TECH CORP RESEARCH

BREAST CANCER - PATENT LANDSCAPE

TECH CORP LEGAL® LLP

GENE THERAPY PATENTS

US: Association for Molecular Pathology, et al. v. Myriad Genetics, Inc.

INDIA: Health Ministry Requests Revokation of Trastuzumab Patent

Breast Cancer Patents – A Landscape

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Executive Summary

Introduction

Breast cancer is a malignancy that effects women across the world and is most prevalent among various types of cancers.

Patents are jurisdiction specific exclusive rights that are sought by innovators across various technological fields. However, patent rights become questionable and debatable when these are sought in respect of pharmaceutical drugs, medical devices, surgical techniques, diagnostic tests, personalized medicines and research tools related to healthcare. Across Western jurisdictions, patents have been sought for artificial plant varieties (hybrid plants, genetically modified plants etc.), animal species created with human intervention (Harvard Oncomouse, Dolly the Sheep etc.), and methods of human treatment. Due to the presence of numerous patents in the field of healthcare, it imminently results in the requirement of large number of licenses to access patented technology, which subsequently leads to increased cost of treatment because of accumulation of royalties (royalty stacking) to be paid to the patent holders. Therefore, in developing countries like India, it becomes highly controversial as to whether to grant such patents to protect Intellectual Property Rights (IPR) or to focus on affordable healthcare by rejecting such patents.

Strategy, Scope and Focus

With a view to discuss implications of patents specifically related to breast cancer, we have researched and analyzed the breast cancer patent landscape in India and US, in light of latest legal developments, with special focus on Trastuzumab (a medicine which treats a form of breast cancer) and US Supreme Court judgement to overturn Myriad Genetics' patents on the "breast cancer genes - BRCA1 and BRCA2".

Breast Cancer and Patents

Basics of Patent Rights

As it is well known that patent protection is granted for a limited period of 20 years, wherein the patent holder holds exclusive rights for exploitation of the patented invention.

Generally, patents are aimed at encouraging innovations by providing incentives to the patent holders by offering them recognition for their creativity.

Biotechnology Patents

In the field of biotechnology and healthcare, the cost of reparation is crucial, as the research in these fields is highly expensive. The financial investments can only be paid off if the companies can protect results by exclusive rights (patents) and gain the competitive advantage.

Gene Therapy Patents

Historically, there has been a close relation between gene therapy, patents and scientific advancements.

Large pharmaceutical companies have invested huge amount of capital in patenting genes, either on their own or by acquiring small biotech companies.

For example, Swiss pharmaceutical company Sandoz (subsidiary of Novartis) acquired Genetic Therapy Inc. of Gaithersburg, Md. In 1995, for about $295 million.

NOVARTIS

SANDOZ

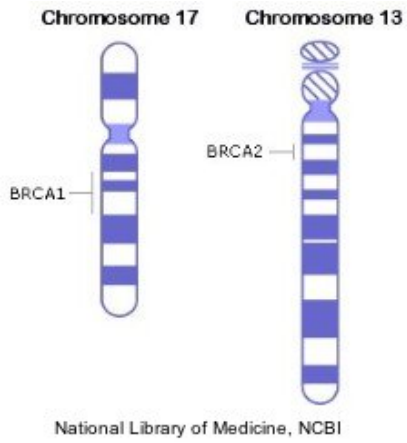
At that point of time, Genetic Therapy held exclusive license to a patent received by the National Institutes of Health for ex vivo gene therapy (somatic gene therapy), which involves taking cells out of the body, treating them with altered genes and replacing them in the body, with a view to compensate for deficient or defective genes. However, Novartis shut down Genetic Therapy after approximately 8 months because expected results could not be achieved, thereby bringing out the risks involved in such investments.

Patents for Breast Cancer Genes

Although disease-associated genes involve meticulous research and development, patents granted for protecting such innovations are at epicenter of various debates as they may hamper future R & D activities, in addition to leading to cumbersome costs of treatments. These concerns are presently being debated across various jurisdictions with regards to breast cancer genes (BRCA 1 and BRCA 2). In past, patents for these genes have been granted by EPO and USPTO.

Myriad Genetics

Myriad Genetics, Inc. is a molecular diagnostic company based in Salt Lake City, Utah, and holds hundreds of patents worldwide on BRCA 1 and BRCA 2, including the genes and diagnostic methods based on them. Many parties fear that due to such exclusive rights, the research may become impossible to carry out in public laboratories, or will become highly expensive.



National Library of Medicine, NCBI

Commercially, Myriad Genetics has become a forerunner in the healthcare industry for diagnostic testing of BRCA1 and BRCA2 gene mutations, which are closely related to breast and ovarian cancer. In recent past, such diagnostic tests created controversy and were heavily debated when Angelina Jolie announced she had been tested positive for the mutations, whereby she voluntarily had a preventative double mastectomy.

Association for Molecular Pathology, et al. v. Myriad Genetics, Inc.

In light of Myriad's wide patent portfolio covering the BRCA1 and BRCA2 genes and corresponding diagnostic methods, Myriad's patents were challenged in court, in the interest of the public's right to affordable access to medicines.

On 13 June 2013, the United States Supreme Court, in a unanimous decision, held that the mere separation or isolation of naturally occurring genomic DNA is not sufficient human intervention to give rise to a patentable invention. As stated by the Court, it was held that: "*Myriad did not create or alter either the genetic information encoded in the BRCA1 and BRCA2 genes or the genetic structure of the DNA. It found an important and useful gene, but ground-breaking, innovative, or even brilliant discovery does not by itself satisfy the §101 inquiry.*"

However, surprisingly, the Court further stated that Complimentary DNA (cDNA), which is a synthetically created form of DNA corresponding to a gene sequence, is indeed patentable under §101. Generally, cDNA contains the same protein-coding information as found in a segment of natural DNA, excluding the DNA segment that do not code for proteins, i.e. introns.

Accordingly, cDNA only contains nucleotides that are known as "exons". In this regard, the Court stated: "***Its order of the exons may be dictated by nature, but the lab technician unquestionably creates something new when introns are removed from a DNA sequence to make cDNA***".

With a view to obtain clarity and understand this judgement from the perspective of future patent applicants, it is advisable to analyze the patent claims at issue, such as claims 1, 2, and 5 of **U.S. Patent No. 5,747,282** ("the '282 patent"), identified as representative of the claims at issue in Myriad case.

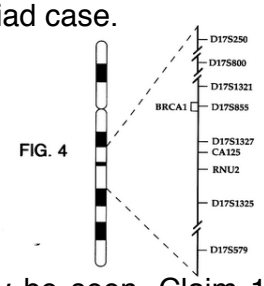


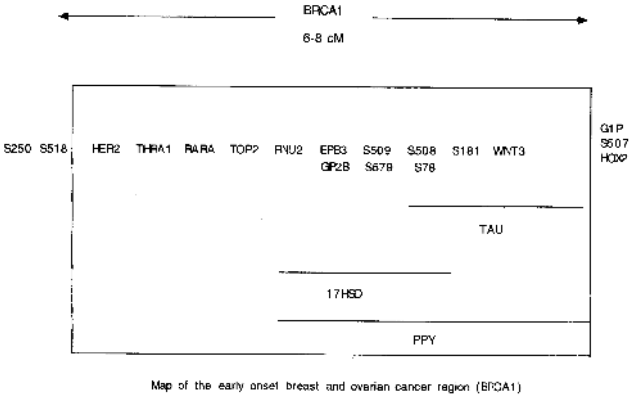
FIG. 4

As may be seen, Claim 1 of the '282 patent claims "***an isolated DNA coding for a BRCA1 polypeptide, said polypeptide having the amino acid sequence set forth in SEQ ID NO:2.***" This claim is clearly invalid as it pertains to a naturally occurring DNA sequence, and the Court has explained that "***Myriad's claims are not saved by the fact that isolating DNA from the human genome severs the chemical bonds that bind gene molecules together.***"

However, Claim 2 of the '282 patent is a dependent claim that claims "the isolated DNA of claim 1, wherein said DNA has the nucleotide sequence set forth in SEQ ID NO:1."

Since the Court has noted that SEQ ID NO:1 is an isolated full-length cDNA sequence, which, according to Myriad, is non-naturally occurring and therefore patentable. Therefore, Claim 2 seems to be a valid claim.

Additionally, Claim 5 of the '282 patent is a dependent claim that claims "an isolated DNA having at least 15 nucleotides of the DNA of claim 1." This claim also invalid in view of the Court's observations.



Map of the early onset breast and ovarian cancer region (BRCA1)

FIG. 1

In spite of above clarifications, the Court did not specifically state anything with respect to "**the patentability of DNA in which the order of the naturally occurring nucleotides has been altered.**"

Accordingly, **future patent applications are advised to present the subject matter to be claimed as "synthetic," such as in a recombinant form, which may include describing the chemical composition of the molecule to differentiate it from its natural counterpart.**

The decision created a stir of controversy, wherein certain commentators termed the judgement as a victory, while others called it catastrophic, thereby further resulting in complicating the debate surrounding "gene patents."

SUPREME COURT OF THE UNITED STATES

Syllabus

ASSOCIATION FOR MOLECULAR PATHOLOGY ET AL.
v. MYRIAD GENETICS, INC., ET AL.

CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

No matter whose side of the debate says what, the impact of this judgement will be seen globally, and it will take years before a resolution is achieved.

MYRIAD®

Breast Cancer related Patents: Indian Scenario

Recently, the Indian Health Ministry has asked for a cancellation of patent to Trastuzumab - a medicine which treats a form of breast cancer. Specifically, the health ministry had suggested that the government use powers under section 66 of the Indian Patents Act to revoke the patent in public interest. In accordance with provisions of the Indian Patents Act, Section 66 states that:

Revocation of patent in public interest: "*Where the Central Government is of opinion that a patent or the mode in which it is exercised is mischievous to the State or generally prejudicial to the public, it may, after giving the patentee an opportunity to be heard, make a declaration to that effect in the Official Gazette and thereupon the patent shall be deemed to be revoked.*"

This provision is rarely used by the government, and previously, the government has used the provision to revoke patents only twice. In 1994, it cancelled a patent given to a US firm for developing cotton cells by tissue culture while in 2012, it used this to revoke patent for a medicine made of jamun, lavangpatti and chandan meant to treat diabetes.

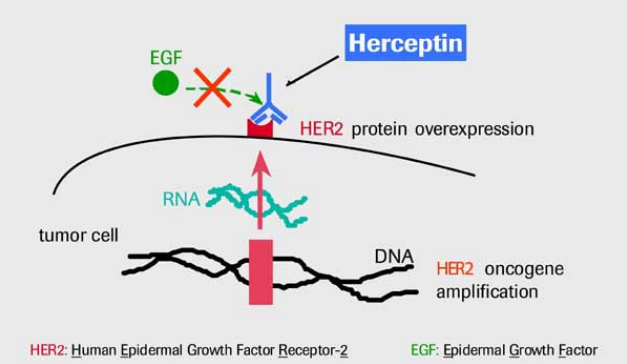
In recent past, the health ministry had asked for the use of compulsory license provisions for Trastuzumab, along with Ixabepilone and Dasatinib, which are also anti-cancer medicines.

The Indian government is already at the receiving end of criticism from developed countries, including US, for awarding compulsory license for a renal cancer medicine, which is patented by Bayer, with a view to bring down the treatment cost.

Earlier this year, in a landmark ruling involving Novartis's anti-cancer drug Glivec, the Supreme Court rejected the patent application, thereby upholding the validity of the provisions to check frivolous patents.

Breast Cancer Patents – A Landscape

Trastuzumab is a monoclonal antibody that interferes with the HER2/neu receptor and is a commonly used trade names of Herclon and Herceptin. The development of trastuzumab has led to new therapeutic strategies for patients with breast cancer. Trastuzumab has been shown to be effective in those patients whose cancers are HER2 positive by either immunohistochemistry (IHC) or fluorescence in situ hybridization (FISH).



Generally, the HER receptors are proteins that are embedded in the cell membrane and communicate molecular signals from outside the cell (molecules called EGFs) to inside the cell, and turn genes on and off. The HER proteins stimulate cell proliferation. In some cancers, notably certain types of breast cancer, HER2 is over-expressed, and causes cancer cells to reproduce uncontrollably.

Relevant International Patent Classifications [IPC]

1. A61K

Preparations For Medical, Dental, Or Toilet Purposes (devices or methods specially adapted for bringing pharmaceutical products into particular physical or administering forms A61J 3/00; chemical aspects of, or use of materials for deodorisation of air, for disinfection or sterilisation, or for bandages, dressings, absorbent pads or surgical articles A61L; soap compositions C11D).

2. A61P

Specific Therapeutic Activity of Chemical Compounds or Medicinal Preparations.

3. Co7K

Peptides (peptides containing β-lactam rings C07D; cyclic dipeptides not having in their molecule any other peptide link than those which form their ring, e.g. piperazine-2,5-diones, C07D; ergot alkaloids of the cyclic peptide type C07D 519/02; single cell proteins, enzymes C12N; genetic engineering processes for obtaining peptides C12N 15/00)

4. C12N

Micro-Organisms Or Enzymes; Compositions Thereof

(biocides, pest repellants or attractants, or plant growth regulators containing micro-organisms, viruses, microbial fungi, enzymes, fermentates, or substances produced by, or extracted from, micro-organisms or animal material A01N 63/00; medicinal preparations A61K; fertilisers C05F); Propagating, Preserving, Or Maintaining Micro-Organisms; Mutation Or Genetic Engineering; Culture Media (microbiological testing media C12Q 1/00)

5. C07D

Heterocyclic Compounds

6. G01D

Measuring Not Specially Adapted For A Specific Variable; Arrangements For Measuring Two Or More Variables Not Covered By A Single Other Subclass; Tariff Metering Apparatus; Measuring Or Testing Not Otherwise Provided For.

7. C12Q

Measuring Or Testing Processes Involving Enzymes Or Micro-Organisms (immunoassay G01N 33/53); Compositions Or Test Papers Therefor; Processes Of Preparing Such Compositions; Condition-Responsive Control In Microbiological Or Enzymological Processes

8. C07H

Sugars; Derivatives Thereof; Nucleosides; Nucleotides; Nucleic Acids (derivatives of aldonic or saccharic acids C07C, C07D; aldonic acids, saccharic acids C07C 59/105, C07C 59/285; cyanohydrins C07C 255/16; glycals C07D; compounds of unknown constitution C07G; polysaccharides, derivatives thereof C08B; DNA or RNA concerning genetic engineering, vectors, e.g. plasmids, or their isolation, preparation or purification C12N 15/00; sugar industry C13)

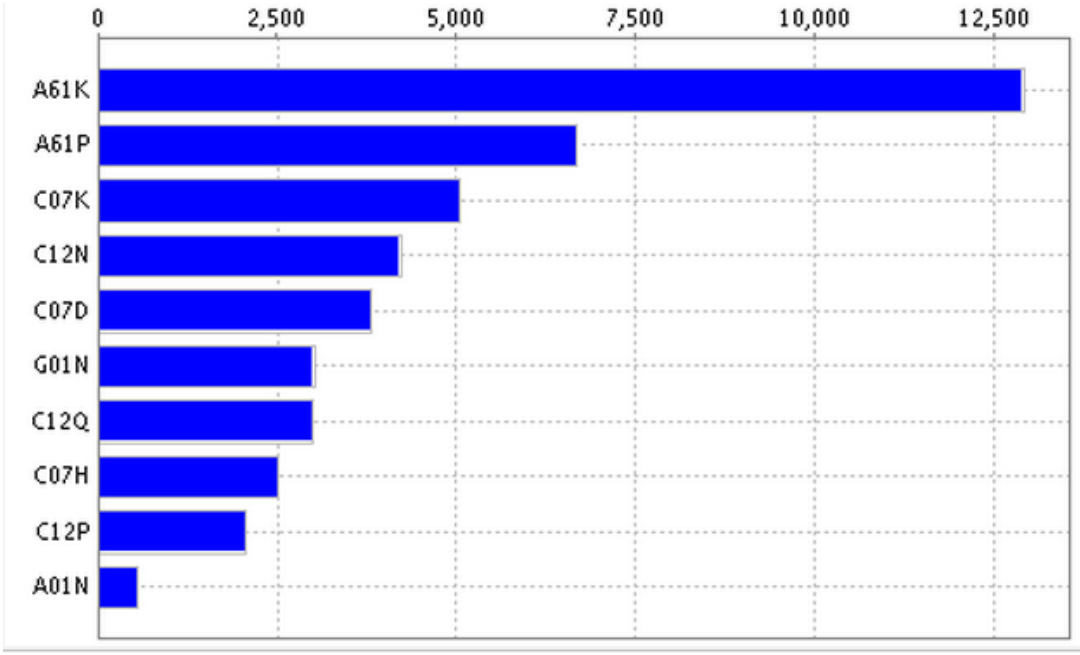
9. C12P

Fermentation Or Enzyme-Using Processes To Synthesise A Desired Chemical Compound Or Composition Or To Separate Optical Isomers From A Racemic Mixture (fermentation processes to form a food composition A21, A23; compounds in general, see the relevant compound class, e.g. C01, C07; brewing of beer C12C; producing vinegar C12J; processes for producing enzymes C12N 9/00; DNA or RNA concerning genetic engineering, vectors, e.g. plasmids, or their isolation, preparation or purification C12N 15/00)

10. A01N

Preservation Of Bodies Of Humans Or Animals Or Plants Or Parts Thereof (preservation of food or foodstuff A23); Biocides, e.g. As Disinfectants, As Pesticides

Or As Herbicides (preparations for medical, dental or toilet purposes which kill or prevent the growth or proliferation of unwanted organisms A61K); Pest Repellants Or Attractants; Plant Growth Regulators (mixtures of pesticides with fertilisers C05G).

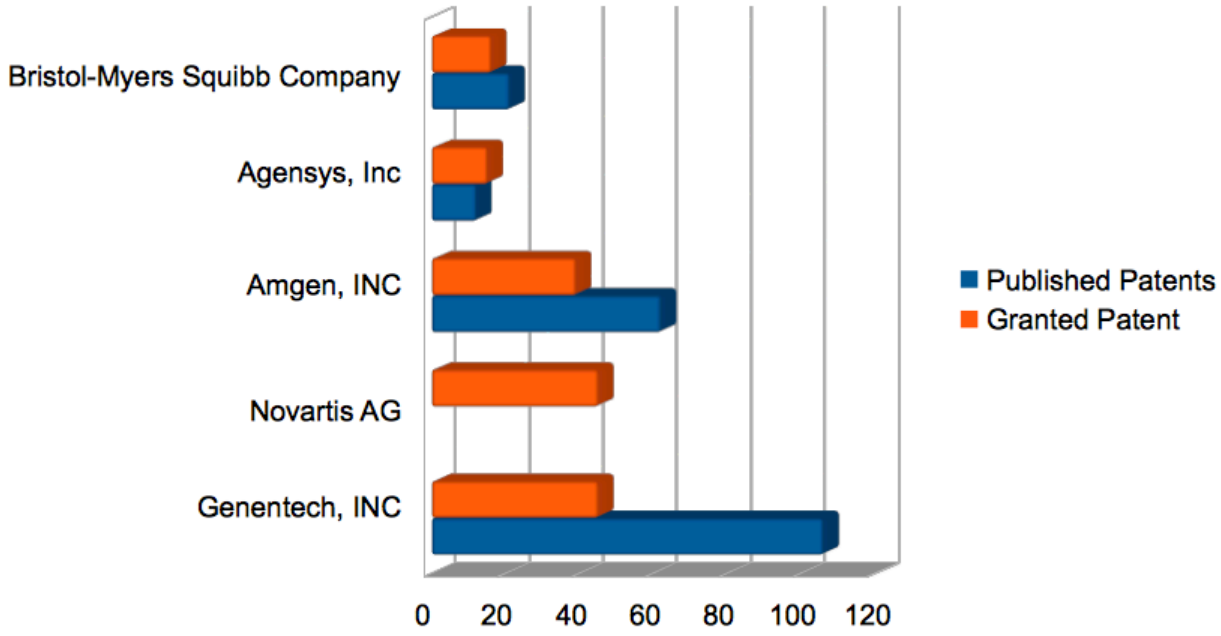


No	
Name	No
A61K	12910
A61P	6670
C07K	5039
C12N	4219
C07D	3813
G01N	3005
C12Q	2990
C07H	2512
C12P	2066
A01N	552

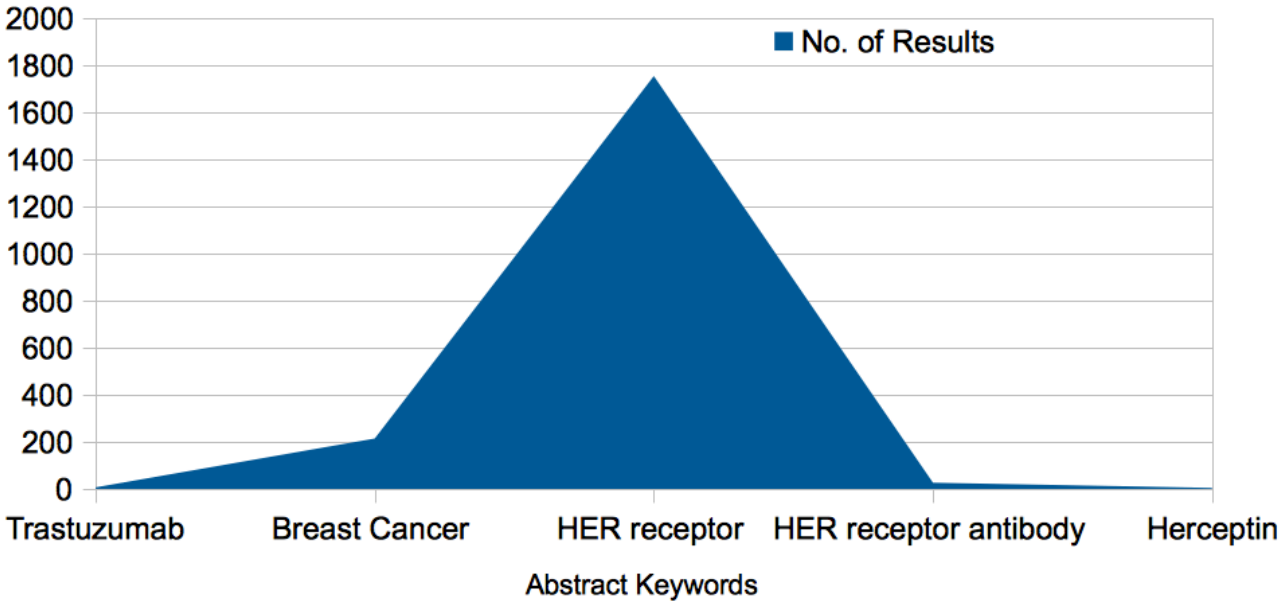
Number of Patents filed before WIPO in each IPC

Main IPC		Main Applicant	
Name	No	Name	No
A61K	60	MYRIAD GENETICS, INC.	100
C07K	46	MYRIAD GENETICS, INC	18
C12Q	40	BOARD OF REGENTS, THE UNIVERSITY OF TEXAS SYSTEM	2
C12N	25		
G01N	17	UNIVERSITY OF UTAH RESEARCH FOUNDATION	1
C07D	15	INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM)	1
A01N	9	ABBOTT LABORATORIES	1
C07H	6		
C12P	4		
G06F	4		

Number of PCT Patents filed by Myriad Genetics (Singly & Jointly) in each IPC



Number of US Patents by Major Players



Number of Indian Patents related to Trastuzumab