

## GENE THERAPY TO TREAT CARDIOVASCULAR DISEASE A SURVEY TO DETECT THE POSSIBILITIES OF PREVENTION AND MANAGEMENT WITH GENETICS USING DATA MINING

*K.Ashokkumar<sup>1</sup>, Dr.S.Sheeja<sup>2</sup>,*

### ABSTRACT

The coronary artery disorder and cardiac arrhythmias are diseases which are the major causes of death in the many countries. Heart diseases can affect people of all ages. Pharmacologic drugs and device treatments have multiple limitations. There exists more need for better-quality clinical outcomes without side effects. Interventional procedures including angioplasty and ablation have improved the prognosis for patients with ischemia and arrhythmias. However, large subgroups of patients are still left with significant morbidity despite of those therapies. This limitation have prompted extensive investigation into new treatment modalities. Sequencing information of the human genome with the development of gene transfer vectors and delivery systems is done by the researchers. There are tools to target specific genes and pathways that play a role in cardiovascular diseases. Early-stages of clinical studies have been demonstrated in the promising signs of efficiency in some trials with very few side effects. The field of myocardial genetic manipulation is vast because of complex and multifaceted disease mechanisms in myocardial genetic gene products. Many different gene products can be targeted to ameliorate clinical phenotypes. There are several delivery vectors used in the clinic. This review focuses on three main cardiac diseases that are currently being evaluated for therapeutic benefit of gene therapy: (i)coronary artery disorder and (ii)heart failure[3]. There was a survey to trace

Cardio Vascular Diseases[2] to heredity and an attempt to detect the possibilities of prevention and management with genetics using data mining is proposed in this paper.

*Keywords: cardiovascular disease, Gene therapy, data mining, heart failure*

### INTRODUCTION

Data mining is a process of filtering data that are available from the large databases. It explores the large database to get the required data filtered from the entire environment. The First step is to select the data from the large storage area(database) with techniques like filter approach, wrapper approach and embedded approach. The second step is to use a filtering method. There are classifications like Bayesian, decision tree, rule based, neural networks etc., Genetics is a branch that deals with every individuals pattern for individual genetics. It is a branch of biology concerned with the study of genes, genetic variations and heredity in living organisms. Individuals of every human various on the pattern by which DNA[1] strands are arranged in and by chromosomes. Each individual has a set of 23 chromosomes where 22 of them are character deciders and 2 namely X and Y are sex chromosomes. The molecular basis of genes is deoxyribonucleic acid (DNA). The DNA[1] is composed of a chain of nucleotides, of which there are four types: adenine (A), cytosine (C), guanine (G), and thymine (T). The genetic information exists in the sequence of these nucleotides, and genes exist as stretches of sequence along the DNA chain. The viruses are the only exception to this rule but sometimes the viruses use a similar molecule RNA instead of DNA as their genetic material.

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<sup>1</sup>Research Scholar, Department of CS, CA & IT, Karpagam Academy of Higher Education, Coimbatore, India

<sup>2</sup> Professor, Department of CS, CA & IT, Karpagam Academy of Higher Education Coimbatore, India

**GENE VECTORS AND DELIVERY**

The heredity remedy represents the relocation of genetic science[4] which aims in cell or a part of the body to cure or intercept conditions. The victorious payment of a genetic science is to be attacked in the predominate remedial edges. It is manageable to understand variations of a touch dungeon to exude hormones are the unit developed element; at intervals alternative exacting prevalence, required could also be in depth as a variations of exceptional or all dungeon in attack of body-part. A personality of a genetic science transportation[5] procedure has been literate utilize the each infectious agents and non-viral establishment values. Non-viral performance incorporates applied in exposed polymer single or composited with liposome. The undraped genetic info values are unit straight-forward immune. This is to publicity of genetic info plasmids, the smallest amount is concerned a staging insistent to genetic science of the involvement for polymer space. The undraped genetic info values are unit unsuitable, utmost of minimum quantitative relation of attack dungeon intimate journalist of genes following macromolecule. Obviously, The genetic science is concerned without any need in every mysterious of specific dietary compound to the remedial advantage.

Adenoviruses (ADs) or Adeno Associated Viruses (AAVs) had the worth of moving Non dividing slot. A sizeable constraint of (Ads) vectors is that trigger of white blood cells response that eventually restrain ADs-moderated genetic science conveyance of a long-time of days and weeks when genes relocate. AAVs had extra-large restrained

hypersensitive white blood cells response; modify AAVs-moderate genetic science statement utmost significant above Ads. A touch of stage of medical educations have be persistent AAVs-moderated statement yearly forthcoming vector remittance, and a hereditary lack of a clotting factor and treatment of actual patients stream registered resolute expression in muscle 365days when AAVs dose. Downside of AAVs lined restricted size of the cistron insert (4.5 to five computer memory unit total) and also the required of help virus or completely different risk perform for polymer sequences.

The non-target is a undesirable impact of a medical treatment to be a line once the, viruses rate is often treated in blood to check distribution and also the genetic science land up within the individual part to deliberate. The uniform at intervals in aim of part unrestrained variation of the Transistors could also to be unsafe. The proposition of desired performance of cistron variation involves in the utilization of condition- or material. These specific helpers that might unambiguously indicate below obvious background (eg: An inadequate blood offer to an organ) or in evident specialized (eg: heart precise protagonist).The scope of generating a malignant from the viruses rate appeared as a regard to genetic science is a remedy at intervals. The reasoning to abnormal leucocytes beside genetic science is a remedy at intervals is an immune deficiency medical case. The scope of most likely infections are hundreds of their polymer issue in a cellular organism. This cause with the complicated polymer to indicate the fit and incorrect space and enhance tumours.

**Table 1. Delivery Techniques for Gene Therapy**

<b>Gene Delivery Technique</b>	<b>Pro</b>	<b>Con</b>
Myocardial injection	<ul style="list-style-type: none"> <li>• Great density of gene transfer limited to cardiac muscle</li> <li>• Simple and safe, able to inject percutaneous</li> </ul>	<ul style="list-style-type: none"> <li>• Small area of gene expression</li> <li>• Multiple injection sites needed</li> <li>• Acute inflammatory response and potential scarring from the injection</li> </ul>

Gene Delivery Technique	Pro	Con
Coronary perfusion-antegrade and retrograde perfusion	<ul style="list-style-type: none"> <li>• Delivers genes globally across the myocardium</li> <li>• Distributes gene vector more homogeneously</li> <li>• Cardiac specific</li> </ul>	<ul style="list-style-type: none"> <li>• Inefficient</li> <li>• Delivered into systemic circulation</li> </ul>
Aortic cross -clamp LV cavity infusion <sup>4</sup>	<ul style="list-style-type: none"> <li>• Increased gene transfer efficiency</li> </ul>	<ul style="list-style-type: none"> <li>• Accessibility, need open chest</li> <li>• High risk of myocardial injury</li> </ul>
Cardiopulmonary bypass perfusion and “closed-loop” system <sup>25</sup>	<ul style="list-style-type: none"> <li>• Specifically enhances coronary perfusion by separating it from systemic circulation</li> <li>• Allows for temperature control of solution, cold increased transfection efficiency</li> <li>• Increased contact time with gene vector through multiple - pass cardiac recirculation</li> </ul>	<ul style="list-style-type: none"> <li>• Not cardiac specific</li> <li>• Significant morbidity risk from cardiopulmonary bypass procedure (CBP)</li> <li>• Intended for patients undergoing CBP</li> </ul>
Ultrasound and microbubbles <sup>26</sup>	<ul style="list-style-type: none"> <li>• Increased permeability of capillary and cell membrane</li> </ul>	<ul style="list-style-type: none"> <li>• Only slightly improved gene transfer efficiency from myocardial injection alone</li> </ul>

**Gene Remedy for the Treatment of arterial illness**

A generality to a muscular-walled tubes activity blood to the guts incapacity is that arise and in 2009 counted for 1 of every half-dozen dying within the USA. The many amount of your time survival of tolerable delays with AN artery activity blood to the guts incapacity has most edges in medication concern effects and modes of action of medication and revascularization technique. Still a bunch of patients in United Nations agency area units with unmanageable to straightforward remedy has come into the view. These patients suffer from severe high blood per unit area despite of giant as doable medication remedy even to be no more cured at intervals settled through the skin associated with mediation. There are an activity bloods to the guts transplanted surgically. An auxiliary remedy replacement to be the entity established, named meditative<sup>[6]</sup> of latest blood vessels. The medical care concerned with managing the genes for antigenic growth factors to enlarge evenly as a default vessel enlargement. A stage of medical education

outcome to a dream that regular person can be allotted to a result toward the continued medical issued. It is stream by lacking in vitality force of medical trials has uninteresting this hope. The variety of individuals ending those analysis in that vessels may be complicated to implement. It requiring precise temporal arrangement of multiple growth factors working on transmits a sign to nerves to stimulate, and to sustain new blood vessel constraints. The VEGF may be a stimulated the cell division for vessels single layer of cells encouraging transhumance and fast copy of a cell.

This additionally shown the vessel permeability and cytoprotective reactions. The quick medical work seems sensible contract for remedial reaction with VEGF cistron treatments. The differential part of one trials showed that VEGF cure sorted with coronary artery bypass graft reduce the manifestation and development of muscle in the guts tissue.

The difficult inquiry is to inert prevail the relating locus of remedial blood vessels. It reluctant express if the cases

**Table 2.** Gene Therapy Targets for Coronary Heart Disease

Molecular Target	Stage in Development	Findings	Model	Reference
Vascular endothelial growth factor (VEGF)	Clinical trials, phase 2/3 Continued safety and efficacy	Safe but not consistently efficacious with increasing myocardial perfusion. Success with secondary end points, ie, increased exercise capacity and reduction in ischemic area	Human	Hedman et al, <i>Gene Ther</i> , 2009 <sup>46</sup> Stewart et al, <i>Mol Ther</i> , 2009 <sup>47</sup>
Fibroblast growth factor (FGF)	Clinical trials, phase 2/3 Continued safety and efficacy	Safe but most trials have not increased myocardial perfusion. Some have improved exercise capacity and symptom alleviation	Human	Kukula et al, <i>Am Heart J</i> , 2011 <sup>48</sup>
Hepatocyte growth factor (HGF)	Clinical trial, phase 1 Preclinical	Safe with negligible side effects from ADs; HGF in serum not detected after 35 days Increased capillary density and end-diastolic volume Improved cardiac perfusion and reduced apoptosis	Human Rat Pig	Yang et al, <i>Mol Biol Rep</i> , 2009 <sup>49</sup> Jin et al, <i>Gene Ther</i> , 2012 <sup>41</sup> Yang et al, <i>Mol Biol Rep</i> , 2010 <sup>42</sup>
Platelet-derived growth factor (PDGF)	Preclinical	Increased capillary growth and collateral formation from single naked DNA injection	Rabbit	Li et al, <i>Microvasc Res</i> , 2010 <sup>43</sup>
Hypoxia-inducible factor (HIF 1a)	Clinical trial, phase 1 Preclinical	Preliminary safety of ADs after 1 year Increased myocardial perfusion and improved LV function but no improvement in bioactivity end points	Human Pig	Kilian et al, <i>Circ J</i> , 2010 <sup>44</sup> Heinl-Green et al, <i>Eur Heart J</i> , 2005 <sup>45</sup>

ineffective since be an absence in advantage of the ordering of another organism (while had suggested that many vessel factors could also be the result) are unit establish to insufficient genetic science conveyance or unsuitable goal assortment. A supplementary treat escalated by Lee et al and Liuet al propose the possibility of a little remedial aperture at intervals. The overconsumption of the vessel component manufacturing hemangioma and coronary-artery disease of these problems have to be compelled by the classes out a head growing cistron medical care turns possible.

#### PROBLEM IDENTIFICATION

- To identify the hereditary diseases and possible genes to be relocated.
- Whenever the gene transplantation is made possible with modern facilities there is a hunch between identified gene pattern and result.
- The current tools such as cluster analysis will be very helpful to predict genes reason for the illness and to replace gene with various data from the parental sources.

#### OBJECTIVE OF THE RESEARCH

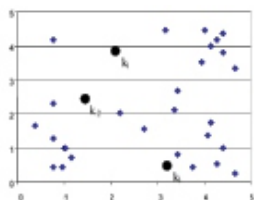
- By treating the diseases with gene therapy is more promising and can develop personalized treatments.
- By simplify the gene identification using clustering and interpretation can make them easier to analyze and necessary steps faster.
- The reliability and accuracy is basically achieved faster in predicting future observation.
- It saves life even by birth time

#### CLUSTERING PATTERN

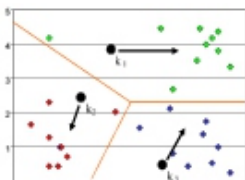
- The Idea is to cluster the  $n$  genes into  $k$  clusters, where each gene belongs to the cluster with the  $\square$ closest $\square$  mean[7]
- Algorithm:
- Locate initial positions for the  $k$  means[8]
- Associate every data point to the nearest mean, giving  $k$  clusters
- Recompute the  $k$  mean points for the new  $k$  clusters[9]
- Go to step until convergence
- Goal is to minimize

$$J = \sum_1^k \sum_{n \in S_j} \|X_n - \mu_j\|^2$$

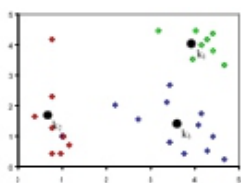
BEGIN



MIDDLE



FINISH



**MEANS CLUSTERING**

The K-means clustering is a method vector quantization, originally from signal processing, that is popular for cluster analysis in data mining. This results in a partitioning of the data space into voronoi cells.

**Result and Discussion**

This system compared the gene data of male and female, analyzed the pattern of among the womb and allocated the gene that can be reallocated.

The risk factor of not only diabetics but also other hereditary diseases also found using KDD and clustering model. ANT colony optimization model can find the exact pattern for reallocation. The results of gene therapy have modified a gene or genetic pathway to provide therapeutic value as shown in the tables, it also prevents from the number of diseases mentioned in the list shown above, and it also reduces disease by the methodologies in provided. It shows that t it has found the importance of development methods that is safed and effectual for the resent of human disorder which has been mentioned and incorporated in the table results and analysis.

It also categorized the important issues such as tolerance of the diseases using KDD environment and this also found the ease of management process need to be change the clinic.

This discussion extends the results of cardiovascular disease, gene therapy has been found to be limited in the form of medicines and treatment issues due to the transportation vectors and delivery to the target cell resulted in clustering model. The long-term expression with ADs is found to be limited in the resulting process. It has been previously present in the literature, The AAVs provide longer-term expression as found to be moderate and to some area it can avoid the host resistant system of the target cell. The existing endogenous antibodies to AAVs have been found to limit AAVs-mediated gene transfer in some patients. This was done in the CUPID trial of the system generated issues of the target cell, it is been prescreening for AAVs antibodies is important for finding a viable population in the resulted target. These show every extracted genetic material intrinsically possesses superior discriminate influence and we can finish that only few genetic materials are necessary to attain the high-quality molecular categorization recital. These comments are accommodating in influential appropriate and in our projected algorithm by arranged genetic material selection.

**CONCLUSIONS**

The genetic screening is unlikely to be practical on a broad scale worldwide. At more research needs to be conducted in the area of gender inequity for CVD, examining the reason that the majority of CVD victims are women. It will become increasingly necessary to simultaneously study genes encoding a variety of proteins that participate in both pharmacokinetic and pharmacodynamic[10]□pathways□ to evaluate the full contribution of inheritance to variation in drug response. This will require large, well- controlled studies that have been designed especially to test pharmacogenomic hypotheses. This system compared the gene data of male and female analyzed the pattern of cardiovascular disease flow among the womb and allocated the gene that can be relocated. The risk factor of not only cvd but also hereditary diseases may be found using KDD and clustering model. ANT colony optimization model can be found the exact pattern for reallocation.

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