International Journal of Trendy Research in Engineering and Technology
Volume 4 Issue 7 December 2020
ISSN NO 2582-0958

NETWORK OF DISEASES AND ITS ENDOWMENT TOWARDS DISEASE UNDERSTANDING

Tripathi Rajesh Kajal
Maharashtra institute of Pharmacy, Pune, Maharashtra
ktripathi285@gmail.com

Received 05 December 2020 Received in revised form 18 December 2020 Accepted 20 December 2020
Available online 26 December 2020

ABSTRACT

Disease Network is the science that has emerged to diagnose a disease from a network aspect specifically. Networks are the group that interconnect to each others similarly disease networks are the one that reveal concelled connection among apparently independent biomedical entities like physiologic process, signaling receptors, in addition to genetic code, also they prove to exists intitutive in addition to powerful way to learn/discover or diagnose a disease.Due to these networks, we can now consume the elderly drugs and its method to learn/discover the new drug accordingly.Example- Colchicine is used in gout but after repurposing it is also used in mediterranean fever. This is because there are many factors that affect the body during mediterranean fever and gout, we know that gout is a form of arthritis that causes pain in joints also mediterranean fever is the one which is accompanied by pain in joints, therefore colchicine is used as a repurposed drug again.In repurposing of medicines or drugs we first analyse the change in symptoms and identify the target organ and accorgingly we produce a drug that is compatible with pharmacokinetics of the body. As the availablity of transcriptomic,proteomic and metabolomic data sources are increasing day by day it helps in classification of disease .Also there are some networks reffered to as complex networks which can be called as collection of linked junctions/ nodes.

1.INTRODUCTION

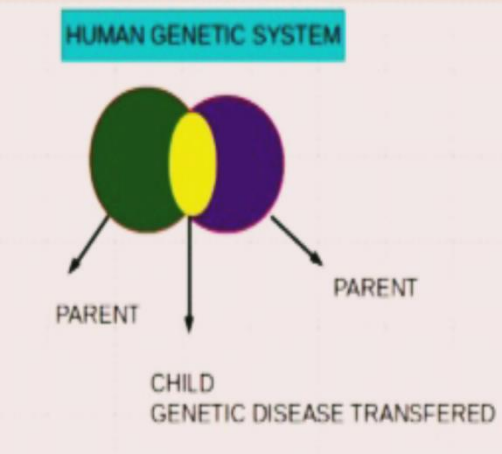
We understand disease when we diagnose it through symptoms. And when we understand the disease we get to know about the particular bacteria,or virus or any antigen affecting the body harmfully, also we get to know about various factors affecting the bacteria or virus in a particular tempreture/pressure etc therefore we design an antibody which helps us to get rid of bacteria or virus, but we cant forget that disease networks play a very important role here. Disease netorks are the one that tell us about the understanding of disease. Only through these networks we come to know about the disease. As we know due to functional interdependencies in molecular compounds there arise abnormality in gene but this is rarest because initially the molecular compounds only deals with other cellular components except genes.and show their symptoms but when heriditary is considered some of the disease come from gene where the abnormality arises from phenotypic character of previous one.

However ,networks define symtoms which have important role to play in every disease. Therefore network defines symptoms. Scientists named Erdos and Renyi created the network theory based on the mathematical model which was used to scrutinize the structural properties of a random network where pair of nodes were connected and an obvious expectation was observed which was reresented in the form of probability was observed.There is a graph theory in network theory which relates to nodes and edges having attributes. Network theory is a part of graph theory where graph is made by vertices connected by edges and network is made by nodes connected by links.

Actually network perspective is to look beyond formal, and simple designated relationships to complex connections between people, (if we call in terms of eukaryotic beings) but when we talk about bacteri,virus or germs then the network between them and the body is very complex. Complex network theory is an interpretation of statistical data (physics) of old graph theory aimes at description and understanding the composition that was created by connections between elements of a complex system. These elements are connected by junctions/nodes in a pairwise manner and in links whenever a relationship is observed between corrosponding elements. The resulting composition can be described by many topological metrics and can used as the base for reshaping the system.

Also disease networks expresses connections among junctions and edges in a graph, where G=(D,W), D represents set of disease called as junction/ nodes and W represents set of connections/ relationships (edges) based on similarity.Here meaning of similarity varies depending on data used to build the network which can be biologicsl or phenotyphic among other approaches. Therefore, through this article

we get to know that concept of disese network is just on limited to disease but to various other aspects like symptoms,treatment, precautions,etc .



2. ACCESSING METHODOLY

Due to alot of research was carried out on disease network and their contribution to understanding of drug and its repurposing we found out that there were five databases including Medline , Web of Science, Springer, ACM digital library and IEEE Xplore. The results were confined only in English language studies published from 2007 to September 2008.

Terms such as disease network, network medicine, drug repurposing, pipeline and many more were used for the search. The acquired studies and their results were analysed by a single researcher and evaluated by various co-authors so that now it can be considered as the systematic validation. Based on the eligibility criteria, there were analysis of articles, the study was included in the evaluation if:

(a) The studies inscribe the application of biological network to disease understanding and/or repurposing of drug.

(b) Process to build a network.

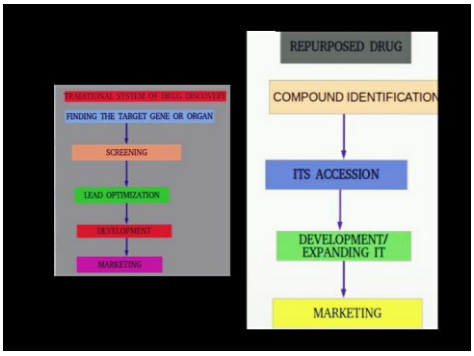
(c)Also if qualitative and quantitative information of the generated network is provided.

3.MODIFICATION IN NETWORKS OF DISEASES AND THEIR APPLICATION.

3.1.PRIOR STUDIES:

Human disease network was invented by Goh et al , he created a disease-gene bipartition network type of graph called “Diseasome” using information from OMIM database, and they discovered a human disease network(HDN) where couple of disorders are connected to each other if they have common genetic code.Therefore Drug repurposing plays an important role in disease networks and its understanding, drug repurposing is also called as drug repositioning where we utilize the medical indications of previous drug and can use our time ,cost and other factors for the disease that are really needed to be cured.Traditional drug development consumes alot of time ,energy and cost therefore disease networks are the one that help us to overcome the difficulties that we face during inventing a drug. As we know that we dont have the medication treatment for HIV virus, but by giving them the treatment we can prolong the life of a patient. Traditional drug development As we know all the drugs do have some side-effects , some diseases are acquired by the environment while some are inherited from genes, even if we try to cure a genetic disorder it has some or the other side effects, therefore we cannot cure genetic disorder by traditional means of research. Genes are the segments of deoxyribonucleic acid(DNA) and riboxynucleic acid (RNA) which have 99.99% similarity only 0.01% is the percentage which are our own characteristics.

One of the research says that diseases are prone to assemble by their classification and degree of distribution that follows a power law,which means only few diseases are connected to a large number of diseases, whereas most diseases have some links to others.In the year 2008, Lee et al created a metabolic disease network where two disorders were linked if the enzymes associated with them catalyze adjacent reactions. In 2009, a complex disease gene network was created by Barrenas et al using GWA(genome wide association), this network showed that disease which are under the same classification do not always share the common disease genes. Therefore complex disease genes are primarily used compared to monogenic disease genes in human protein. The business application of drug repositioning and engrossment showed by pharmaceutical companies have led to increase educational activity in this field.



3.2 NETWORK MEDICINE

Through network we can discover many drugs and those drugs can be used for either symptom based or genetic disease or disorder. Medicines can be made from networks through gene mapping, diagnose the symptom, or through prognostication. When we approach to a human disease through network, it becomes easy for us to identify what kind of disease is it or whether it has genotypic or phenotypic characters present in it.

Rzhetsky et al took the initial step and started his research in network disease using the phynotypic sources in 2007. The disease history of 1.5million peopleat columbia university medical center concludes the comorbidity links between various kinds of disorder and prove that phenotypes set up a highly connected network of strong pairwise relation.In 2009, Hidalgo et al raised phynotypic disease network (PDN) adding the connections of more than 11 thousand disease obtained from a pairwise comorbidity relations restored from over 30 million records from medicare patients.

Actually phenotypic disease network(PDN) help in understanding the genesis of many disease and their connection with each other.

Phenotypic disease network are the network which affect one or more physiological system in a living beings. Phenotypic disease network is not aware to the mechanism which is underlying the observed comorbidity but it shows that patient tend to spread disease in the network surrounding of disease they already have. It is also found that succession of disease differs across genders and ethinicity.

Recently an epidimeological HDN(eHDN) was created by jiang et al using data from taiwan national health insurance research data base and concluded that two diseases are connected to eac other if the probablity of co-occouring in clinics diverges from what was expected under self rule. Despite their illustrated potential in pathological analysis , the access and use of clinical record in medical research is restricted by several issues including heterogenity of sources, which are ethical and legal.

An analysis was done by okumura et al in which there was a plotting between clinical vocabularies and findings in medical litreature using OMIM as a knowledge source and metmap as NLP tool was done, following his design rodrigues et al found out diagnostic clinical finding from medline plusarticles by using the web scraping and the combination of NLP techniques using metamap tool. In further analysis the same team compared the performance of metamap and c in the same work.

Zhou et al constructed a human symptom diseasse network (HDSN)using symptom information from PubMed, in 2014. In HSDN the influence between the two disease quantifies the resemblence of their respective symptoms. In 2015, hoehndorf et al used a similarity measure for text minded phenotypes and created another human disease network.In both the cases the disease share relationship with number of genetic union .They also indicate that not only common ones are prone to be grouped into classes but also the mendelian diseases.

3.3.INTERACTIONS OF PROTEIN AND DISEASOME

As we know diseasome means a group of diseases and disorder including problems in genetic code too. Due to the complexity arising between disease and disorders, the consideration of a single factor whether it is a symtom disease, or a gene disease or a drug disease was a restricting factor to obtain new findings and predicting the drug to be repositioned, understanding this concept of disease networks various scientists came forward to give their contribution towards it, it is also called as HDN(human disease network). In 2012, Goh et al suggested that all the disease contributing factor have to be integrated in a context dependent manner for example molecular linkage from protein interaction, co – expression, metabolism, genetic interactions and phenotypic comorbidity links will be accordingly if we only consider them under symptom or gene associated disease. But if the

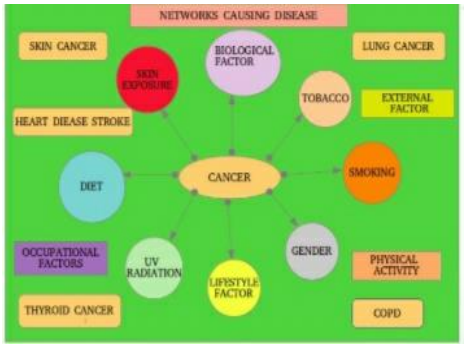
disease is drug based then, drug chemical information, toxicity and non biological environmental factors will be considered. The result will be the integration of common bipartition network which will be represented as single, complex , k- partite heterogeneous network , they are also called as complete diseasome. After doing research Gottlieb found out the solution in the same lines he made a wider collection of information sources and created five drug drug similarity measure with two disease – disease similarity measures. It means there will be interaction among five similar drugs with each other which will treat two similar diseases at one time. He used this similarity measures for predicting calculations to find out novel drug which can be useful for any kind of disease. Then scientists like Sun, Albornoz, Daminelli, and Wang combined various data sources and created tripartition network of gene – disease – ppi , gene – diseease – pathways, and drug – target – disease to predict which disease is associating with each other and which drugs can be used for repositioning. In 2012, heterogeneous networks are created from 17 different public data relating to drugs, chemical compounds, protein targets, etc. This was done was Chen et al. Later Zitnik accelerated the research on disease networks by incorporating ontology and molecular interactions by linking them to each other and created another heterogeneous network by linking 11 different types of data on metaphysics and molecular bond interaction, but when this heterogeneous networks were getting evaluated one of the most notable points were genetic interactions are most informative property as they are complicated and play their role in both chemistry and physics. In both the studies, logical thinking on phisophical networks as well as metaphsics in molecular bond were applied to illustrate the edges. A meritorious example is Hetionet which is an integrative network born after the studies of millions of billions of biomedical research. Its data was combined from 29 different sources to connect disease, pathways, biological processes and many more. However the disadvantage was lack of standard i.e a standard which was not established for calibration and this may lead to uncertainity in link description which may lead to misleading interferences. As shown in fig1.

As there is advancement in technology, this has resulted in the tools/ gadgets for the prognostication of treatment of new disease called as DTI drug target indication. example Rephetio , it was an activity based on hetionet which anticipate almost 3394 repurposing applicant drugs by calculating the algorithm for social network analysis. Another meritorious example is DTInet where DTI prediction system is based on how low dimensional feature vectors present a superior performance than other state of art prediction methods and created a potential applied to COX inhibitors to prevent inflammatory diseases.

4. DATA PIPELINE TO BUILD DISEASE NETWORK

As discussed in previous sections about diseasome, and various types of disease networks, the research in this field has resulted in expanding the knowledge and trying to search for more innovative ideas reguarding disease networks. We always consider similarities between diseases or we try to find out some of the similar link when we want to connect one disease to another, though we have aother approches to find out disease networks for example - computational approach or biological or experimental approach is also useful but we always try to find similarity among disease for its repurposing, this is because the target organ of a disease is same if they are related to each other so we have to block or stimulate that part of the receptor which can block the antigen to enter the body. Both the drugs are having same target because they are arrived from same network, the symptoms may differ because antigen may attack different part of the receptor or due to some other biological issue.

The function of the original drug and the repurposed drug differs by some points that is why the drug is repurposed. Additionally the drugs (both repurposed and original) share common phases like modelling, visualization etc also can be represented as functional unit of data science.



4.1.DATA SCIENCE NETWORK AND ITS PROCESSING

As there is growing availablity of information due to technology and other traditional methods there is improvement in the understanding of disease and its networks in various perspective. Data acquisition is something which is the first and the initial step, in data acquisition pipeline acquires data from different sources and present itself. In the second step pipeline consists of making the work more appropriate by transforming and mapping the given data. There are some literature sources such as PubMed or GWAS catalogue which is used for significant number of studies. Due to all these resources the standard of drugs and its application has improved alot. Researchers use biological means of data like KEGG,Biogrid or OMIM along with its type and and description for its use in network study.

Data science pipeline also processes action towards reproduciblity and similarity or differences among studies as a whole or in phase level. Recent studies collect data from books, experiments and various sources to give more accurate prediction capacity. This creates challenges for identification of a proper network source, for all these solutions, scientists used a word finder which addressed terms like MeSH, SNOMED ct or code listing. Including all the logical and hierachial source, we can allow maping data such as disease code or any medical term. In medical literature sources Metadata is more often mixed up with the word extraction tools such as Metamap.

4.2.DATA COMBINATION AND ITS STRUCTURING

To find out the answer to our question of our study, we have to process the integrated data and analyse it properly. After this, networks of disease are constructed from the output data of the previous stage and a model is made out of it. As they are made of nodes and edges, they can or cannot be directed or weighted. Depending on the type of node and its features they connect to each other. Due to disease network, the complexity in understanding the disease has led to various perturbations especially in human. In data combination and structuring there arises there arise molecular complexity between protein interaction and disease networks which become more stabilized when we know that the structure of protein and the combined data are related to each other.

Diseases are conneted to each other when they are connected to a particular gene or its part or if its a symptonm based disease then we can connect to both of them by finding out the hidden link or network between them that makes them connected. Due to various incomprehensiblities arising in drug formulation disease network has made it abit simple and appropriate.

4.2.1 SIMPLEST HOMOGENEOUS NETWORKS

They are the fine projections of heterogeneous networks, and are the most simplest one. Disease - disease networks are usually validated by using standard network method. In an uncomplicated approach the link weights results in disease – disease network that represent link abundance from the previous projection data. Methods such as hyperbolic weighting and resource allocation weighting can be used as alternative though complex but are useful. As we know homogeneous networks are built on similarity networks. In these networks if the comparison of i and j takes place and if the similarity points is greater than zero then the corrosponding vertices are connected and a network is created.

Homogeneous networks are the simplest networks coming from human interactome and are based on various types like its composition, duration of action, etc. The structure of protein influences function by determining molecules ith which it interacts and outcome of interaction.

5.CONCLUSION

At the end, we can say that network of diseases are complicated to identify but once we get also know the network we can easily find out the disease and take precautions if possible. We can get to know the approach of virus or bacteria in it's particular way. It may or may not be connected to genes but they are surely connected to a network coming from other diseases.

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