

Dean Goldschmidt's Interview with Tatjana Rundek, M.D., Ph.D.

April 23, 2009

PJG: Tatjana, thank you for joining me this morning. As you know, this is an interview that you and I will be working on and then will be available to people who want to learn more about your work and what you do. It's a way for me to tell people about the medical school without having to always talk about the things that I am aware of, but more to give people in the school, who are very young and bring a lot of expertise, the opportunity to tell what they do. There will also be an article summarizing the interviews, that will be in the magazine referring to the interviews and that will be the way to get people to look at the full interview. I really appreciate you taking the time; I was wondering if you could tell us about your life and how you grew up and how you came to the United States, because I understand that you came from central Europe?

TR: Yes. Well, first of all thank you so much for inviting me and giving me this incredible opportunity to be able to talk a little bit about my work and actually have the personal contact with you as well. I think it's a great format. So my life story in brief? I was born and raised in Croatia in a small family...

PJG: What city?

TR: In the city of Zagreb, which is the capital, and my mother is German and my father is Croatian. It is kind of an interesting family story as well because part is Jewish and part is Catholic, so they all just think that I'm a child of a conflict, but the two families actually work very well together. And so, I've done many wonderful things as a kid – enjoyed my life in Croatia, finished medical school there as well but then later on for training I went to Germany. I

did my residency and my Ph.D. at Max Planck in neuroscience. Then I decided to go back to Croatia because I love the country and I love the people and the climate, so I went back. Then, unfortunately the war in the Balkans started. At the time I did not want to leave, so I was enlisted and I did spend almost a year in the war zone. I was a physician in a small team consisting of a surgeon and an anesthesiologist and I was a support physician. Fortunately it didn't last too long, so I survived and got back to Croatia, but my life was changed at this point and I was a different person. Then, actually, my mother suggested that I needed to change environments and that I needed to do something because it was obviously "post-war syndrome, post-traumatic stress disorder," so I applied for the Fulbright Scholarship and by some kind of stroke of luck, I got the scholarship at Columbia University in New York.

PJG: Let me ask you a couple of questions. I understand that during the Balkan War, you were a physician on the frontline and you mentioned that it changed your life. Can you tell us a little about that?

TR: At the beginning I didn't even know what it meant. We all saw the movies and then you go see those productions and you think it's something heroic, it's something great to serve your country, but right there on the field, it's really sad. It's really, regardless of which side, it's just destruction and killing and loss of human lives for no comprehensible reason – it's just unbelievable. To watch that every day... we were like five or 10 miles from the real battle... and then after everything comes down during night, you go there and see who you can help and who you can't and then go back to the base... it was just too much to take sometimes. And then you go through the processes. First, you're terribly afraid. I couldn't function for three weeks because of the sounds, and then after that you start to kind of accept things, start to recognize that "oh this is going to go over," recognize even the types of weapons, then you lose fear and that's

the most dangerous part. The last phase was you completely lose fear and then you do stupid things. You just go. You try to help somebody under fire. That was the moment they decided that I must go because this was not a good time for me to be there. But then they couldn't find anybody to replace me, so I stayed longer and I didn't want to leave; I wanted to stay. Then they changed the surgeon and said I must go too – that's it. So then I got back home and actually I did almost want to go back... because I was trying to help so many young people there, you know, losing their arms, legs, I mean it was really tough.

PJG: And that must have been in huge contrast with your Ph.D. work at the Max Planck Institute?

TR: Completely different story.

PJG: Tell us about that because Max Planck Institute is a great place...

TR: It's a great institution. They have wonderful teachers and a great system, however it's very specialized. You get into the program and you immediately start working on your Ph.D. and you get into a very narrow field.

PJG: How do you pick it?

TR: It's pretty much if you have your own interest. My interest at the time was to understand the vascular basis of Alzheimer's because even at that time I thought it cannot be pure Alzheimer's disease, it must be some kind of a correlation of another type of dementia? I wanted to investigate that part and I wanted to do it clinically. I said, "I can do little mice models, but I, somehow, want to connect it with humans."

PJG: So what did you discover for your thesis?

TR: What did I discover? Actually, it was published in a little German article that basically 20 to 30% of Alzheimer's patients would have vascular changes in the medial temporal lobe,

which would be associated with the memory impairment in this region. It was a small study, but it was accepted at that time – we're talking about 20 years ago, this was some kind of a novel finding.

PJG: That's terrific. And, of course, about the same time, people doing genetic work on Alzheimer's, in particular Peggy Vance, who discovered the ApoE gene...

TR: Right now, this University's genetic research is unbelievable ...

PJG: But that was very consistent with your work because ApoE, that's not a nervous system gene, that's a vascular gene.

TR: Exactly. It's really interesting. I do have a paper in preparation to look at ApoE and the presence of carotid plaque and we do have a strong correlation, however more among women than men. In many other kinds of genetic polymorphisms, we do find some kind of sex-related differences. I am still not sure how to explain that.

PJG: Interesting.

TR: I don't know how much of that really is the part of the interaction with the environment and sex specific genetic markers – they are connected with metabolic syndrome, but interestingly none of those polymorphisms are on sex genes.

PJG: Yes.

TR: It must be some kind of association and maybe it's because of post-menopausal status. Maybe it is really environmental, but there has to be a connection... and if you look at any of those clinical trials where they tested lipid lowering therapies of any kind, there is a relatively smaller, or lower response among women. That is something that also focused my interest as well.

PJG: Yes, it's extremely interesting. In small vessel disease, women usually have a tendency to have more of that than men do, men having more the proximal atherosclerosis. You have your Ph.D. with a publication in Alzheimer's from the Max Planck Institute, you apply to the Fulbright, and you get to the US...

TR: By some kind of stroke of luck, yes...

PJG: I'm sure. You get the grant, and then here we go, you're on your way to America. What year was that, by the way?

TR: 1996

PJG: 1996 – which date?

TR: Actually it was late November.

PJG: Late November...

TR: But my chairman at the time, allowed me two weeks to settle down, so I actually started in 1997.

PJG: Fascinating. So you did get a bit of time in the United States?

TR: Yes, two or three weeks.

PJG: That's a very good idea...

TR: When I arrived, my English was very poor. I arrived in front of his office and he just looked at me and said, "Who are you?" and I said, "I'm Tatjana;" he said, "okay" and I was in shock. It was the first time I was in the United States, so it was a cultural shock, it was a language shock. I did learn English as a kid, but I never really practiced speaking it.

PJG: At that point you spoke fluent Czechoslovakian and German?

TR: Yes.

PJG: Then English was your third language?

TR: Yes. I always read English literature, but I never really expressed myself in English until I arrived in the United States. But do you know what the first question from people here was? “How is your Spanish?” I thought, “What?” I don’t even speak English and they’re asking about my Spanish? But Columbia University is in an area of Washington Heights, the part of northern Manhattan that is highly populated by Dominicans.

PJG: Oh, that’s interesting.

TR: 80% of the population there speaks Spanish. So his question was, “How is your Spanish?” I thought, “Spanish? How am I going to overcome this?”

PJG: That was a perfect preparation for Miami, right?

TR: My Spanish is still poor.

PJG: Tatjana, you arrive to Columbia University, you start in January of 1997, and here you go – America watch out, here comes Tatjana! You start to do your work – what struck you?

TR: I arrived with a very clear mind of what I wanted to do. At that time, I was in neural network analysis. I forgot to say that in college my major was in math and I was competing in the math Olympics. I had a pretty good, skillful, reasonable knowledge of mathematic topography and multi dimensional spaces at that time, so my idea was that by coming to the great United States, I will be able to work on what I really want to do since I was never able to do it in Europe. My idea was to simulate the disease process in a multi-dimensional space and do some kind of prediction model which would create the links between important biological nodes. Then by cutting certain nodes, it will simulate various types of brain diseases. That’s how we can start understanding the complex circuitry of brain processes and also build up the therapeutic pathways. Then they looked at me like, “you want to do what? No, that’s not possible here.” So I thought, “Well, then I will familiarize myself first with what we have here.” I later said “Okay,

then can I do stroke research?” Everyone said, “Oh no, that’s boring. Who wants to do stroke? You want to do some real neurology like ALS, multiple sclerosis.” I said, “Yes, but there’s no action there. It’s nice, but I like something with more action.” He said “Okay, go, but three months. I’m sure you’re going to get to see what’s going on with stroke, you’re going to be back, and you’ll want to do something else.” So I said, “Okay,” then I went at that time, and met with Dr. Mohr and Dr. Sacco and have stayed with them since. I worked with stroke neurologists in the past, but the pathways and the way of approaching a stroke in the United States was completely different. We did have a concept of urgency in Europe, but not as much as it was in the United States

PJG: Sure.

TR: Of course, technology was not great at the time. I was from the time where CT was introduced, other imaging techniques and biomarkers came later, so it was definitely a very technologically advanced approach for the patients. I really liked it. I started to be a part of what I call the “Ralph Sacco school of epidemiology;” it’s how I got interested in his Northern Manhattan Study, joined the stroke epidemiology group and started to like it. I didn’t like epidemiology at all before coming to the U.S. because I thought, “This is counting death. Who wants to do that? Just counting people – have disease, no disease, exposed, not exposed...” But then I realized there are so many factors one can really detect in the populations – small signals in the population which understanding this can make a big difference. Then one can bring back the important factors to the clinical and bench research.

PJG: Let me see if I understand, you come to America with the idea that you would look at the brain as a network with nodes and links, and that what an injury would do to a disease process would disrupt the nodes and links, and you would be able to reconstitute the disease process by

looking at your mathematical model of disturbance of normal connection and perhaps redundant pathways and all kinds of consequence. Is that what you had in mind?

TR: Yes.

PJG: Then here people tell you we don't do that kind of thing?

TR: Because they were not familiar with the concept, they thought, "Okay, but we don't even know how to help you to start this type of research. But we do have many other exciting areas in neurology you may want to explore." I agreed and I grabbed that opportunity. I also had skills and knowledge of ultrasound, which was very helpful in stroke research because a system of learning and performing ultrasound is quite different in the U.S. than in Europe. Here, they were done by technologists who do not have much of the opportunity to advance the ultrasound field.

PJG: I was very interested by that.

TR: Right, and I was surprised too. How do you train technologists to provide the expertise that you need for your patients? Ultrasound is a tool that helps to diagnose, predict, and follow-up with patients. How do you rely on someone who doesn't have enough medical knowledge to provide that information? Then I realized, with the proper training and supervision, you can train a very experienced and good technician. I didn't have that concept at the time when I arrived, but I had a pretty good knowledge of ultrasound. I do have another interesting story about ultrasound. Early on during my neurology training, I heard about technology called Transcranial Doppler and I thought, "Wow, how interesting, one can measure blood flow in the brain non-invasively by ultrasound through the skull." Then I got in contact with Dr. Rune Aaslid, who was the inventor of TCD. I asked one of my neurology professors, "What do you think about that new technique called TCD?" He said, "Oh that's nonsense. But yeah, go there and learn what this is about, but there is no future in it." I thought, "I do not agree, but I don't

know anything about it, so I am going to learn it.” I went and met this incredibly smart person who used to lock himself in a room for two months and work on the project because he had to solve certain puzzles of his prototype machine. He was actually constructing and testing this equipment on his own.

PJG: Interesting.

TR: I saw him one day; I think I had been there two months because he was locked in his room in the hospital. It was really funny research— we had to wait for him to give us pieces of information and equipment to test it on the patients. I liked it instantly, learned how to do it, and the future was made. Now it’s really an indispensable tool for stroke diagnosis and following up the success of stroke treatments.

PJG: I remember very well when it came out... transcranial ultrasound? What the heck is that? That’s great. How did you adapt your thought process to a much more translational aspect of work than what you had initially anticipated? It was quite sophisticated in the applied mathematics of domain... what you were thinking about doing and then now you’re doing translational work where your math knowledge is helpful because...

TR: Oh, extremely!

PJG: It’s a lot of statistics and so forth.

TR: For epidemiology, extremely.

PJG: It’s really good to be good in math for that type of work, but is that how you...

TR: Envisioned?

PJG: You adapted?

TR: That’s how I adapted, but I haven’t abandoned my original idea.

PJG: I’m glad.

TR: Yes, because I think it all goes in cycles, right? You start one way, go up, and then go down, and I think I'm going to go back to finish the loop. I look at it as a necessary experience because if I go straight to do what I wanted to do then, I believe, I would miss the whole other unknown area at the time. I think I broadened my knowledge and I can now go back with a better knowledge of what this process and the problems may be because my initial approach to medical problems was a bit naïve. Although you can explain or describe systems wonderfully by mathematical equations, they still do not really capture the complexity of the real biological system. I think this knowledge I gained through my "sidetracked" path, knowing that there is a lot of individual unpredictability in responses to therapy, will allow me the opportunity to put this knowledge back in the mathematical model, which for a while we considered to be an error in the system, but it's not an error, it's a biological reality. I think when I go back to my original idea, it's going to be much more advanced model than what I was originally anticipating.

PJG: That's great. Tell us what are the studies? I was, of course, looking at your CV, but I wanted to speak about you. What are the studies that really have you the most interested?

TR: Right now I think I'm fascinated by genetics, polymorphisms and understanding the genetic basis of health and disease. I think understanding health is the first step in understanding disease, from normal vascular aging, normal functions of blood pressure to arterial walls, understanding what's normal, what's not normal. I am now fascinated by the complex nature of the environmental and genetic interactions.

PJG: That's wonderful. You know one of the things that really fascinated me in doing genetics is that in a very simple way, we had the idea that we could take mice, put them on different types of diets and then study the gene expression profile and link gene expression profile with diet. Simple idea.

TR: Brilliant.

PJG: We were funded for it and we had plenty of money to do that study and then, in spite of the best mathematicians in North Carolina, we could not find a link between the diet and gene expression.

TR: It's hard to believe.

PJG: It was very hard to believe; it was contrary to anything I've ever thought. It was very upsetting and the mice had a response that was all over the place, and there was no relationship with their gender and with their age. We were frustrated but then did something different. We modified the model to actually make the mouse sick. We made them genetically prone to atherosclerosis using the model Dr. Jan Breslow developed by knocking out the ApoE gene and sure enough, the gene expression profile was completely predictable and very monotonous and worsening with age. What it means to me is that if you look at it from a mathematical standpoint, disease is the loss of degrees of freedom.

TR: Yes.

PJG: But there is an extraordinary variety in response to an injury for a normal organism because there are infinite degrees of freedom, but not for a sick organism. The ability to adapt to a new injury is very limited, actually almost depending on how sick the individual or the animal is, nearly zero. It's very interesting because the degrees of freedom of the model also have a lot to do with society and why we care about diversity in society. Well, here are your reasons for it.

TR: Yes, that's exactly how I think about it. This is really interesting, which coming back to my mathematical model, I think it's going to improve significantly one day.

PJG: If you think about it, due to chronic damage to nervous tissues, it eventually it has to go all through one pathway that may be incapable or insufficient to really provide the kind of brain function that people want to have.

TR: It's very complicated at this moment.

PJG: But there are some breakthroughs. I don't know if you have looked at, for example, the use of a cochlear implant. The brain essentially is made out of receptors, processors and connections. You can have complete absence of a receptor like the ear system and bypass it electrically to the ear nerve, the auditory nerve, and it can result in people able to hear speech, music, and children's sounds.

TR: Yes, it is incredible.

PJG: It's exciting because here you bypass the receptor, you plug in the sound sensitive device that produces the electric signals of the ear system and you get all the processing right – right?

TR: Yes.

PJG: Hopefully, there can be a time where we can bypass it.

TR: Yes, I think something similar was done for the vision as well.

PJG: To some degree, yes.

TR: To some degree. Now they can have an artificial intelligence – robots or computers that actually have vision that can decode images and processes to see the shapes and colors as well; this is fascinating. What is going to be a little bit difficult is our cognition and intellectual function. Memory – there's a lot of work on memory already, however that is also very complicated, when we get to the higher level processes, then we always get stunned with the complexity and beauty of nature. It's unbelievable.

PJG: That's exciting. And also emotions – the thing that's very interesting is this kind of unbelievably diffused connectivity of emotions with everything else. That is fascinating because there must be some kind of evolutionary advantage to that, right?

TR: There must be.

PJG: Yes, there must be.

TR: Because we survived all these years.

PJG: I know, I know. Tell me, when Ralph Sacco came here, I was very impressed with the fact that you were someone he immediately wanted to bring to Miami as well. How was that episode of your life?

TR: When he announced he was going to leave, he did talk to us as a group. He asked us if we would consider coming to Miami. Some people didn't want to leave their lifestyle because it's New York with a different environment. For me, it sounded like an extraordinary opportunity and it still is; I believe so because we heard about you, we heard about the genetic group and of the Vance's coming down, and that you already started to develop a very strong research and clinical environment. I already had a candidate gene grant in atherosclerosis funded and that was available to be transferred because data was collected, ultrasound imaging and questionnaires were completed. However, I needed the genetic expertise to continue with my research; for me, there was a lot of appeal for coming to Miami, and it was a promotion as well. But the people at Columbia University advised me, "No, you don't want to go"... and I thought "Why not?"..."Because you will always be considered as Ralph Sacco's person, you'll never gain your independence – you're always going to be labeled," and I thought, "That's not true." It's not really... maybe that's the system here, but in Europe actually...

PJG: That's the classic thing that we say to everybody...

TR: Really?

PJG: ...who we want to keep when they want to go with somebody else. It's a classic...

TR: Do you use it?

PJG: Of course, of course.

TR: But everyone, my close colleagues, chairman, colleagues from other departments with whom I had been collaborating on various projects, said, "No, you don't want to go... you're never going to be independent." Then I consulted my parents, and my father who was alive at that time said, "Well I don't know how it is in the United States, but in Europe if a professor asks you to join him at a new institution to continue the work you started, it's the greatest honor you can have." For me, that was the most important opinion. One conversation with my parents, and I made my decision. I called Ralph and said, "I am in – I'm coming to Miami."

PJG: That's great. Tell me, how has it been? I'm sure that there were both great things and hurdles. Tell us about that.

TR: Work wise, I've seen incredible changes and progress. We started small and now we excited people in the department about clinical research. We got more cohesive with the basic science group. We have monthly meetings with them, we have weekly research meetings, and I see residents, fellows and other faculty excited, motivated and stimulated. That's been a great experience. We extended our group with terrific faculty members; and I was very excited when Clinton Wright, my colleague from Columbia University, also decided to join us. He is a great addition to our team. Ralph brought really extraordinary people to our department. I see an interest in clinical research. I always thought you can't have clinical work completely separated from research, but you have to have both – great clinical work and great research at the same

time. The hurdles... maybe adjustment to life in Miami, but then I'm sure that you've heard the same thing from many people.

PJG: How do you like it?

TR: It is very different. The first part – driving everywhere, that's very different from New York... jumping on the subway was easy. Now I have to drive everywhere. I used to race cars when I was a kid, but on the racetracks (that's another story). Now I'm racing like everyone else, so I adapted to that one easy. Still, because Miami is so spread out, I still do not quite understand where the boundaries of downtown, midtown, uptown, the beach, Coral Gables are, and what is happening in each of these parts of Miami. Actually it took me a while to understand that these areas are different towns. What I was able to do in New York, to work until eight, meet my friends, cut my hair, have dinner and be home by midnight is impossible here. You have to be well organized... decide what to do first, plan how to get from point A to B, do one thing, and then if some time is left, try to get to point C... I would say, for me, it's less efficient.

PJG: Interesting.

TR: But, it has other charms.

PJG: Do you like the international character of the city?

TR: That, I love.

PJG: It's interesting.

TR: I love being in the international city. I usually get asked, "Where are you from?" I say, "I don't know... I'm a citizen of the world."

PJG: Good for you. It's my understanding that Ralph is very generous to the people who work with him in terms of allowing them to get credit for the work that is being done and so forth. He very strongly felt that you should be the person interviewed for this work.

TR: Yes, he has been an incredible leader, teacher and supporter of my career development. Even in New York when he was leading the division, he would never take credit for anything alone. He would always acknowledge his team, his coworkers, research assistants; whoever contributed, they were always acknowledged and appreciated for their work. He's been a great leader.

PJG: I'm thinking here... you were racing cars when you were young, you went to the war and then you are a great mathematician. I wonder if you could give a phone call to Larry Summers to let him know that his...

TR: I would love to!

PJG: His understanding of women and mathematics is...

TR: I would love to! I couldn't believe that he would say something like that. Even at Columbia, people at the time supported his views....

PJG: Really?

TR: Oh yes.

PJG: Unbelievable!

It's interesting to see how much the ability of an individual to contribute to the understanding of the disease process is so much a function of the kind of mindset that the individual approaches the problem with. Yours was so interesting because it was really a mathematical network model.

TR: Yes.

PJG: Tell us about stroke today – the way you look at it.

TR: A general approach – this is the environment of reality, of biological processes of stroke, and it depends on what kind of mask you put on it, that is how you see this process. If you put a mask of imagers, you can see the lesions, locations, and the size. If you put the mask of

epidemiologists, you'll see the person's demographic characteristics, predictors and outcomes. Is a patient of African-American background, woman or a man, more prone to high blood pressure or lipid disorders? If you put the mask of a resident, it's, "Oh, look at the time... time is brain, must rush, must give tPA, must call attending, interventionalist..." Looking from a researcher aspect, it's incredible – we still don't understand the pathophysiology of the stroke types, what the small vessel disease is. What is the real process behind? Is it partially embolic? Is it lipohyalinosis? Then we must understand the whole ischemic process and how we can successfully intervene. I think how one sees the same biological reality depends which mask one puts on. I've tried to approach it from as many aspects as possible, almost like 360° approach, to understand the most global process and then see how we can help intervene and how we can actually prevent it. It's real interesting to see stroke treatments evolve. We still struggle with specific therapies for various stroke sub-types. Now we're pretty good in identifying hemorrhagic and ischemic stroke. But our therapeutic options are still quite limiting. We are venturing in the interventional therapies following successful experience from cardiology world, but we are still years behind. Certain types of stroke are going to be similar to myocardial infarctions – but not all. Therefore we are developing stroke specific therapies based on stroke science while also following science and evidence from complementary fields such as cardiology and endocrinology.

PJG: It's very interesting because the artery of the nervous system is much more challenging than the artery of the heart. I always tell Ralph, we can go into coronaries with a bulldozer and then practically never get a bleeding problem. With a little bit of a careful approach, of course, we practically never get a bleeding problem. But with brain arteries, they are so finicky ...you do one thing wrong and you've got a major bleeding problem on your hands. That's very

different and the concept that we had where we can apply thrombolytics and we can apply GPIIb-IIIa blockers, it's all going to work exactly like coronaries, were completely wrong. That was a good lesson of humility, for sure. But what is also very interesting is the response of the brain to stroke; some people who instantly start to recover from the injury versus other people who have an injury that is relatively small but then it gets worse over time – it's a little bit like with your redundancy idea. It seems that for some people, when one epicenter of the stroke is destroyed, there is that variety of alternative pathways that allow them to compensate for whatever damage happens almost within hours or days, and others who are totally unable to do that.

TR: It's incredible how early on in ischemic lesion, the brain has an unbelievable autoregulatory response to minimize the lesion. This is where the difference comes in – some people are with a heavy burden of risk factors, the small vessels cannot react and provide that essential collateral supply, while the healthier brain can successfully autoregulate and defend against injury. The normal brain has an incredible ability to protect itself from ischemic injury; when stroke happens, it's a huge event because the brain already tried everything it could to prevent the event. We can use a very simple test, Transcranial Doppler (TCD), to test for brain autoregulation in people at risk for stroke. For instance, in patients with high grade carotid stenosis, a Transcranial Doppler may show a lower velocity in the ipsilateral middle cerebral artery (MCA) and a good collateral pathway through this interior circulation to the posterior. But on top of that finding, we can challenge the brain circulation with a mixture of air, with a little bit more of CO₂ through the mask. If there is a good response in which the cerebral blood flow velocities in the MCA increase because CO₂ dilates the small arteries, patients are less likely to have a very high risk of developing stroke. There is a certain range of velocities that we would

expect the brain to react in a situation of high grade carotid stenosis. However, if that response is absent, the brain is in great danger, has impaired vasoreactive reserve, and the patient is at high risk for developing stroke. These are patients, we believe, who need to be revascularized. Even for asymptomatic coronary artery disease, I don't think we utilize enough simple neurosonology technology to target people who may be at a high risk of developing stroke.

PJG: I see. You're essentially looking at the reserve? You're trying to find out in situations where the brain reacts to the lack of oxygen or excess of CO₂, which is interesting because CO₂ was the vasodilator.

TR: Yes. CO₂ is a very strong small vessel dilator, so you can really challenge the small vessels in the brain and test to see how they react to it. We use this procedure in many situations where we want to estimate the imminent risk for stroke.

PJG: That's awesome. I must say that it is really a pleasure and an honor to have you at UM. I'm just wondering, did you ever think about the possibility of being a big physician-scientist with a huge reputation and working at a major center in the United States when you were a little girl in Croatia? Was that something that you were thinking about?

TR: No, it never crossed my mind. I always thought that I was going to be a teacher.

PJG: School teacher?

TR: School teacher for little kids.

PJG: How interesting.

TR: But then I was going to be an astronomer, astronaut, astrophysicist and then mathematician, physician and then neurologist, and now I'm thinking I'm finally on the right track.

PJG: That's great. That's wonderful. I'm sure that your parents must be very proud of your career?

TR: Yes. Unfortunately, my father died...

PJG: So I heard.

TR: ...a couple of months ago. But my mother and father were always very proud of me. They were my greatest supporters, even though sometimes they thought that some of my decisions might not have been the greatest. But they always trusted my judgment. They would tell me, "we are not sure and we don't quite agree with you but we trust your judgment and we know you're going to find your way and it will be the proper way for you." They've been supporting me all the way, to the point where I am now.

PJG: That's wonderful. And your mom – is she a physician too?

TR: No, my mom is a lawyer.

PJG: A lawyer.

TR: She wanted me to go to law school but I wanted to stay away from those difficult cases and arguments in court.

PJG: There's a great song of Bruce Springsteen where he said, I think it goes something like this: his father wanted him to be a lawyer and his mother wanted him to be a writer, and he said they were always fighting. Father wanted me to be a lawyer and mom wanted me to be a writer, and so he said, "Well then Mom and Dad, tonight, you're just going to have to settle down for rock and roll!"

TR: Pretty good.

PJG: I must say, he's my favorite singer, but it's really wonderful to have you and I hope that you know this University and this medical school are proud of having you here and of the work

that you do and the entire team. We're looking forward to great breakthroughs because stroke is a huge disabling disease process that we're just going to need to manage for years to come because people won't be able to afford to have a stroke. At a time when humans are challenged with working later and later in life and staying very functional for a long, long time for a variety of reasons, it's not going to get easier to be able to prevent stroke, treat it when they come up, and get people back on track. It's critical, otherwise...in a way, have you ever gone through the Sequoia Forest in California?

TR: Oh yes, it's beautiful.

PJG: You know there are these forest fires that come regularly... it's important because they need it to compete with the otherwise expanding ground vegetation.

TR: They need it, yes.

PJG: The fact that I find so interesting is that every time there is a fire, a sequoia will lose a root and as a consequence a branch or two. Successive strokes are really like that. When you see a patient that has gone through successive strokes, it looks like in some way what happens to the sequoia tree where functions disappear one after the other. The work that you do is really of extraordinary importance for the future of humanity and we wish you great luck with it. Let me say thank you on behalf of the school for the work that you do and for all the patients that you help in the world because of your work.

TR: Yes, thank you so much.

PJG: Thank you very much for the interview.

TR: Thank you.

