Chemistry Nobel Laureate Prof. Ada Yonath's dialogue with high school students at the Stamford American International School in Singapore on Wednesday, March 4, 2015, as part of the ASEAN event series "Bridges - Dialogues Towards a Culture of Peace" facilitated by the International Peace Foundation.

Good morning, I am very happy to see so many young students who are interested in science. Thank you for coming, and as promised I will tell you what we are doing in our lab and what we have learned there, scientifically.

The process that I was very excited by, that caught my attention when I was your age, was the translation of the instructions that are in the DNA, namely the genes, for the formation of cell “workers”, called proteins that perform most of the cellular tasks. I guess that you know what DNA and what genes are. However, when I was your age DNA and the genes were just discovered, and for me these finding were most fascinating. DNA is the genetic language for all forms of life. This language has just 4 (four) letter. When it was discovered I was in school and for me it was fascinating. Indeed, even now it is still fascinating. I was very curious about how this process is performed and this curiosity inspired my studies when I became a young scientist. Now, one word about proteins: I am sure that most of you or all of you are told by your parents or other adults that you should eat proteins, because that’s good for your health, therefore you are eating eggs, or cheese, or steaks. But do you think that we eat eggs, because we want to have chickens in our bodies? No. The eggs are cooked anyway, so they can’t turn into chicken. The same is true for the steak or the cheese, which won’t become cows inside us.

In fact, the proteins that we’re eating are being chopped in our body into their building blocks by our own proteins, and the building blocks are then used to make the proteins that we need for facilitating our life. Did you hear about hemoglobin? It is a protein that transports the oxygen from the lungs to the muscles. Muscles are also built of proteins, part of the specific body

proteins that are made from the building blocks from the proteins we've eaten. Each protein has a specific structure that is designed for fulfilling its task, which is dictated by the sequence of its building blocks according to the instructions that are provided by their genes.

What was known when I was a young student was that in every living cell are particles, called ribosomes that function as "factories", which translate the genetic code into proteins. The ribosomes are made of many components, and within the cells they are among the largest particles, although actually very small. They know to read the genetic code and to decode it into growing proteins. They function continuously, very quickly and very, very accurately. From our point of view, they are fantastic molecular machines.

I want to give you an example. They are making the chemical bonds between the building blocks of the newly born proteins, called amino acids. In one second they can make up to 40 bonds, actually from 5 to 40 depending on the complexity. They hardly make mistakes that we could catch, namely about one mistake in one million bonds. It is likely that they make more mistakes, but they get rid of them because they possess a proofreading machinery. A normal protein has about 200 amino acids, hence a typical protein is made in a few seconds. New proteins are formed constantly because proteins don't live long, just about 3 or 4 days, and then they need to be remade. Sometimes we need specific proteins. For example when dust comes into our eyes, we have tears, like we are crying. These tears wash out of the dust, as they contain salt (I am sure some of you tasted the tears and noticed that they are salty). But the function of the tears is much more complicated, as they also contain a protein (called an enzyme) cap, that is able to chop the wall of every bacteria. Therefore, in the case that there are bacteria within the dust that could cause an infection in the eye or something else which isn't wanted, then this enzyme, which is made immediately when the dust enters the eye, can chop it. This protein is called lysozyme.

The instructions how to make this and all other proteins are in their genes, which reside in the DNA and are collectively called genome. Each of the proteins is formed only when it is needed. There is no point in having this protein just running around.

Another example are the proteins that can deal with a few cases of heart attacks. A heart attack is usually happening at the age of 60 or over, therefore there is no point in having these proteins when you are younger. Even in older ages they are produced only when they are needed, although the instructions for their formation are always in the DNA

Now let’s come back to the efficiency of the ribosomes. As I said, they can make up to 40 bonds in one second. I was a good student, I was a fast student, and it took me 6 hours to make one bond

I just want to share with you my enthusiasm about ribosomes. What I wanted to understand is how they work, and this was just plain curiosity. I didn’t think about selling my knowledge or expecting profits. Just to understand, and add important knowledge to humanity. Before I started several distinguished scientific groups have been trying to shed light on this process, but failed. However, although we all wanted to understand the same process, I had a different point of view, and after many years, eventually we succeeded, and understanding how the ribsosomes work was for me unbelievable and unexpected. I was so overwhelmed that for months after seeing how it functions and works, I couldn’t see anything else. It was in front of my eyes for a few months.

Owing to the fundamental role played by ribosomes, many antibiotics paralyze them. What are antibiotics? Antibiotics are medications that are used against bacteria that cause infections, like pneumonia, antibiotics will take care of it, many by interfering with the production of the bacterial cell

workers, the proteins

The antibiotics are very small, with molecular weights of around 500-900, and bacterial ribosomes are much larger, with molecular weight of about 2 million. How can the antibiotics achieve their aim? This question was very interesting for me, although originally I was not sure if I could solve this question.

The natural antibiotics are the weapons that one bacteria uses against other types. Understanding how antibiotics work was above my dreams. This is a great bonus that I got when deciphering the ribosome modes of action. Now we know how all the antibiotics that paralyze ribosomes are working, which consist about half of the useful antibiotics. This is our contribution to medicine. Above understanding, we are trying to provide answers to a major problem in modern medicine, namely the resistance to antibiotics. We are suggesting how to design better antibiotics that will have less resistance.

Question:

Your Nobel Prize was awarded to you in honor of your contributions to science, along with that you became a role-model to women all over the world. What advice can you offer to us as we get ready to graduate high school and to make our mark in the world?

Prof. Ada Yonath:

You might not like my answer. I don’t wish to be a role-model, because in my opinion each of us, each of you and everyone in the world should progress according to what one wants and can do. I cherish originality, not

copying someone else. I may be inspiring but please don't try to copy me. First, because in general I think that one should be developed according to what one has and can do by her or his own, and second, because my life was not always that easy and there was not always so much glory. I am not sure that many would like to go through what I experience that was at times more difficult than normal. Going through difficulties may be inspiring, but I wish you a much better life.

Question:

It was nice to interact with you in our lab class this morning, when we were using hydrogen peroxide as the catalyst for our reactions. I would like to understand what it really is in the catalyst molecule that helps to break down a hydrogen peroxide.

Prof. Ada Yonath:

Because of time limitations I cannot explain catalysis in detail, except than saying that each molecule that has the capability of breaking or making chemical bonds or transferring materials in cells or between cells in living organisms is called an enzyme. Catalyzing chemical reactions mean performing the reactions efficiently and fast. Many reactions would have happened anyway, with no enzymes, but not so fast and not so accurate and not so well as by the enzymes.

The main property of these molecules is that they posses an active site, usually an internal pocket containing several components that interact with the substrate. In your case it was a catalyst in decomposing hydrogen peroxide. Even ribosomes work this way, except that they are not just proteins.

Question:

What do you think about ethics, and to what extend should ethics basically constrain the development of science and the knowledge in science?

Prof. Ada Yonath:

Ethics should be the basis of everything, also in science. Ethics is the basis for our wellbeing. Understanding is very important, but is has to be ethical.

Question:

Do you think it constrains the development of science?

Prof. Ada Yonath:

I think science is ethical, and when its observations are used correctly, then there is no constrain. Of course, if a scientist uses knowledge to make an atomic bomb, it is not ethical, similar to cases in which human beings use their brain for theft or murderer, it’s also not ethical. There are always possibilities to be right or wrong. Basically science has to be ethical as well as everything else we do, at work, at home, in life.

Question:

How do you see the prospects of bacteria becoming resistant to antibiotics all over the world?

Prof. Ada Yonath:

Needles to say, this is very worrying. I hope it doesn't happen, because then we would go back to pre-antibiotic times. It is indeed a very big problem, and I hope that we will find a way to control it, if we're not able to get rid of it completely.

Do you know how old Mozart was when he died? He was 36, and he died from an infectious disease. Importantly, 200 or even 100 years ago life expectancy was around 50. Most people died when they reached the age of 45 or 50.

Question:

Considering that the IB program does not permit the use of animals for research, although sometimes first-hand experience leads to better understanding. Are there criteria that can be developed to justify the use of animals in research?

Prof. Ada Yonath:

Well, this is a complicated question. Animals should not be used for anything except for life saving or high quality medicine. Clearly not for cosmetics and things like this I am totally against the use of animals in such research, even if people may look be less beautiful because of this.

In addition, since molecular biology developed, many models can be made in the lab without using animals, like tissue cultures. Therefore, wherever it is possible to use them, they should be preferred on animals. However, there are some scientific and medical issues that cannot be investigated without animals. Some of these may lead to life saving or advanced therapeutics. In my opinion, these directions should be performed under utmost control, by using animals.

Question:

I imagine that you spend a lot of time in the lab doing research. I am curious if you could share with us the kind of activities you like to do in your free time.

Prof. Ada Yonath:

I indeed spend a lot of time in the lab, but I also spend a lot of time with my family. I raised my sister when she was young, because my father died and my mother wasn’t so well. So although my free time is scarce, it exists. I like to swim. I also like reading or listening to music, especially classical. I am also spending time with friends and have discussions with them.

Actually, when I was young I had two dreams. One was to be a fiction writer, but I wasn’t good enough for this. Science was easier for me. Also, I wanted to work at a farm and raise cattle, mainly calves. These were my dreams, not science.

Question:

Every cell in the body contains a whole genome, yet at any given time most genes are switched off rather than on, hence they are not expressed. What is the mechanism which determines whether any particular gene is or isn't expressed at a particular time?

Prof. Ada Yonath:

This is determined by the need of the body. I was talking about it in my little opening speech. I gave two examples of genes that exist, but are not expressed most of the time. One is turn on when dust enters the eye, which doesn't happen constantly, and the second is heart events. Let me elaborate a bit more on that now.

I am sure that within this audience there is at least one person with parents or a family member or someone they know, who had a heart event, but once coming to the hospital and being examined by doctors, they would find that their own body took care of the problem, by its own enzymes. Clearly these proteins must be made exactly at the right time. Therefore they are not expressed when in young age or in healthy persons. Only when they're needed.

This is an example, but the general idea is the same.

Question:

What is your view on personalized medicine and ethical implications behind it?

Prof. Ada Yonath:

My view on personalized medicine, if it works, which it already happens in some cases, is positive, and I am very exciting by it.

Question:

To what extend do you think scientists have a unique responsibility within democracy?

Prof. Ada Yonath:

I think that science can contribute a lot to democracy or to increase peace, because science has no limits. Collaborations between scientists promote understanding of peoples and cultures, and thus should contribute to democracy.

Question:

My question is how does the body know when it is needed to express the gene, how does it anticipate when an event is about to happen, so it can express the gene to aid the body?

Prof. Ada Yonath:

This is called regulation or transmitting of signals, and it is being studied very thoroughly around the world right now. From what I understand about science is that this question won’t be answered fully by the time you can

become a scientist. Thus, you have a really great project to work on!

Question:

Biology isn’t the easiest subject, so I just want to ask if going through medical college and years and years of hard work in bio - is it really worth it?

Prof. Ada Yonath:

If you look at me, of course it is!

But a more general answer, difficulties in life are associated with everything one does at its best. This is part of the definition of professional life. Therefore difficulties should not be the measure according to which one makes the selection. In my opinion anybody should choose the most interesting and exciting profession.

To be a good dancer is also difficult, even if you have all the right properties for doing that. To be a politician is difficult, maybe the most difficult. Studies are usually difficult, but there is a pay off, there is a reason to do this. You enrich yourself and your knowledge, you may also enrich society, the whole humanity with new knowledge that you produce.

The years of studying - for me they were a lot of fun, difficult yes, but also pleasurable. Many more reasons should be determining what one chose to do rather than just difficulties. Much more suitable values are enrichment or expression or achievement

Question:

Do you think that being a woman stopped you from doing something?

Prof. Ada Yonath:

Well, it stopped me from being a man.

Also, I cannot compare how my live would have been if I was a man, because I just am not a man. I know that being a woman gave me some benefits that men don't have. I can become pregnant and deliver a child and raise the child as a mother, this is something that females do and males cannot. Many people consider children as a burden, as a difficulty, but I look at it with a lot of pleasure, and this can never be experienced by a man.

In science and in school I didn't feel that it was more difficult for me, because I am a woman. Maybe it was, but my project was so difficult by itself, that the gender-point didn't even come into it. I think that science is gender independent. Indeed, science is demanding from men as well as from women. Clearly when men are competing in science or in politics or in arts, they're tough to each other as they are to women, or maybe even more so.

In short, I consider being a female as a blessing, not as something negative.

Question:

You said earlier that you were studying on your subject many years, did you ever feel like changing your field?

Prof. Ada Yonath:

In my opinion the driving force is the problem that is interesting to the scientist or for humanity. The field, like chemistry or biology are only the tools to answer a problem. I did not want to change my goal, namely to answer other questions.

Yes, there were many interesting questions, but I was deeply engrossed into mine, and I couldn't do more than what I did. But if I had failed, I would have looked for another problem that would have been interesting to me and be of significance for other human beings.

Question:

Was it difficult to publish your research?

Prof. Ada Yonath:

Yes, it was and still is. In order to publish scientific results one has to convince the reviewers, that they carry significant importance and that the studies were carried out correctly. Since other scientists may have different opinions, sometimes it's not easy to convince them. In short the scientist has to think about a problem, to design the experiment, to convince a funding agency to support it, to attract students to join and to perform the experiment. The publishing is minor compared to that.

Question:

After winning the Nobel Prize and making a major scientific breakthrough I wonder if you still feel passionate about your field. Do you still feel an urge to keep on working, or do you like to spend more time with your family now and away from the labs?

Prof. Ada Yonath:

The Nobel Prize is a point in my live, but it is not the most important one. In science most important is the achievement, namely the discovery. In my opinion we still did not discover everything. I am still working in the lab, I still have a running group and I am still doing experiments. I am working on improving antibiotics, on finding new ones, on finding ways to discriminate between bad and good bacteria and on understanding how ribosomes were made in the beginning, which means on the origins of life.

Question:

What’s your opinion on pharmaceutical companies in America and their monopoly on prescription drugs?

Prof. Ada Yonath:

I can tell you my opinion on pharmaceutical companies all over the world, but I cannot say anything about monopoly on prescription drugs, because I

have no knowledge on that. But I do have knowledge on pharmaceutical companies that stopped the development of new antibiotics about 20 years ago, which is very sad for humanity.

Question:

When you were younger, who was our role model?

Prof. Ada Yonath:

I had no role model. I appreciated my mother very much. She had no knowledge in science. Nevertheless she supported me throughout. Consequently I consider that the ability to give to others, her daughter in this case, is something I would like to have. I also was inspired by some scientists like Marie Curie, but I didn't think I could do what she has done.

Question:

I was wondering how many years of research did it take you to become a Nobel Laureate?

Prof. Ada Yonath:

You want to ask how many years it took since I started studying ribosomes until I got the prize, or how long I worked on the project that brought the prize?

Question:

How long did you work on the project that brought the prize?

Prof. Ada Yonath:

20 years, minus 2 weeks.

Question:

Do you have any other projects on your mind for the future?

Prof. Ada Yonath:

I already told on what I am currently working, but of course everything can develop into something else. When I started with ribosomes, I didn't think that I will become an antibiotic specialist.

Question:

I was wondering how does being famous help you advocating for some things you believe in besides in the field of science? I've read for example that you have some unique perspectives on current events and politics. So does being famous help you do something about these issues?

Prof. Ada Yonath:

Getting the Nobel Prize in Chemistry gives other people the idea that I understand everything. They ask me everything, not only related to chemistry or medicine. Also questions about physics or even philosophy, politics, art and whatever. But we are not more knowledgeable after we received the prize than we were before, so from this point of view there are expectations which I often can't fulfill. From another point of view, becoming a Nobel Laureate allows me to meet people like you, young and curious people. I could do this before receiving the prize, even here in Singapore, but not in such an amount and so intensive as it is now, and it gives me a lot of pleasure.

Question:

You have studied ribosomes for a very long time, but everybody knows that the cells in our body will eventually die off, so I wonder is it possible with today's technology to artificially create what the cell does naturally?

Prof. Ada Yonath:

It may be possible but I don't know anything about it.
In my opinion the body and nature are so clever that to create something as clever as natural cells or cleverer, is still not possible.

Question:

I was reading in the write-up that you pioneered your research line despite

skepticism from the international scientific community, and I was wondering what pushed you pursuing the research of this line despite the skepticism?

Prof. Ada Yonath:

First of all, I was a skeptic myself. Until we got to the end, I was not certain that it would work. But my curiosity, the magnitude of the question and the expected contribution of the result pushed me to continue, although I did it in a way that was not the common one. We designed new procedures, and create new concepts. The reasons for going on despite the skepticism, was the progress that I saw, although difficult to explain. Consequently the skepticism grew and grew, and I became the “village fool” or the “crazy” person in the scientific community. Nevertheless, we continued, not always in a way that I could explain and mostly not in the traditional way.

Question:

I was wondering, during the approximately 20 years that you have been working towards your goal, did you want to give up or had trouble continuing your work?

Prof. Ada Yonath:

There were technical obstacles, problems with the funding, conceptual difficulties and so on. One occasion that was really devastating was when we could not use our samples, namely our crystals, after 6 years of preparation, because they decayed during the measurement. Namely it took us 6 years to obtain these crystals, and then lost them within a second. At that time I was afraid that we would never make it. But trying to understand why this happened and to overcome it, we developed a new

unexpected method, which is actually mentioned by the Nobel Committee, called cryo bio-crystallography. This new method allowed not only us to measure, but also almost instantly became routine in almost all labs all over the world. Thus, the number of known structures (the result of our studies), when we installed the new procedure, was about a 100s, whereas currently, about 2 decades later there are more than 60,000, and 99% were determined with our new methodology.

Question:

How does your upbringing influence the way that you see the world?

Prof. Ada Yonath:

I was born in a very poor family, and my father died when I was young. Most of my childhood was dedicated to survival, to help my mother generate enough income for the family to go on. For example, in order to attend school I had to get fellowships.

Question:

Our school is very prestigious. Do you think that we actually have a benefit from it in terms of succeeding, or do you think that you get more out of the passion and drive for your own work than you would from the good upbringing?

Prof. Ada Yonath:

The school I attended was excellent, but here is paradise compared to the ability of my school with equipment and the numbers of students and teachers. So please take advantage of it. I am not sure that being poor and going through problems is the best way. You can become a great scientist or a great person with a great personality when you study in a very good school like what you have here. Take advantage of it!