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Research Article
A Data-driven Approach to Allogeneic Stem Cell Transplantation

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Abstract

Background: Healthcare organizations today are capable of generating and collecting large amounts of data. This increase in volume of data requires automatic way for these data to be extracted and analyzed when needed. Millions of people would like to store cell specimens, for use in all sorts of contingencies. This study explores innovations in life sciences sector with the case of stem cells, an emerging and promising field. Stem cells research plays a key role in regenerative medicine because of the variable potentials it offers in basic, clinical research and development. **Methodology:** Applications from the stem cell research and developments can be categorized into four key fields as the application of the pluripotent cells, application in the field of drug discovery, cell therapy and diagnosis for example in identifying new treatment options forany organ failure or any fatal disease. Stem cells have the unique ability to become any cell in the body. This can keep on renewing themselves. These basic building blocks of life are fast becoming the ultimate repair-kit of the future. **Results:** Statistics show that there is a greater chance for success in a stem cell transplant between siblings (syngenic) as well as there may be chance to solve the disease of unrelated donors (allogenic) and recipients. **Conclusion:** Basing on these findings, it can be concluded that the data-driven approach to retrieve the knowledge from the stem cell database helps to solve the disease of unrelated donors and recipients also. This offers a new insight to the data mining techniques in the field of medical practices.

Key words: Stem cell, syngeneic, allogeneic, autologous, embroyonic cells, aminiotic fluid, bone marrow cells, pluripotent cells

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Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Stem cells[1] are the basic building blocks of the body. All the cells in the body are not stem cells; this is a special type of cell, which can rejuvenate themselves with a more specific function, such as blood cells, brain cells, heart muscle or bone. No other cell in the body has the natural ability to generate new cell types.Stem cells sources need to be identified in human body. The stem cell mostly lives in embryos, bone marrow, regular adult cells reprogrammed into induced pluripotent cells and amniotic fluid[2].

The several sources of stem cells:

- **Embryonic stem cells:** These stem cells come from embryos that are 3-5 days old. At this stage, an embryo is called a blastocyst and has about 150 cells
- **Adult stem cells:** These stem cells are found in small numbers in most adult tissues, such as bone marrow or fat. Compared with embryonic stem cells, adult stem cells have a more limited ability to give rise to various cells of the body
- **induced pluripotent stem cells:** Adult cells altered to have properties of embryonic stem cells scientists have successfully transformed regular adult cells into stem cells using genetic reprogramming. By altering the genes in the adult cells, researchers can reprogram the cells to act as same as the embryonic stem cells
- **Perinatal stem cells:** Researchers have discovered stem cells in amniotic fluid in addition to umbilical cord blood stem cells. These stem cells also have the ability to change into specialized cells

Transplantation of stem cells[3] helps to save the life of patients. Now a days stem cells are stored in laboratories mainly umbilical cord stem cells are widely collected and preserved. They were maintaining a complete record over this data for future medical processing needs. When these cells are shared between unrelated people this will bring drastic changes in the medical field. It will be achieved by connecting all the donor registries for matching, bone marrow worldwide registry is already sustaining for storing these data. Stem cells are the blood (hemat) cells for the human body, so called as hematopoietic transplantation. This was the recent work in medical field to find the parameters for unrelated donor transplantation.

Stem cell study[4] is one of the recent works in medical field; self-renewal is its hallmark property. It is collected and cultured for long duration for mutation and researchers have developed many methods to find the various parameters for transplantation.

Human embryonic stem cells[5] are collected from spinal muscular atrophy patients. These cultured embryonic stem cells have undergone various methods for finding the changes in their genes. Defective genes have been identified and the pluripotent changes can be resolved. Stem cells are useful for finding defects in genes as well as mainly used for transplantation.

Recent researchers[6] have tried to deliver better health by transplantation. This will help to reduce the risk like red blood and white blood cell disorders, platelet disorders and related diseases. Stem cell transplantation has been great leaps in haemotological research and patient care. Actually, there is a still more work have to be done in this area to improve patient care in medical field.

MATERIALS AND METHODS

Methodologies of transplantation: The different methods of transplants[7] include:

- **Autologous:** A transplant in which one's own peripheral stem cells are collected and given back to them after high-dose chemotherapy treatment
- **Allogeneic:** A transplant of stem cells taken either from the bone marrow cavity or the peripheral blood stream from donors of someone other than themselves. This is also known as a Matched Unrelated Donor (MUD) transplant. The stem cells are given back to the same person after high-dose chemotherapy with or without radiation therapy
- **Syngeneic:** The collection of stem cells from an identical twin and given to the patient

In autologous transplantation there is no chance for donor matching.

In Syngeneic transplantation, donor matching has to done, but there is a high chance for matching.

But in Allogeneic transplantation there is a need for high chance of donor matching perfectly, because donors are unrelated persons and their stem cells have to be matched with the recipients.

Analysis on transplantation: Based on the methodologies of stem cell transplantation, the following analyses have done.

Hematopoietic Stem Cell Transplants (HSCT)[8] are used to correct defects that occur in blood cells by supplanting the patient's hematopoietic stem cells with those derived from donors, so that new healthy blood cells can develop to replace the existing defective blood cells. The most important Pre-requisite for performing a successful HSCT is to find a suitable HLA-matched donor. This has been the Goal of World Marrow Donor association that has helped in establishing standards and accreditation of stem cell registries. This will be a vital and vibrant component of patient care in future.

Selling autologous stem cell therapies[9] patients can use their own stem cells to act as a repair kit for many conditions. This leads to clinical trials to evaluate possible autologous (own cells) cell based therapies. This needs to be explored and induces interest between patients and practitioners. Also, there is a need to regulate the development and commercialization of new cellular therapies.

The HLA matchmaker[10] is the computer based algorithm to determine donor recipient HLA compatibility. The HLA antigens are of HLA-A, HLA-B, HLA-C chains of protein sequences. These are referred as class I HLA matching. This algorithm is for assessing donor-recipient compatibility that are shared by HLA antigens, so called CREG (Cross reactive antigen groups). It helps in the concept of kidney transplantation.

Class I and II[11], HLA antigens are assessed for high resolution HLA matching.The effects are classified as high, low or both on engraftment, Graft Versus Host Diseases (GVHD) and mortality. Class I alleles or antigens are HLA-A, -B, -C and Class II alleles are HLA-DRB1, -DQ and -DP. This was performed by Wilcoxon Rank sum test and the likelihood ratio. This will helps us to identify the HLA disparities and to predict perfectly matched donors with high resolution of HLA alleles.

Haemotology stem cell transplantation[12] has developed rapidly as a treatment in India by HLA matching. Three registries from India are considered to collect HLA typing and demographic data. Maximum likelihood method is used as the basis of HLA Analysis. This analysis shows patients in India are more likely to find a matched donor outside of India than within India and this will continue to be the case until the Indian adult donor registry size grows substantially.

A glow of HLA typing in organ transplantation[13], the adaptive immunity is considered as the main response exerted to the transplanted tissue. The HLA antibodies are the important factors responsible for graft rejection in organ transplantation. Methods for HLA typing are described including serological methods, molecular techniques of Sequence Specific Priming (SSP), Sequence Specific Oligonucleotide Probing (SSOP). These methods are used to decrease the rate of rejection with less side effect and complications.

HLA match likelihoods for hematopoietic stem cell grafts in the US registry[14], is a special kind of life saving therapy for cancers and other diseases. In US, they were maintaining a match registry, which helps the unrelated donors for transplantation. The matching was done at allele or antigen level and the likelihood of matching was done. Mostly there will be the chance of finding donors through this registry.

These analyses show the importance of allogeneic transplantation in unrelated donors.

RESULTS

Resulting technology in allogeneic transplantation: The HLA matching[15] is the only way to match the allogeneic stem cells. Human Leukocyte Antigen (HLA) are proteins that are located on the surface of the white blood cells and other tissues in the body. This group of genes resides on chromosome 6 and encodes cell-surface antigen-presenting proteins and has many other functions. Human Leukocyte Antigens (HLA) are said to be a "Match", if their tissues are immunologically compatible with each other. In HLA there are two main alleles class I and II, in class I the antigens or genes are HLA-A, -B, -C and minor alleles or genes are HLA-E, HLA-F and HLA-G and in class II the antigens or genes are HLA -DR, -DM, -DOA, -DOB, -DQ and -DP. Humans may have any combination of these alleles in their chromosome 6. These have to be matched with the donors for HLA matching for allogeneic transplantation. As an example in Fig. 1. It is important to know that HLA is inherited as a "Set" of the three HLA groups, A, B, DR. This set is known as a "Haplotype".

One can inherit one haplotype from each parent. Therefore, there are a total of four different haplotype combinations from 2 parents. There is a basic rule in HLA inheritance. The rule is: One have a 25% chance of inheriting all of the same HLA (same 2 haplotypes) as any one of their siblings, one have a 25% chance of not inheriting any of the same HLA (none of the same haplotypes) and one have a 50% chance of sharing 1 set of haplotype with one's own siblings. Therefore, one has a 1 in 4 chance of being an identical match with one's own siblings.

This can be taken as consideration for matching HLA typing with other donors. There may be chance of this kind of matching might be present in unrelated donor alleles also. The HLA matching can be done manually in clinical labs where

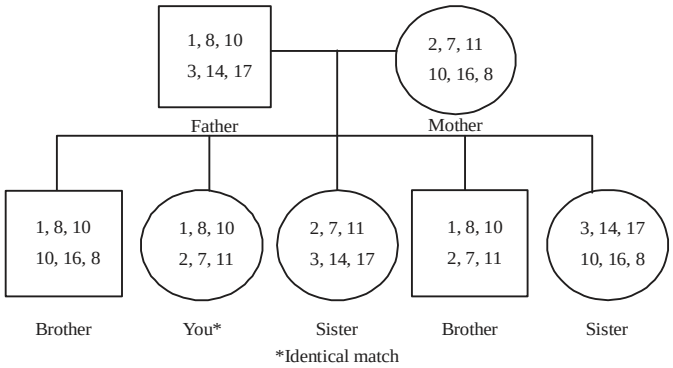

Fig. 1: Chances in HLA typing alleles

matching is necessary, this gives the idea of a data driven approach in allogeneic stem cell transplantation. The HLA typing is the resulting method for identified unrelated donors matching, so a computerized matching algorithm is needed for further processing.

A computer based algorithm called HLA molecular based Matchmaker algorithm[10] was only developed. Yet more effective methodologies are needed. This was the contradiction in previous method. This will be resolved by attributes of HLA typing.

The HLA typing attributes have to be identified when various stem cell laboratories and the methods which are made for matching in medical field have to be identified. This can be converted in an algorithm which improves the efficiency in matching the unrelated donor matching.

DISCUSSION

In this complete analysis, effective study is needed in the database of stem-cell by collecting related samples from various data centers. Based on the methodologies of stem cell transplantation data, HLA typing is needed for matching the alleles based on manual matching at clinical labs. If this matching is done using any classification and clustering computer based algorithms, this will be more useful for unrelated donor matching. This will be preceded with the stem cells datasets by classification and the datasets can be classified by blood group using classification based algorithms. This classification[16] will help to make datasets grouped into limited numbers. Then similarities between alleles are found using clustering[17] algorithms. Dissimilar allele groups are again classified and then clustered using the same procedure. This idea will leads to develop an essential algorithm for stem cell transplantations in future.

CONCLUSION

By summarizing some important issues and research trends in stem cell database, there is no computer based algorithm for this kind of matching. There is a need to identify a proper computer based algorithm. So, the HLA typing parameters have to be identified then classification and clustering of stem cell datasets will helps to identify unrelated donors. Many of the classification algorithms like Decision tree algorithm, nearest-neighbor classifier algorithm etc have to be analyzed and the effective algorithms can be applied over this datasets. After classification of datasets, many of the clustering algorithms like Hierarchical algorithm, K-means algorithm etc., have to be analyzed and the resulting clustered data are the outcome for allogeneic or unrelated donor matching. This methodology will lead to match the unrelated donor stem cell matching efficiently. This study will help the society in allogeneic matching.

SIGNIFICANCE STATEMENTS

This study gives more importance for health care organization. Because a patient history of data have lots of information for mining. This idea leads to mine the information in stem cell database. Currently, all over the world stem cell database entries are more in number and its database keep on growing, which is mainly used for transplantation purpose. So, there is a chance to bring out the importance of transplantation through computer based algorithm, this paves the way to precede this research.

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