3
Curemark Lic	CM-AT	Enhance protein digestion thereby potentially restoring the pool of essential amino acids	NCT02649959	Phase 3
Roche Holding AG	RO5285119 RG7314 RO5028442	GABA B receptor agonist, antagonist of the vasopressin V1A receptor	NCT02901431 NCT01793441 NCT01474278	Phase 2 Phase 2 Phase 1

Unravelling the basic mechanisms of how the body makes and regulates energy metabolism will open up these very important medical and scientific areas of investigation and allow us to discover new personalized treatment approaches.

Also, this study brings to light current perspectives and views on autism research. In these days of hypercompetitive era it is challenging and interesting for researchers across public and private organizations to develop target based diagnosis and treatment strategies for this disorder. It is expected that through white gaps, investments will help researchers to formulate viable R&D strategies, with freedom to operate opinions and bring better returns through technology licensing and promote economic growth. In addition to that demand for promising technologies and fertile areas can be identified where research and development has to be focused for new start-up companies. These are the significant studies giving consideration to the information about patented research trends in the field of autism diagnosis and treatment.

In the current work the status of ongoing research in developing novel diagnostics and treatment methods was outlined. We have discussed about the fore most diagnostic and treatment approaches that have been widely implemented for the past 25 years and highlighted the potential approaches that have shown considerable advancements in last 5 years. We have observed that genetic and biochemical markers have gained attention among the groups that aim to develop novel diagnostic strategies as per the treatment methods focusing on neurotransmitters might reveal novel strategy to cure the disorder. However despite significant scientific advances, development of novel diagnostic and treatment methods is still in its infancy and is hobbled by multiple factors including poor understanding of molecular mechanisms. More intense R&D coupled to setting up inventive strategies is needed to facilitate growing need towards developing novel diagnostic and treatment strategies for ASD.

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