Nobel Laureate for Medicine Dr. Sir Richard Roberts' keynote speech and dialogue "Why you should love bacteria" on Friday, February 10, 2017 at Gadjah Mada University in Yogyakarta (Indonesia)

It is a great honor and pleasure to be here and it is always a delight to talk about bacteria, I love bacteria and I do everything I can to make everybody else love bacteria, and so during the course of this talk I hope to convince you that these should be your friends, that these should be bacteria that you really appreciate, that you love and don't feel that you have to go and wash your hands every time you touch anything.

I would like to start by talking about where bacteria stand within the tree of life and I will do a fairly broad spread of where we find bacteria in the earth, then I will move into humans and talk about bacteria that live with us, and I will explain why they received such a bad name, and then I will tell you why they really do not deserve the bad name that they have received.

If we look at the tree of life, on the top left you can see a big branch and that are the bacteria. Those are the most primitive form of life that we know about of organisms that are actually truly alive. To the right of that are the archaea, for a long time they were confused with bacteria, but they are in fact quite different. They have some very different properties. They typically live in very harsh environments, high or very low temperatures, highly saline environments, and they have a lifestyle that is somewhat different, and in fact they are probably quite close to some of the original forms of life that appeared on earth.

Down at the bottom are the eucarya. These are the eukaryotic organisms which are all the organisms that you typically think of as life. When we walk around outside we see trees, plants and flowers, we see animals and we see ourselves, these are all the eukaryotic organisms and you might wonder that these were perhaps the dominant form of life on earth, but in fact they amount for about 40% of the total biomass on earth. The vast majority of this biomass are bacteria and the archaea and organisms that are microscopic and that you can't see unless you have a microscope.

These organisms live with us, they live with every animal and every plant, they live in the soil. If I dig three miles down into the earth we find bacteria living there perfectly happy. The oceans are full of bacteria, you go to the seafloor and you discover huge bacterial mats living down there. Bacteria are everywhere, and yet we know relatively little about them, as is often the case with things that you can't immediately see, we have not studied them as much as we should. We tend, as scientists and biologists, to investigate the macro side of life, things that we can see. It's been relatively easy for Darwin and naturalists and so on to go off and see and study the animals. This tended to be what we studied.

The bacteria on this tree of life occupy quite a large area on the top left, but I would like to draw your attention to the eucarya where you can find zea, this is maize, a plant and right next to it is homo, humans. The length of the line connecting homo to zea tells us how far apart we are in an evolutionary sense. If you go from bacteria all the way down the tree to get to men then there is huge distance, we are a long way apart, but it may surprise you to know, that you and I are full of bacteria, and if we kill all of your bacteria we would die. Without them we simply cannot survive, we need them, and this is true for most of the organisms that are living one earth. If we kill the bacteria they will die. This is something worth considering when you start taking antibiotics and when you start to kill the bacteria that are normally living with you.

What I want to do is to go quickly through and talk about one or two of the organisms that are essential and have played such an enormous role in this planet. I start with a cyanobacteria called Anabaena St. Johns. This organism is exceedingly old, it is one of the oldest bacteria that we know about, and it had the unfortunate property, when it started out, to finding itself in an anaerobic environment, an environment in which there was no oxygen, because all of the oxygen was tied up in chemical compounds of one sort or another. Anabaena was quite happy to grow this way, but in doing so it slowly hydrolyzed the bonds that connected the oxygen, to say metal or hydrogen or some others, and released it into the atmosphere, in much the way that we today release CO2 into the atmosphere.

What happened to anabaena? It almost wiped itself out of existence, because it had to learn how to adapt, it polluted its environment and most of these organisms were not able to grow, and only a few of them figured out how to change, so that they could live in an oxygenated environment even though they preferred an environment without it. So they were able to survive in very small numbers.

We are in danger of doing the same thing, because of what we are doing to our environment and to our climate. If we are not careful we will suffer the fate of the Anabaena and almost pollute ourselves out of existence.

The myxobacteria are bacteria that I think are particularly beautiful and they are responsible for rotting wood. If a tree falls down in a forest then very soon these trees are colonized by myxobacteria. The myxobacteria are quite complicated as bacteria go, because they can actually form little fruiting bodies that look much like mushrooms. They can produce spores which they can spread around the forest, and in this way, when the next tree falls the spores are there ready to start eating it. So these organisms which you almost never see really play a tremendous role in recycling the wood from fallen trees, and from other kinds of plants that one finds dying in the forests.

This is an example of a spiral bacteria and I want to draw your attention to this particular organism because there are many hundreds of different types of spiral bacteria, and these were some of the very first we have ever seen in a microscope. If you look in the middle of this cell you can see a big black line, this is actually a magnet, it's iron hematite and it senses the earth's magnetic field and this bacterium uses it, in order to know whether to swim north or south to find food. So this is a very sophisticated bacterium that is just a little magnet.

There are many extreme environments on this earth, some of them you know about very well here on Java. You look around at the centre of the Island and you have this constant range of volcanoes, which makes it very nice to fly past the island, but nevertheless these volcanoes cause some problems. The volcanoes are not limited to land, they also occur in the oceans and in the oceans we think of them when they erupt as steamers, black steamers, thermal vents, and they have some very interesting life that becomes associated with them. They poor magma together with hydrogen sulfide and many other noxious gases and minerals, and form this big black smoking chimneys that we call vents. The temperature of these vent's at the sites of eruptions is about 300 degree centigrade, but because the ocean itself is 4 or 5 degree centigrade, there is a thermal climb that takes place, a fast change in temperature, and it is in this region where life grows. You can see some red and white organisms here on the side and these are tubeworms, they are neither true eukaryotic organisms, they are worms in one sense, but they cannot live without the bacteria that live within them, in fact the worm is

just a big case for bacteria that are living of the hydrogen sulfite that is coming out of the vent, they use to break down the hydrogen sulfite to generate the energy that they need in order to grow. These worms produce larvae which is then swimming around in the ocean, because the vents don't last for very long, maybe they are active for 3 or six months or a couple of years, but they aren't active forever, and so these organisms need in order to survive to go and find new ones as they appear. When a new vent appears within a matter of a week or two it is colonized by these organisms. There are many other organisms that grow there, but these are particularly interesting to me, because of the large number of bacteria that they need for their life.

For any of you who have been to the US, and I suspect for those of you who have been at the environments close to the volcanoes here, you are familiar with the geothermal areas that are particularly beautiful to go and visit, and one of those in the US is Yellowstone National Park. It was the very first national park in the US and it is an absolutely fascinating place. It's a volcanic caldera, and the life that lives there, the geothermal activity there is quite extraordinary, it's one of the most beautiful areas in the world and if you get the chance I would absolutely encourage you to go and visit it.

But I want here to point out these areas at a geothermal spring, with a green band where typically the temperature is in between 70 and 90 degrees, and these green bands are photosynthetic bacteria that are living of the CO2 by harvesting the energy from the light, but they also getting some energy from metabolism and from the heat from the spring. On the right side you have some brown and orange parts, and these are also photosynthetic bacteria that are living in very high temperatures, and one of the things that are very nice about these organisms is, that they have very many interesting enzymes in them that find use commercially. This has been a very profitable group of organisms to be looking at, in order to find commercially or industrial use for these enzymes. You probably could do something similar here in Indonesia by looking at the pools and the organisms that are living near the volcanoes and are growing at very high temperature, I am sure they have interesting properties too.

One other thing that happens in Yellowstone is that because of the high concentration of hydrogen sulfite that is coming out of the ground, there are organisms called sulfolobus that will convert the hydrogen sulfite into elemental sulfur, and so you get these huge yellow sulfur-pools all over the place, and these look very inhospitable and they smell terrible, but these organisms, sulfolobus, they love them and grow perfectly happily there.

Now I would like to switch gears a little bit and talk about humans and bacteria. One of the things we have thought about for much of the life of the biological sciences is that the human genome determines our fate, tells us what we are going to be, whether are male or female, short or tall and so on, and when the Human Genome Project was conceived the only target was the human genome, the DNA that was in human cells. However, we forgot the possibility the bacteria that live with us are also a part of the human genome. We forgot that we couldn't kill all of these bacteria and still survive, and so the bacteria and the human genome are really a very important symbiosis, two or more organisms that live together.

If I look at a typical human and ask how man human cells do you have then the answer is about 10^{13}, a goodly number of cells, but then I ask how many bacterial cells live in this typical human, and the answer is somewhere between 10^{13} and 10^{14} bacterial cells, that's between the same or 10times as many as human cells. Among all of these cells you can ask how many strains are there, and for human there is just one, but for the bacteria the best estimate is that there is a minimum of 20 thousand different strains of bacteria that live with anyone of us. The numbers are enormous, and they live all over us, all over our skin, in our hair, under our armpits, in our guts, everywhere we look we find bacteria. When we ask how much DNA in terms of the length of DNA is encoded within a typical human, well, it's about $3x10^9$ DNA bases, and there is an equivalent or perhaps ten times as much bacterial DNA. A bacterial genome is typically 3 million bases whereas the human is 3 billion bases. So there is a lot of DNA present that is actually bacterial DNA that lives with us, and thanks to my discovery we know that human DNA actually doesn't have that many genes, because in humans the genes are really spread out over large distances, whereas in bacteria they are very compact. They do not have these introns that I discovered and that are present in higher organisms. The number of bacterial genes just dwarves the number of human genes, and our best guess is that there are maybe about 23 thousand human genes, that is genes that code for proteins, that make us work and carry out all of our activities, but for bacteria, a million, maybe two or three million, many many more genes.

One of the sad things about biology at the moment, or one of the very good things, is that we don't know a great deal about these bacterial genes, and this means that on the one hand we need to find out more so that we can understand the interactions between the bacteria and us, we need to understand how the bacteria work which means we need to figure out what these genes are doing.

So if you're a young person in the audience I would say here is a wonderful area to do some research. We need to find both, better methods for working out what these genes are doing, and we also need to put a lot of manpower and a lot of thought into being creative so that we can really understand how the bacteria work, how they interact with one another and how they interact with us. Because one of the things we know is that most of these bacteria are not pathogens, they are not dangerous, but they are looking after us. The way to think about this is to think about your home. When you buy a house one of the first things you do is you put a fence around it and try to keep thieves and people that you don't want out of it. You put an alarm system in, so that if a thief tries to get into your house an alarm sounds and the police can come and get rid of them. Bacteria do the same thing, they have made us their home, and so they don't want anything happen to us, they're not interested in us getting ill or causing problems, they would like us to live as long as possible so we can provide them with a good home, and in this way they do us a tremendous amount of good, because they surveil our bodies, they look to see where the bad guys are, and they help to develop methods to kill pathogens. They even have developed methods to kill cancer cells, bacteria don't like us to get cancer, because it means we end up dying and destroy their home. So we just now are starting to learn about some of the very clever ways in which bacteria are protecting us against disease. It is an early phase in this research, probably only within the last 5 to 10 years have there been this realization about how valuable all of this is

One of the way in which we spread bacteria from one place to another is by sneezing, and some bacteria have figured out that this is actually a good way to allow them to spread, and so they make us sneeze. In a photograph of an uninterrupted sneeze, where you let the sneeze just happen, you can see all these microdroplets which you normally couldn't, if you're healthy then this is probably not much of a problem, but if you are sick then this is a problem, so Kleenex or handkerchiefs are a very good thing to help stop spreading bacteria when you are sick.

I previously mentioned that bacteria got a bad name, and what happened, starting in the mid 19th century was, that biologists started to have access to microscopes and to culture media, being able to grow some of these bacteria, and so they started to study bacteria that caused disease. There was a very good reason to this, because at that time average life expectancy wasn't very high, if you lived to be 35 or 40 then you were thought of doing very well - when Mozart was my age he'd been dead for 50 years. People didn't live that long in those days, and that was because of infectious diseases

and because of the effect of pathogens. Slowly the microbiologists worked on individual diseases to find out which bacteria was causing the problemss or whether it was viruses causing the problems, but they were more difficult to deal with and so there was a focus on bacteria. The microbiologists became so obsessed with the bacteria that caused diseases and this was all they talked and about and all that you heard about in radio, newspaper and later on television, causes and cures for diseases and then along came antibiotics after the sulfur drugs and so now we were able to cure disease. But you heard nothing about the good bacteria, and it is a little surprising, because I would ask you, knowing how many bacteria there are that live with us, would you not expect that if all of those bacteria were bad we would have no chance of living? You can't live with ten bad bacterial cells for every human cell. So we should have thought that in addition to these bad ones there got to be some good ones there as well, but no one thought about that, no one looked into it. Occasionally someone would grow one of these, and when it turned out that it wasn't a pathogen they tended to ignored it, they didn't study it or wonder what was going on.

We now know that the vast majority, maybe 99.99% of all the bacteria that live with us are good for us, they are actually protecting us against all these bad guys that they were busy discovering mostly in the 20th century.

Now let's have a look at one or two of the bad ones, just to give you a flavor on what went on. The one I like best of all, it's a personal preference, and it turns out I have done a lot of work on this organism, because they turned out to have a lot of restriction enzymes and DNA methylation, which I am very interested in. Helicobacter pylori is an organism that lives in your stomach, virtually nothing else lives there, because of the acidic PH, but helicobacter pylori can tolerate that. It forms colonies on the epithelium, the skin that surrounds the stomach, and it causes ulcers. For the longest time everybody thought ulcers were caused by too much acid, and the pharmaceutical companied thought that was great, because they could sell you antacids. Antacids do something for the symptoms, but they do nothing for the cause, so if you had an ulcer you had to take antacid everyday, and that's what the pharma-companies love as they don't like medicine that cures disease because you only take them for a few days and then you can stop.

There were two Australian microbiologists, actually Doctors, called Barry Marshall and Robin Warren, and they started to look at the intestinal contents from people who had ulcers, and they noticed this funny looking bacteria there and so they wondered, could it

be that this bacteria caused the ulcers and not the acid. So in a very classic experiment Barry Marshall isolated this organism, grew it in the lab and took a drink of it, and sure enough within a few days he developed an ulcer. He then took an antibiotic, it killed the helicobacter and cured his ulcer. This is a classic piece of experimental science that many scientists over the years have done to prove their hypothesis, when everybody else doesn't believe it they do the experiment and show how it works. For this work Barry Marshall and Robin Warren won the Nobel Prize, for the discovery that helicobacter caused ulcers.

Helicobacter causes other things too, it can also cause cancer for example. It's one of the few bacteria we know about that actively can cause cancer, and this happens when you have a particularly bad infection that doesn't get treated, then the helicobacter makes its way into the human cells around the epithelium, we don't exactly know how it does it, but it can make those cells cancerous and cause stomach cancer. If as a result of refluxing the stomach contents up in the esophagus, then it can also cause esophageal cancer. But life is not all bad, because it turns out that helicobacter, if it's just a mild infection, looks as if it's protecting us from a disease called asthma. In the developing world where almost everybody has helicobacter infections, asthma is an unknown disease, you go to the West where very few people have helicobacter infections, because they have been taking so many antibiotics, they almost always rather have asthma. Asthma is very common in the western world, and we think it is a disease that is cause because we have been interfering with the microbes in our bodies in ways that are inappropriate.

So helicobacter is a complicated organism, but maybe we could fix it with a little biotechnological or genetic modification we could change it so that we could capture the beneficial properties and get rid of the properties we don't want. We don't know if that's possible yet though.

Lyme disease is a very interesting disease and I particularly like the organism that causes it. Lyme disease is a disease where there is a lot of in the area of New England where I come from. It is caused by a deer tick that bites you and transfers a bacterium into you. There is a characteristic red ring that characterizes the point where the tick bit you and where the cause of the disease entered the body. If you treat it immediately with antibiotics you have no problem, however if you don't, then you end up with an infection by another spiral organism called borrelia. It will get into your nervous system, the spinal cord and into the brain, and can cause some major problems. Once that

happens it is very difficult to get rid of it, it maybe a two or three year treatment with specialized antibiotics and you can eventually get rid of it but it can cause a lot of nervous damage in the meantime.

I like vibrio cholera, which is a lovely organism that likes to live in the oceans where it doesn't cause a lot of problems. When it causes problems is when it gets into the drinking water and humans start to drink it, and then it can cause the disease of the same name, cholera. That's a disease that you can cure by taking antibiotics and by drinking very large amounts of water, because basically what it does is it causes you to dehydrate incredibly rapidly.

This is a disease that is very prominent in many areas, I suspect in Indonesia from time to time, in Bangladesh they have major problems with it, and this is because you have very low lying land and when you have a big tide or a storm the seawater get into the drinking water and causes contamination. But there is wonderful remedy, a wonderful way of stopping cholera, and that is due to the dress sense of many of our ladies. In Bangladesh you find the Saris that the ladies wear are made of a very finely woven fabric, and I could see some similar types of clothing of fine silk here. If you take water that is contaminated with cholera and filter it through the sari then you get rid of most of the vibrio cholera, and that is not because it filters out the bacteria itself, but because it filters out another organism called volvox to which cholera binds itself. The amount of free floating cholera is comparably small so by filtering it you would get out most of them.

Typhus is a nasty disease that was absolutely devastating in World War One, where we had no way of dealing with it, which we can do now easily with it with antibiotics. The thing about typhus is that it caused by rickettsia, and that are bacteria that actually grow inside human cells. This is another kind of lifestyle than the organisms we were discussing before, and it turns out that there are many bacteria, hundreds of them, that grow inside human cells and not freely by themselves.

Treponema denticola is another spiral bacterium that you can find in your mouth, and that is not particularly harmful. We don't know what most of the bacteria do that are living in our mouths, we sequence them but we don't know what they do. Some we

know to produce caries and rot our teeth, but many of them are intimately involved in the initial digestion of the food that we eat.

The last one I wanted to talk about is yersinia pestis, the organism that caused the plague in the Middle Ages in Europe and decimated the population. It is a highly transmissible organism, it is transmitted by fleas from rats and it's still quite widely spread. There are many parts of the world where this organism is still there, but today it is easy to treat with antibiotics, provided you catch it early, within six to eight days of being bitten and then it is curable. It is only when people come from an area where plague is rife and say, go to a city where they've never seen it that it isn't getting diagnosed properly.

Now let's switch gears completely. I have given you some idea of how bacteria has gotten such a bad name and shown you many of the organisms that cause disease, and so one has to wonder why we aren't all sick from bacterial infections all the time with so many nasty bacteria around? The answer is, because the vast majority of the bacteria that live with us protect us, they are helping us and are good for us, and they stop all of the nasty bacteria from affecting us. We think of them as probiotics, although that is not the best term I think. There are a couple of them, lactobacillus and bifidobacteria, these are organisms that are present in yoghurt and they are very good for you, they produce lots of good materials and compounds that help you digest your food, and are generally very beneficial. I mentioned already Helicobacter and that they can have both good and bad effects and the question is: What else is there?

Let me talk a little bit about lactobacillus sake. This is an organism that is present in yoghurt and it is one that the Nestle Company in Switzerland started to work on when they bought Danone Yoghurt. They discovered that is possible to actually improve the health properties of this bacterium. By introducing some new genes into them they could make this a much better probiotic than the natural one. Then what happened was that the people in Switzerland were very scared about GMOs, and they were told that any genetically modified organisms are really bad, and so Nestle got worried to get major problems with consumers if they start to genetically engineer the yoghurt, even though we can make it better, and so they stopped research in this area. This is great shame because it is one of many problems that have been caused by the anti-GMO activists.

You will notice, especially if you are diabetic, that you take human insulin every day. Human insulin comes from genetically modified bacteria, because we figured out how to make that from bacteria or from yeast, however these are GMOs where the activists are not arguing against and that is because it's a medicine, because it produces something that clearly has beneficial effects. This I find to be a major problem, and I will return to this topic a little bit later in my talk.

Before that I would like to talk about clostridium difficile, also called cdiff. You can go to a hospital in the US and if you can stay there for about a week, then there is a very good chance that you will come up with a cdiff infection. Because it's rampant in the hospitals, it spreads very easily and it is a nasty organism, basically it causes uncontrollable diarrhea. It doesn't kill you, but there is no cure for many strains of cdiff by using traditional antibiotics, every antibiotic fails, because the bacteria picked up the most immense resistance to antibiotics. However, it turns out there is a way to cure it by using gut bacteria which we normally get by taking fecal samples, because these are the best examples of what's in a normal gut, isolating the bacteria and then feeding it to the people with cdiff infections, and in 95% of the cases it cures them. We don't know how it does it, we don't know what the mechanism is or which organism is responsible for this, but it's a wonderful example of how a normal bacterium is keeping pathogens at bay. And one has to ask with an example like this, how many other pathogens could we treat the same way? We know for example, that in the nasal mucosa, in the nose of many people organisms are growing which will kill staphylococcus aureus and mrsa memacilin resistant staph aureus, the most dangerous staph aureus out there. Again, we don't know how they do it and also not which organism it is that is responsible for doing it, but there is a lot of research in this area.

What I think this is telling us is that there are the most amazing opportunities for research here, because we go from one population to another and the bacteria that live with us tend to be a little be different, depending on location, diet and lifestyle. If I take a typical inhabitant from China and compare them with someone from Indonesia, we will find that their microbiota, their microorganisms are somewhat different. So the question is if there are microorganisms growing in the Indonesian population that would be particularly beneficial for fighting disease and vice versa, in the Chinese or the Indians, in the US and so on. This is a wonderful area for research, and again I address the students, if you want to do some really important research that may lead to some key discoveries then this is a great area to be doing it in.

I want to finish by making a plea for genetically modified organisms. I already mentioned that we genetically modify bacteria to make human insulin, which is very good, and that we could genetically modify lactobacillus to make better probiotics. We have the ability to genetically modify plants and we have been doing this for many times, to make them much better, and in fact the techniques of genetic modification that have been developed in the last 30 years, allow you to make very precise changes in these organisms that can be hugely beneficial across all societies. But you are probably aware that the anti-GMO activists want to tell you that this is really dangerous, that this is a very dangerous thing to be doing, despite the fact that for the last 12 thousand years we have been genetically modifying everything. Every time a couple has a baby they produce a GMO, because it has a mix of genes from the mother and from the father. Genetic modification is not inherently dangerous and particularly using the modern methods it is especially safe. We take one gene, we know exactly what it is and we can put it into a plant, we can monitor where it goes and we can see the products. Traditional breeding which the anti-GMO activists will tell you that it's perfectly safe, here you take a lot of genes where you don't know what they are and put them into another plant, and you test them basically by eating it. In this way we have a large number of products on the shelves that, if it would be a GMO you would not be allowed to eat it. Celery is the example I use very often, because celery has a group of compounds in it called psoralens that can cause cancer. When people used to be harvesting celery and chopping it up to be put into supermarket packs, many of them came down with contact dermatitis on their hands as a result of touching the celery juice in large quantities, and some even got skin cancer from it. Just because of the psoralens and natural compounds that are present, if this would be a GMO it would be banned. But in fact you can eat celery perfectly safely, because your body knows how to take care of this, and so all of these scary stories that you hear from the anti-GMO activists, they really are stories, they are fiction designed to make you want not to support GMOs, but rather to support the organizations. As a result, this has been the most incredibly good fund raiser for the anti-GMO organizations. You may be surprised to know that Greenpeace raises about 500 million Euros every year partly because of their anti-GMO campaign, so for them it's a huge moneymaker.

I have been very concerned about this and I have organized a campaign were we now have 123 Nobel laureates trying to convince Greenpeace to stop spreading this nonsense. What they are saying is not scientifically factual, but it's not good science, and so we want to spread this message as widely as we can. If you want to learn more about this then you can go to our website (http://supportprecisionagriculture.org) where you will find huge amounts of factual information and all of the evidence in support of

GMOs, and why they are good and why we need them, and if you agree then you can join up and sign on.

The bottom line is that for much of the developing world, for many of the poor people in this world, they need GMOs. The big agricultural companies are focused on crops that are good for the West where there are massive markets, but they have not focused on cassava or maniocs and other useful crops that are grown in many local developing countries, because there isn't a big market. But we can fix all of this, one thing that I am particularly keen on at the moment is something called banana wilt, if you go to sub-Saharan Africa then you encounter a major disease of bananas under way, caused by a bacterium unfortunately, and there is no natural form of banana that can resist it. The only way to stop this disease is to spray chemicals on it. However there is a very good GM solution. Sweet peppers have two genes in them will kill xanthomonas wilt and will protect the plant, and we can take those two genes and put them into bananas, and that has been done and then the bananas will be protected against this disease.

In Uganda 30% of all the calories that people consume come from bananas, so why would you not put these genes in and protect the crop, because without it bananas will disappear. With GM methods we can stop this and protect an important food source from being lost. So please have a look at our website and make yourself familiar with the facts.

I would like to thank you and I am happy to take questions.

Question:

What would be your advice to the young students and aspiring scientists in the audience today who will be the next generations of scientists in this country?

Dr. Sir Richard Roberts:

I usually tell people that the most important thing to do is to work out what it really is that you're passionate about, what is it that you love to do, and make a career of it. It doesn't

really matter what it is, it could be art or video games, it could be biology, it could be physics, whatever it is that you really like to do in your spare time, make a career of it, because you can always find a way to do that, smart people never have a problem making a career. Don't worry about money, I think one of the things that a lot of young people do is they think they have got to make a lot of money and I know in many Asian societies parents think that their children have failed if they don't make a lot of money, but that's not true, because money does not bring happiness. Just make enough money to survive and if you love what you do then the money will be irrelevant, you will be successful and everything will go well.

I would draw your attention to those of you who think they should be pursuing a career that will get you a Nobel Prize, I write an article for the journal "PLOS Computational Biology" titled 10 simple rules to win a Nobel Prize and I would recommend you read that. It is intended as a humorous article, but there are some words of wisdom in it.

Question:

We are here in Gaja Mada University and one of our responsibilities here is to create a vibrant scientific atmosphere so that these future leaders can flourish. What in your view are the key conditions to ensure in this campus to do that?

Dr. Sir Richard Roberts:

Not knowing how you teach at the moment it is always difficult for me to suggest changes and so maybe some of the things I am saying you're already doing. I think one of the key things that is absolutely important in education is to make sure that the kids, the young people who are being educated feel that they are part of the process, feel that they have the opportunity to ask questions and to explore things for themselves and are not just taught to memorize facts and then regurgitate them at an exam.

I had an extremely good chemistry professor who taught chemistry as though it was a puzzle, and at the chemistry exams you never had just to regurgitate anything but all of them were really puzzles that you had to solve, and I think this method of teaching where people have the possibility to explore what they are interested in, to ask questions and to get on and do experiments in the lab that they thought of and not ones

that some textbook suggested or the professor thought about. This is a very good way to teach.

If you go back and think about the time when you were very young, three or four years old, what were you interested in exploring the world, to see and touch everything and to find out how things work and if you were lucky your parents would encourage that, if you were less lucky then they tried to stop you from touching some of the things that you wanted to touch. I say: go out and touch everything that you can. You never know if you are going to find something that is so interesting that it can become a passion for your life. I would also add a corollary to that which very much applies to my own life, and that is if you doing something, let's say you decided that you want to be doctor and so you are pursuing this career, and then all of a sudden you come across something that is very different but you think it would be even more interesting and more fun, don't be afraid to change course.

Don't be afraid to rebel. I have always been a rebel and I always feel if people tell me I should be doing something I usually want to do the opposite, because I think it's probably boring. But when people tell me not to do something I always think there is probably some really interesting worth doing there. So don't be too strong in following rules, do the things that you think are important and remember that it is the young people in this world who are going to run the world in the future. The old people who run it now are going to disappear and they oftentimes don't know what is best for you.

Question:

In recent decades the world has faced so many diseases like antrax, ebola, cholrea and all the viruses, and some say this occurs as natural phenomenon, but some say that they were produced or engineered by a highly facility and a highly secret institutions. Do you think that is possible?

Dr. Sir Richard Roberts:

No. There is no credible evidence to support such a theory, but more to the point, we know that these diseases have been around forever, long before we had any ideas of using them in some ways as a conspiracy to kill people by this method. They are a

natural process, new viruses or bacteria arise all the time where some cause disease and some don't and that is called evolution and we've known about this for many years since Charles Darwin formulated his theory, and there is no evidence supporting anything else.

Question:

You just mentioned evolution and also that all the bacteria are already intact within us to support our lives and this leads me to an epistemological question: What is the purpose of all this life? The life supported by this bacteria, is there any grand design of meaning for man or is it just coincidence occurred by evolutionary process?

Dr. Sir Richard Roberts:

All of evolution happened by chance where whatever is fit survives. So the symbiosis that took place between us and the bacteria that live with us was a pure act of chance. There was no grand design, no one came along and said we make it this way, it's purely by chance and in my case I think it was a happy chance. We see this everywhere, it isn't just human and bacteria, all animals and plants have bacteria that live with them, the soil is a massive bacterium, they are everywhere and they form these relationships, because they need a home to live in and if the organism that they choose to make their home is better than they will make itself more hospitable to the bacteria, so this is two way street.

Question:

I am particularly interested in the subject of GMOs. People are afraid that GMOs cause cancer and other diseases, which is a problem I face in my start up where we are working with cassava. SO I am wondering what you would recommend us to do and how we could persuade the markets and the people to reconsider their stance about GMOs?

Dr. Sir Richard Roberts:

First of all I would recommend you to direct people to the homepage I mentioned and that 120 Nobel laureates attest to the safety of the GM method. There is much material on the website that people can read.

The bottom line here is that once people get scared it is quite difficult to reassure them. It takes a lot more effort to reassure people that things are safe than it is to get them scared about the dangers of things and so one of the things our campaign is trying to do is to get people like the pope, like the major religious leaders in the world to speak out about the safety of GMOs and if we could get the green parties to admit that this is just an area where they made a mistake that might help too, but the problem with them is that this has been such a success for fundraising for them that they like the money and so far haven't shown any willingness to follow the science and accept that they made a mistake.

The more people talk about this and the more people know the fact the easier it will be. There is a very good movie that has been made recently and that soon will be distributed, it's called "Food Evolution" and it is a very powerful movie, showing how good GMOs can be.

Question:

In your talk you mentioned clostridium difficile and that is has become resistant to antibiotics. I wonder how scientists can use the good bacteria to curb this effect or if it's already too late for that, and if we should worry about antibiotic resistant bacteria?

Dr. Sir Richard Roberts:

As far as antibiotic resistance goes, this has all come about because of misuse of antibiotics. We tend to give them when they are going to have no effect, we tend to overuse them and make them available over the counter, and we just need to recognize that the antibiotics that we have can still be useful, provided we don't overuse them.

When it come to the result that we have now with difficile, I think we are going to find that there are many bacteria that are doing interesting things in our body and our microbiomes to stop pathogens from growing. There is a worldwide effort now to start to study these mechanisms to see if we can find out which organisms are doing it, how they do it and how we can use them. I think we are going to find over the course of the next 5 to 10 years that there will be a big change in the way how we treat diseases of viral, cancer and bacterial infections.

Question:

When we create and consume GMO products is that the same as if we would create a new kind of organism that is totally different from the organisms that we already know and will it influence the tree of life?

Dr. Sir Richard Roberts:

I think if you look at what happens during traditional breeding of plants, where we try to take plants that are very different from one another but can still form hybrids of some sort and move hundreds of genes from one place to another. That seems to me inherently much more dangerous than the GM method were we are taking one gene and putting it into a plant where we know it can be useful and where we can monitor exactly what it does. Any act of logic is going to tell you that the GM method is going to be safer than anything connected with traditional breeding.

Will it affect the tree of life?
Almost certainly not. When you look at the tree of life you would have to make pretty large changes, because you cannot get plants or animals to interbreed. If you look at bacteria on the other hand, they are constantly changing genetic information and in fact it is no longer really clear what is a species of bacterium. I don’t think we do anything that is inherently dangerous in any way whatsoever. Nature has been doing this for many millions of years, and the way the GM method arose was when we followed what a natural bacterium was doing, agrobacterium was finding a way to put its genes into a plant and we have used this exact mechanism. As we sequence more and more genomes in plants and animals we find bacterial genes everywhere, so there is a lot of transfer of genetic information that takes place naturally.

Question:

Does genetic modification change the evolutionary process and is it ethical to make changes in organisms around us?

Dr. Sir Richard Roberts:

So what about dogs?
For many of thousand years we have been breeding dogs and these are not at all products of nature. If you look at any crop plant that we eat and you go back and look at their wild relatives then you wouldn't recognize them as they don't look anything alike in most cases. So this isn't something new but we have been doing for thousands of years and we do even more inadvertently every time we have an oil spill for example, we change the ecosystem in major ways. We allow bacteria to recombine and to form organisms that we haven't seen before. I think the problem is that it isn't possible to have life on earth, whether it's us or any other form, without changing the way that nature evolves. Evolution is a natural process so nature evolves anyway, and we are a result and part of that process and I don't think that we are capable of doing anything that is inherently more dangerous than what nature does all by itself.

Question:

Is it possible to genetically engineer bacteria to fight pathogens and cancer?

Dr. Sir Richard Roberts:

I think the answer is a clear yes. We already know that there are some bacteria that produce anti-cancer compounds and that will stop cancers from growing. There is work coming out from the University of Chicago that shows quite clearly that with the right bacteria cancers can be stopped from growing. Can we do it for all cancers at the moment? No, but maybe we could do that in the future.

We are only at the very early stages of learning of what bacteria can do for us and how they influence out lives. There is a massive research area opening up, that I think over the next few years will find out that bacteria are way more important than we ever thought in the past.

Question:

I would be very interested in your involvement in the Combrex Project. I think everybody here would like to know how we actually can utilize computer to aid our research in biochemistry, and what software is being used?

Dr. Sir Richard Roberts:

The Combrex Project is something that was started a long time ago, we had funding for it for a while and we had funding a little bit in between but now we have no funding. One of the reasons is that the government does not understand how important this is.

Let me tell you what the Combrex Project is. Basically we are finding out the DNA sequences of humans and pretty much all organisms around us, like bacteria and it is quite easy to get a complete DNA sequence of bacteria today. In time we are going to know the DNA sequences of every organism that lives on this earth and we are going to know about the biology, because of our ability to interpret those DNA sequences. And interpreting means that we read the sequence, we identify the genes and then we predict what protein is going to be made and what that protein will do. This is the area where we are slipping behind and this is the area that the Combrex Project was intended to form, to work out which were the important genes that we need to understand the function of. For some reason the administrators in the NIH in the US and in fact in most funding agencies around the world don't think this is an important project and I think they're sadly mistaken because if we don't get going soon there will be no point in determining all these sequences because we won't know how to interpret them or what they mean.

For me this is an absolutely crucial project. It is not expensive and a nice aspect about it is that scientists from all around the work can participate in and you can just have as big as an effect on it if you are in Indonesia or in China, the US or in Europe. Maybe you could start something small here and I can help you with doing this.