Comprehensive Molecular Diagnostics and Advanced Gene Expression Analysis

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Lecture 56 : Pharmacogenomics and Personalized Medicine

Namaskar. Welcome back to our module 12 of Comprehensive Molecular Diagnostics and Advanced Gene Expression Analytics course. The module is title quality control ethical concerns and futuristic trends. So, we will be learning new concepts over here and today's concept is a brief overview about pharmacogenomics and personalized medicine. So, we will cover these all aspects, we will be discussing on what are the factors that affect drug response right. What are polymorphisms? How the drug action varies based on the genetic variation of individuals right and then we will introduce the concept of pharmacogenomics, what are the technologies that are used, testing protocol, what are the common tests that various types of test for what drugs it is most useful right.

We will also briefly discussing the overview of role of pharmacogenomics in drug development will be exploring what are the benefits, limitation, future directions and will be paving the road for initial discussion on personalized medicines. We have a lot to cover. So, first of all you would agree with me that just forget about pharmacogenomics, just imagine a situation if you are a medical practitioner the better, if even if you are not you have this experience from your knowledge that one same drug do not act in the same way to different individual, one same drug may prove to be very good, very beneficial for one person, but the second person may not be at all treated or the treatment efficacy may be different. Again you and I may be are able to tolerate one drug very easily, another person may develop some allergy or drug rash right.

So, there is a variation how a drug acts and most of it actually are dependent on various factors there is no single factor right. Majority is a genetic variation because it is because of the genetic variation that is how we are brought up right. For example, if you consider the demographic factors that is age, gender, ethnicity, BMI, various other comorbidities alright, various family history, circadian rhythm basically how when we sleep when we wake up what is our sleep cycle. Another thing placebo effect in some cases it may happen that someone might think that the drug is very good the doctor who is prescribing it is very good and automatically he feels better right. Although the drug

may be a total I mean it may not be a drug at all just to test the this factor which is known as placebo the physician in clinical trial may give a sugar coated tablet which does not have any drug, but it still proves to be some degree of efficacious right.

So, these are various factors that may affect drug response. Again if you can see here gender, ethnicity, BMI etcetera these are basically indirectly based on our genetic makeup right. And if you consider the genetic factors definitely the our entire genome, transcriptome, proteome, the whole thing how central dogma varies from individual to individual, how what are the metabolic enzymes right, what are the various epigenetic modification even after the DNA synthesized, what are the various changes, what are the various areas of methylation. The various microbiome in our gut right the microbiological environment that is present in our gut have got a huge role in all these drug effects alright. Needless to say environment also plays a big role for example, nutrition what are the various drugs that are being taken together for example, drug-drug interaction, what are various exposure to various chemicals.

Again circadian is what I told you it is also an environmental thing if the environment is very cool and calm and it is very dim you may feel like sleepy, but everyone is a loud music going on it is very well lit sleep may be hampered right. And moreover compliance and adherence to a drug, a drug may only act if we take it for a consecutive 4 or 5 days for example, anti allergic drugs they take some time to act. However, if I just take one drug and in the next day for example, I take 5 days and then I discontinue the drug might not have the same efficacy compared to an individual who takes the drug for a long time alright. So, these are various factors, but among them the most important factors are the genetic factors, because all other things can be modified, can be instructed, can be monitored, but the genetic makeup is not in our hands. The doctors we doctors who prescribe medicine can definitely instruct a patient, a patient relative or a caregiver so that the compliance is very good.

So, the sleep is much better so that life is modified, but the genetic makeup of the patient based on which the drug action may vary is beyond our control right. Now we will have some idea brief discussion about polymorphism. Now polymorphism is actually the structural variation in the DNA sequence right and it is present an allele frequency of 1 percent of or greater in a population right. So, polymorphism actually I mean two same individual having the same DNA sequence, similar DNA sequence doing the same function can have some minute variation. Now this variation obviously happened due to mutation right, change in the nucleotide structure right.

You already know the basics of why there might be a variation in the DNA sequence. Now there are two things that we should be aware about. There might be single nucleotide polymorphism I mean these phenomena can be divided into two cases, two

user case scenario. Number one where this variation is present frequently right. I mean for example, there are 100 individuals or 1000 individual and this variation is present in more than 10.

So, more than 1 percent when this is the case this is known as single nucleotide polymorphism all right. So, greater than 1 percent all right. However we need to know about another phenomena specific that is known as insertions deletion indels that are very uncommon that are not actually common right. They are also variation in sequences, but in case of indel or insertion deletion the short acronym that we use indel right insertion deletion they are much less frequent that is less than 1 percent. So, a variation that is happening frequently that is an alteration or a modified gene sequence and that is quite frequent more than 1 percent of the population.

Then we refer to it as a polymorphism right. Now when the polymorphism is present due to a change of a single nucleotide that is known as single nucleotide polymorphism. However in general we use this polymorphism and S and P synonymously right. So, you might find in some text book that they are referring S and P's as the change in more than 1 percent and in some text book polymorphism again they have divided into two cases. However you should know this that indel is not a polymorphisms for polymorphism it has to be more than 1 percent right.

These are the two types of sequence variation in types of sequence variation there can be one insertion deletion and one polymorphism. And in polymorphism it can be single nucleotide multiple nucleotide like that right, but most common that we are interested in for genetic variation in relation to drug response are S and P's or single nucleotide polymorphism where there is a variation in a single nucleotide that occurs in a specific position in the genome right. So, it is in this position only where the gene I mean the nucleotide is varying in majority it is present I mean the A base is present. However in some cases there might be a G variation in some cases there might be P variation. So, among 100 of cases right there might be.

So, 75 individuals have got this genetic structure where this nucleotide in this position of the gene have got A base whereas, in 23 individual G is present and in 2 individual T is present. These two are actually polymorphism why because it is greater than 1 percent if it is less than 1 percent we will not consider it as a polymorphism. So, polymorphism are genetic variations that are frequently found. So, what will happen right? Now basically this figure you will be able to understand after we have discussed the concept of pharmacogenomics, but let me tell you pharmacogenomics drug is a drug that is specially designed for the ones who have a genetic variation. Why let me tell you for example, this is how the drug looks like there is a triangle there is a ball attached to it and the drug receptor for example, the protein on which the drug need to act has to be a

of a complementary shape.

Now as you can see this is the shape of the target protein and the drug can easily come and bind because the drug is shaped like this it can easily bind and act. However, in case of a genetic variation for example, S and P the gene will quote for a protein we see that the target drug is like this the shape. So, the circular part is absent. So, the drug cannot go on attach and if you use the same drug for all for without looking into the genetic detailing the drug will be inefficacious in that patient. Hence we are using this concept we are designing a drug which is tailored to the genetic makeup to the proteomic makeup of the patient the protein target and then that can actually be successful in exerting its therapeutic efficacy right.

So, this is a very brief early concept of pharmacogenomic drug that you need to know alright. You should have some idea going forward. Now basically why do they happen for example, two individuals why they are having a different action why the same drug is not acting in the same way. The issue is this is a concept of pharmacology these two terms pharmacokinetics and pharmacodynamics right. Pharmacokinetics means basically what body does to the drug.

For example, I take a drug then it is absorbed it goes through some tissues it is distributed and finally, it reaches the target organ right. So, these are basically what a body does to the. So, there are multiple steps which a drug need to cross in order to reach its destination right. Therefore, this can vary from individual to individual because two individual might have different absorption, two individual might have in different accessory pattern, two example two individual might have different metabolism, two individual might have different gastric acidity right. Two individual may have different levels of circulation, so distribution of the drug might be different comparing a baby and a healthy adult a baby might require I mean might have a very small volume of blood.

So, the distribution will be much more whereas, in case of a normal adult in which the drug is prescribed for it will act normally, but in case of a individual it heavy body weight is body mass may be so that the drug may be distributed in a very less amount. So, all of these factors fall under the pharmacokinetic property and definitely with genetic polymorphism with differences in these phenomena the action of what body does to a drug will be different. Again what is pharmacodynamics? Pharmacodynamics deals with what drug does to the body. So, when drug goes inside the body it will exert various effects on various receptors, it will reach various chemicals, it will influence various ion channels, it will lead to I mean induction or inhibition of various enzymes, proteins etcetera. Anything that is also driven by the genetic makeup of the individual all right because some receptors might be drug resistant therefore, the drug might not act right as I as you see right.

For example, here the this drug will never act on this individual therefore, we need a new drug right. So, both pharmacokinetics and pharmacodynamics affect do affect how a genetic variation can influence the drug action on any individual. So, basically if you summarize this whole thing I mean in layman's language basically when medications are consumed they are broken down into various components or various enzymes right. And in theory this should be absorbed in a similar way in all human beings right because we have we share the similar genetic makeup compared to any other species, but there are so much variation in human species because of the different genetic makeup that is these subtle changes can alter the pathways that the medicine does not work similarly in two different individual. In fact, it may have radically different action from one individual to the other right.

So, here the pharmacogenomic testing is of particular importance why because it targets particular biomarkers very important that pertains to a specific class of medication. It explores so pharmacogenomic testing mind it we have not still yet defined what is pharmacogenomic testing we are discussing something about it right. So, pharmacogenomic testing what it does it explores. So, whether some possible areas can be determined so that we can design the drug in such a way in which a drug can be most effective for case to case for SNP to SNP for variation to variation right. So, take an example for example, one person I would say majority metabolizes a drug very quickly metabolizes means whenever I am taking the drug the drug is cleared from my system based on my circulation for example, it is excreted in the liver or it excreted in the kidney it goes at a very rapid rate the drug is very efficacious mind the drug exerts its action and it is rapidly cleared.

So, to treat me for example, I am a normal person I do not have any genetic variation you need a huge amount of drug for example, 10 gram per kg alright 10 gram of the drug per kilogram of body weight right just an arbitrary example. Now we are dealing with a similar disease where we need to prescribe the drug, but that individual has got some genetic variation where the drug is metabolized slowly it is not cleared as quick as compared to normal individual. So, what will happen the drug will be efficacious the drug will exert some action, but it will be very slowly cleared, but it will be cleared nevertheless right if we wait for some time the drug will be totally cleared. However if we already know if we already find out that there is a slow metabolic rate then that person in reality will need a much lower dose of the drug to attain the same efficacy because the efficacy of the drug is based on something called half life that is the amount of the drug that is present in the system. So, here that individual who is a slow metabolizer of the drug will need lower doses in order to avoid a side effect because if the drug is not cleared it may lead unwanted to unwanted effects fine.

Now in case of very small individual they might have two genetic variations just an example and that has led to a problem where only the very fine portion of the drug right is metabolized, majority is not cleared from the system. So, what will happen they have got a high chance of very serious side effects even on small dose even on minimal dose you get my point. So, first there was a individual who was having the drug it was very easily cleared we need suppose this much amount of drug for the normal individual. Now we have got a case of poor metabolizer for that one who is rapidly metabolizing the drug not rapidly metabolizing the drug slowly we need lower dose and one who is not at all metabolizing the drug. So, for them we need to be cautious for them we need to avoid the drug totally because even a small amount can lead to toxicity right.

So, based on all of these genotypes I mean how patient do behave when a drug is taken they can be classified into four types right. Number one for those are known as extensive metabolizers. So, what happens in those individuals they have two normal genes right and they metabolize the drug normally fine absolutely right no problem to the physician to the patient. Next intermediate metabolizer means a patient those who have one I mean for normal metabolism both the genes needed to be active if one is active one is inactive they are slow metabolizer. So, they need lower doses in order to attain some efficacy.

So, these are moderate cases or rather normal cases there might be there is a high probability for example, I showed you 75, 23 and 2 these patient with slow metabolizer you can consider them as 23 percent of the cases that is very frequent, but not majority. However, we can get to extreme cases for example, those 2 percent they can work in both way. Number one ultra rapid metabolizer means they have something called gain of function gain of function mutation means they are rapidly metabolizing more so than the normal individual means in that in these individuals the drug is getting cleared a much earlier than how it was supposed to be. And in another case the person is not clearing the drug at all in which the both the genes are non functional right. So, what can be the consequence right so based on that you can think of right.

For example, the in case of the person who is slow metabolizer all right and who is fast metabolizer and the one who is rapid metabolizer and the one who is non metabolizer you analyze them one by one. Here for the one who is rapidly metabolizing ultra rapidly metabolizing there the drug is not remaining in the system at all right. So, for them the drug is neither beneficial nor toxic because even before exerting action drug is being cleared all right. For normal individual with normal genetic makeup right the drug is beneficial it is not toxic because it is remaining the system exerting its action and it is being cleared right. For slow metabolizers right the toxic word is being hidden in the animation you should note this class that is the one who is a moderate case and who is slowly metabolizing the drug is beneficial, but toxic.

So, we need to be cautious we need to lower the dose and for the who is not metabolizing the drug at all right even before exerting its beneficial effect there will be manifestation of toxic effects of the drug. So, drug will be not beneficial, but toxic. So, these two are extreme cases and these two are moderate cases ok these are extreme this one and this one extreme case right these two are moderate case I hope it is clear all right. For your convenience I will just erase the whole arrows and let you decide because it is so much scribbling it might not be easily visualizable for you leave it to you to decide which case will be extreme case and which one will be moderate case all right. Next, we have seen due to this phenomena majority of the drug are ineffective for many.

You can see these are the percentage that have been procured by various studies for example, these are very common drugs that are used cholesterol drugs, anti cholesterol drugs for high cholesterol statins, statin group of drugs are only efficacious in 30 to 70 percent right and rather you can see the I mean if you say 30 to 70 percent efficacious it is again ineffective for 30 to 70 percent right. So, considering asthma drugs for asthma selective beta 2 agonist 40 to 70 percent anti depressants very common use drugs. Hypertensive drugs very important antihypertensive drugs ineffective for 10 to 30 percent drugs for congestive cardiac failure again ineffective for 15 to 25 percent. So, imagine the situation where the patient is actually spending money going to the right consultant following the right advice following the right lifestyle modification, but only to see that the drugs are not exerting any effect right. We may often find it is a I mean we often can explain it in many different ways, but the truth problem I would say concern lies in the genetic makeup of an individual how it happens all right.

So, we introduce the term pharmacogenomics. So, what is this? It is basically the study of the role of a genome in drug response very important. So, what pharmacogenomics does it aims to develop rational means to optimize drug therapy with respect to the patient's genotype to ensure maximum efficacy with minimal adverse effects right. Mind it pharmacogenomics aims to develop this means of drug therapy right. This drug therapy has got a different name if you have guessed it right it is personalized medicine that is coming later, but pharmacogenomics helps us to get there. So, what will pharmacogenomics allow? It will allow individualized medication that can be used based on genetic determined variation right.

So, it is it will not be the same I mean the average drug for everyone right. Based on the genetic makeup genetic structure we will prescribe what drug you specifically in what drug I specifically need I do not need to take one drug which may be efficacious for everybody because it might not be efficacious for me if I am having the genetic variation alright. Again use of medication otherwise rejected because side effect again that individual might not have that side effect proven by genetic makeup we can use that medicine. Method of accurate dosage very important right accurate dose determination

by pharmacogenomic testing very much possible so that unwanted side effects are avoided. So, there is one term I mean that are often you might often find that is pharmacogenetics and pharmacogenomics both are used interchangeably.

However, mind it pharmacogenetics is an older term that was used that was we introduced much earlier it is basically difference of genetics versus genomics you can apply here. So, pharmacogenetics is often the study same thing we are studying a drug response with response to a gene right. However, we are only targeting a singular group of functional related genes right one doing one single function. However pharmacogenomics right targets a blanket thing. So, many drugs many genes right a group of genes allow predicting the response to multiple drugs fine.

So, pharmacogenomics is much broader concept pharmacogenetics single gene single drug pharmacogenomics multiple gene multiple drugs. So, that we can take an informed decision about many drug interaction many things are taken into account in pharmacogenomics, but not in pharmacogenetics again let me say tell you they are often used interchangeably the concepts fine. So, what are the technologies that are used in pharmacogenomics? Number one DNA microarray. So, now we are getting into familiar grounds because you already know these techniques.

So, we need to find out with the help of testing. So, whenever pharmacogenomics testing it is referred basically we are studying the genetic makeup of an individual right. We are doing various assays to test the genetic makeup. So, that we can get an information about what is different in this individual or what is right or wrong with this individual. So, DNA microarray, pyrosequencing, mass spectrometry, any fluorescence based platform, RFLP, RTPCR you just name any study you can think of to study genetics the protein proteomics we can apply that in pharmacogenomics right. So, there are few drugs which are actually the major culprit what led the physicians to think like that that this drug is not having the similar effect or side effect to many individuals right.

And that is why these drugs are the ones which have been targeted based on which various polymorphisms have been studied. So, this is the chart this is very important for those who are actually preparing for various competitive exams right. And for those who are doing disease specific and drug specific research like for example, very important warfarin CYP2C19, VKORC1 very important you can find multiple articles. Again see the drugs that are mainly of the concern warfarin again clopidogrel another anticoagulant very important pharmacogenomics testing is often done. Antineoplastic drugs so cancer chemotherapeutic drugs, ironotecans, 6 mercapto purine, azathioprine, tamoxifen, antirepressant, amitriptyline, nortriptyline also nortriptyline used for neural pain right.

Narcotic analgesic, codeine, tramadol same anti I mean pain killer you can say pain killer in layman's language narcotic analgesic which kills pain right is not efficacious for any two individual. Two individual might be writhing in pain one acting magically to another is not reactive. Again there might be problem or change difference in the genetic polymorphism immunosuppression drug tacrolimus same story. So basically we are exploring whether these drugs are having I mean whether the individuals are having these polymorphisms and that will want the physician to predict the side effect to lower their dose to treat the individual cautiously. So what are the basically test protocol or workflow you can say? So I mean contrast to traditional way of prescribing patients the individual the modified way will be physician orders a pharmacogenomics test to start with right because I think that I need to prescribe this to the patient.

So I will order a test samples will be collected will be sent to the laboratory the specific pharmacogenomics testing will be run on that specimen the data will be analyzed and the report will be reviewed with the physician right. So that now I know that the drug is actually safe to prescribe that patient right not just family history. We often this is a growing field right it is not adopted universally it is being done in few user cases specially in western countries. However nowadays even in peripheral set up we just incur whether there is any family history of allergy whether you have any allergy to other food and then we empirically prescribe there is no window of that as the medicine is advancing right. So what are the various types of pharmacogenomics test? If you can target the various specific drugs you can easily categorize the test for example, human leukocyte antigen the reason of various genetic makeup difference of various individual.

So HLA test Abacavir right HLA-B5701 anti convulsants HLA-B1502 close up in all these anti psychotic drugs or psych and psychotropic drugs they are have got their specific human leukocyte antigen HLA based tests right and they can reveal various polymorphisms. Again drug metabolism related gene test for thiopurine right mercapto purine, fiprocel all these anti cancer drugs tamoxifen, ironotecan right UGT1A1, delucose transferase in the liver right UDP glycorine transferase in the liver they actually affect again cytochrome P450 based enzyme very important for assaying drug metabolism whether a drug will be fast metabolized or slowly metabolized. Next so drug related gene test trastuzumab, dasatinib all these are related to anti cancer drugs and immunosuppressants mainly for various drug actions. So some drugs may be tested for both combined metabolism as well as genetic testing example warfarin it is we are being testing for both VKORC1 as well as the cytochrome P450. So this one is the metabolic part, this one is the genetic part of the individual that needs to be tested before we are subjecting the patient to a dose of anticoagulant or warfarin.

Now whether these are all theoretical possibilities or whether they do exist definitely they do exist for this amplichip which is was initiated or introduced by Roche

technology Roche diagnostics Roche diagnostics it is an array basically a microarray of CYP P450 enzyme mainly 2D6 and 2C19. It helps us the doctor to understand whether the drug will have a side effect etcetera. So all these things that we have discussed it is possible right. The first FDA approved testing that was actually approved way back almost 20 years right and things are advancing since then right. So already approved things are being done, but in western world.

So again do pharmacogenomics have any role in drug development definitely they do how they can contribute to a smarter drug development process. All these I mean features all these phenomena all these concepts that I have discussed right now you can actually write this answer in your own I mean without me discussing anything. So prediction of efficacy and toxicity definitely better drug which will act better which will be less toxic which have less side effect definitely pharmacogenomics having a role in drug development. Next again so by looking at the genetic makeup of the individual we do not need to recruit so many individual just to test the efficacy of the drug empirically right. If we have got small number of samples to define genetic makeup right we can easily conclude that this the efficacy of the drug is due to this genetic makeup and that will definitely does reduce the number of patients that are involved in clinical trial once we incorporate pharmacogenomics testing as a part of the drug trial right.

That will indirectly not indirectly directly reduce the cost because of the manpower if a huge sample size huge number of patients to test huge number of patients to monitor the side effects that increases the cost. So when that is reduced the cost to bring the drug to the market the time to bring the drug to the market is also reduced. So remember pharmacogenomics help in drug development in these ways. So what are the benefits I mean there are multitudes. Number one personalized medicine which will be discussing very soon.

Just to give an idea what happens to develop customized prescription whatever I want I will be given that I will not be given a universal prescription not a trial prescription that works for everybody and that will work for me no right. So very important to screen monitor various diseases to predict a patient response to a drug if I have a genetic makeup I know I will warn the patient that this drug will have this side effect the moment you see it you discontinue. Generally it is also warned everywhere. However I will be confident enough to not give the drug to the patient at all. So in case the patient might be learned I mean might be demanding I need this drug I can definitely have evidence that why I am not giving the drug it may prevent legal implications right.

Again improve drug efficacy reduction of side effects, optimize drug development as I told you very important develop power and safer vaccines. Same way drug same way vaccine development. So definitely I explained how it save the cost. So when a patient

knows that I am 100 percent sure this drug will be most efficacious this will be least exerting any side effect the acceptance will be much more.

So patient compliance very important it will be very high. Prevention of drug resistance the genetic factors can be easily identified in advance and the drug may be designed in such a way that there will be no drug resistance there will be 100 percent efficacy right. And again very important chemotherapeutic drugs have got a high percentage of inefficacies. So the same chemotherapeutic drugs might not act for example, two individuals having cancer, but if we increase this compliance if we increase this efficacy very important precision, oncology, personalized medicine for oncology a big area where pharmacogenomics have got a huge benefit right. And lastly not lastly one of the major area that I have enlisted last is a R and D for development of new drugs. Purely pharmacogenomics testing can lead to drug development based on tailored needs of the patient.

So what are its limitations? The limitation being the data is very less whatever study have been done have been done in western world and in smaller population for limited number of drugs right. There are variation in test to test there is a limited data in validating these results all right. So, that being said so limited variability and limited clinical evidence western data of population right. Moreover there is a most of the test have been done targeting one or two genes. However as we know we have seen in the very first slide there is a multitude of factors there is a multitude of genes that might affect a drug response.

So we need to improve mind it I have told you multiple limitations at the portal are the ways how we can improve. So we need to still work how we can introduce multiple gene generic test for a single drug. Cost accessibility it will reduce the cost however in order to perform the test it is costly right. Not only that there is a issue about insurance there is a issue about reimbursement so regulatory and reimbursement charges challenges so whether they are being reimbursed right.

These are all very much challenges that needs to be addressed. Moreover the knowledge of various physicians right so they need to be well made aware they need to be made I mean cautious about this mode of treatment and you know the basic individual nature we resist changes right. So there should be a whole lot of integration of the thing into clinical practice in order to make it most effective and very important the dynamic nature every day new drug is being added every day new gene action is being discovered. So a constant knowledge database to maintain is a huge challenge in itself right. So what can be the future advancement? So future advancements of the work flow I mean in an ideal situation we are designing appropriate drugs based on a profile we need to prepare the ethnic profile of an individual the racial diversity considering

everything right and based on that we are designing the appropriate drugs right. After exploring the ethical diversity we are again going deeper and determine the location of the exact proteins and metabolites that are non functional that may be different right.

Based on that we are preparing an index right of the pharmaceutical sensitivity what are the food sensitivity everything right by analyzing each and every variation we need to make a profile SNP profiling and then based on those profiles we can create some laboratory markers those markers can then be analyzed and then it will easily help the physician to prescribe the drug that is necessary for personalized medicine. This is the last concept we will be discussing it in very brief. So what is personalized medicine? It is also known as precision medicine mind it it refers to healthcare approach that customizes medical treatment intervention to suit the individual characteristic of each patient. So whatever I need I am being treated. Pharmacogenomics is a way of going of attaining personalized medicine mind it those two terms are different right pharmacogenomics actually the study of genetic variation of a drug.

Why you are studying pharmacogenomics? One is for personalized medicine. So what does it do? From the definition itself it is very easy to know tailors medical treatment of an individual such as genetic makeup lifestyle environment everything is being taken into consideration when the medicine is being given right. It helps us to optimize again the outcome minimize adverse effect almost similar you can find very similarity between the pharmacogenomics benefits and the personalized medicine features right. So we are considering the patient's unique biology unique health profile unique cellular environment and then we are prescribing the drugs. So it encompasses various approaches including pharmacogenomics various biomarker driven therapies targeted treatments so multiple factors are playing a role but pharmacogenomics is playing a major role. So we will have individualized treatment plans right basically not one size that fits for all.

So one medicine that fits for everyone does not need to be prescribed to me or I will not take that medicine I will only be prescribed one medicine which has been specifically designed for me that will be the most efficacious that will be the least having the least side effect that will be the least dosage and that will have the best outcome right. So patient centered care across medical facilities right not a generalized care not a cocktail on the drug regime will not be based on the average patient alright the concept of average patient will be abolished and it will be case to case person to person. So basically this is the network or the framework how we can attain personalized medicine we will need genetic data the drug response phenotype we need to consider various environmental factors pharmacogenomics of course plays a key central role. Again we need medical professionals to be educated right we need various insurance issues to ensure whether they will cover the medical expense or whether the regulatory body allows such

medicine treatment there will be privacy issues because there might be some tabu or I mean social agenda that this medicine might be needed for this individual whether I will at all take this individual or not so we have to abolish or we have to look into all those privacy issues and sort them right and healthcare cost as always will everything will help us to attain this personalized medicines which is the end goal that in the current prescription whenever we are prescribing a drug 100 percent patients are never getting treated only 30 to 60 percent of the patient responds to one drug the doctor is absolutely fine very experienced the patient follows the drug regime the patient sticks to what the doctor has told still he is not getting treated. However, as the day advances in medicines when we are prescribing with respect to genetic makeup the individual we can be 100 percent sure that the patient will respond to the drug in with 100 percent efficacy.

So, to summarize pharmacogenomics enables personalized medicine by prescribing drug response reducing adverse reaction optimizing therapy it has got role in multiple domains for example, oncology precision oncology including I mean increasing patient compliances tailoring prescription helping in disease screening. Next very important new molecular tests are crucial for detecting genetic variation and therefore, pharmacogenomics and pharmacotherapeutics are fundamental in diagnosing and treatments so the day will come when pharmacogenomic testing will be incorporated in medical treatment. So, overall pharmacogenomic revolutionizes the health care by improving drug efficacy and streamlining drug development as well as the approval process. So, these are my references for today's class and I thank you for your patient hearing.