**Transcript of RPS Pharma Scene podcast #23**

**RPS Chief Scientist, Professor Parastou Donyai, interviews Miraz Rahman, Professor of Medicinal Chemistry at King’s College London.**

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PROFESSOR PARASTOU DONYAI: Today I'm joined by Professor Miraz Rahman, Professor of Medicinal Chemistry at the Institute of Pharmaceutical Science, King's College London. Miraz is also the Director of the MRC-IK Doctoral Training Program at King's and in addition to that he is the antimicrobial research theme lead at King's College London. Welcome Miraz.

PROFESSOR MIRAZ RAHMAN: Thank you and thank you for giving me the opportunity to speak to you with this podcast.

PARASTOU: You're very welcome. I know a little bit about your career journey and I think that our listeners would learn a lot from listening to the journey that you've had, from being an early career researcher and arriving in the UK. I won't give all of it away and the resilience that you've shown throughout your career. What I want to do is take our listeners through that journey that you've been through and the first question I've got for you is to ask you how did you get into pharmacy and what did you study?

MIRAZ: So I grew up in Bangladesh in different districts because my father was a government officer, and we used to move from one city to another. When growing up I don't think I had pharmacy as the profession that I will be taking as a carrier I must say. I wanted to be a cricketer. My father used to look after all of our siblings, the education and we never went to any tutor or in coaching centers which was the norm at that time. I left home at around 15 to move to Thaka, the capital and there I first saw the pharmaceutical industry because Bangladesh is a very different country in terms of healthcare and pharmacy. The pharmacies dominate the healthcare settings and the pharmaceutical industry there. So that was the first time I thought about studying pharmacy. In Bangladesh if you want to study pharmacy you have to be at the very top of the ranking in the university admission test. So that's how I ended up in pharmacy.

PARASTOU: Can I ask you Miraz? Didn't you get a job working in a pharmaceutical company while you were studying pharmacy?

MIRAZ: So the pharmacy training is again quite different compared to the UK where I'm now part of the pharmacy education system. In Bangladesh the degree is very much industry focused and in year three of your degree you have to spend at least 40 days at a pharmaceutical industry which is considered as in-plant training and then you are exposed to the R&D manufacturing formulation, quality control. So you visit different departments and then you are expected to write a comprehensive report which you present to the management and they evaluate it. So it's a mandatory assessment which you must pass to graduate as a pharmacist and then you do an M-farm which was two years. So I went to one of the largest pharmaceutical industries which is called S-KNF Pharmaceuticals which was used to be Smithland and French and then when they left the country then it became a more national pharmaceutical company. It was fantastic seeing how actually everything works so you can put the theory into practice. When I wrote the report I ended up writing a highly critical report. So I was a good academic student so when I produced that report the management was very surprised that a undergraduate student coming in without any industry experience is essentially criticizing one of the largest pharmaceutical industries. Now my theory was quite strong I must say so I was able to defend my report. I also put an action plan at the end what the company could possibly do. I said why not? If you give me the authority I'm sure I can do this and in that meeting they offered me the job of technical development officer reporting just to the executive director.

PARASTOU: Fantastic I mean it illustrates quite a lot of confidence but I suppose it's the bravery isn't it because you were clearly rocking the boat quite significantly. So was the company able to implement the changes as a result of employing you?

MIRAZ: I didn't just back down when I was challenged. I think that confidence that despite being an academic question I was probably not a conventional academic student because I was the captain of the cricket team. I was doing a lot of extracurricular activities. So that gave me the courage and now by looking back I just think oh my god I probably want people to do this at this age. How was I able to take that on and when I was only about 19 or 20? So I started to implement the action plan that I wrote. I kind of made a whole so change in some of the practices so the staff were really happy because they felt that they are getting a bit empowered and learning about different things but at the same time I was learning. My knowledge was theoretical I must say so there were senior pharmacists there who helped me to understand and helped me to implement some of the proposals that I was proposing because some of them were unrealistic having no background in industrial pharmacy at that time. So yeah I had a really good time so I decided to continue doing this full-time job while studying for my firm. Did you end up with a first-class degree with your MFO? So you have to take a kind of a mentor as a research supervisor. So I took up a mentor professor, Chodri Mamudha-san who was the director of the drug administration before coming back to Dak University and he gave me a lot of freedom saying, whereas whatever you feel you can do just go ahead and do it. So I know that he will be doing well in research because he was very organized and you have got the exposure and the experience that many students do not have but where I was really suffering was the academic because we had five subjects to where we had to sit for the exam and that exam will be happening not when you finish your theory but when you have finished your whole theory and research. I don't know how I managed it but I ended up being first-class first again. I think I was probably in a bit more mature the way I approached those questions because some of those I could write or respond from my practical experience in the industry which the students didn't have that exposure.

PARASTOU: Well I'm not surprised the commitment that you shown and of course that learning that you would have had in practice. What did you end up doing after you finished your MFO?

MIRAZ: So I was still at the scale where I was working in the industry at that time as a pharmacist so I just moved up to a more senior role but then I realized that I was not quite sure I wanted to be in the industry. There were a number of reasons. I was enjoying the job but then I realized I might want to move into a different industry that was one option. The other option is life can be quite difficult because I remember sometimes I will be getting in in the say at 3pm for my evening shift and the monsoon rain is quite heavy in Bangladesh and the roads sometimes can accumulate quite a bit of rainwater and the security officer will tell me Mira's you cannot get out now because we have but almost needy water or even higher and so we have to wait until water receives a bit more than the car can get out. So I just felt no I want to probably do a bit more academic job or academic environment to do some research work at that time. So I ended up joining a private university which is called the University of Asia Pacific which was one of the first university in the country to offer pharmacy and stayed there for three years before I moved back to Dakah University as a lecturer in 2003.

PARASTOU: And you were presumably employed as a lecturer but yet to get your PhD and from speaking to you before I know that you undertook your PhD in the UK so could you tell us a little bit about how it was that you arrived in the UK?

MIRAZ: In 2005 I finally managed to secure the communal scholarship for a PhD in the United Kingdom. So one of the conditions was that I had to secure an offer letter from one of the universities in the UK. I managed to get admission at this I usually useful of pharmacy at the University of Oxford and the University of Nottingham. So it was a quite tough decision at that time to decide whether I would like to go to University of Oxford during a PhD in carbohydrate chemistry or come to school of pharmacy or PhD in a cancer drug discovery. So I remember one of our very senior founder of the pharmacy department in Dakah University Professor Duljabbar. He said why are you thinking? Just if you get to go to school of pharmacy you just go there you don't think about this. And then I also liked the field of research which was the cancer discovery and working with an industrial setting because my supervisor was Professor David Thurston and who founded a pharmaceutical company called Spireen at that time. So I just felt okay I will be probably more able to use some of my industrial experience coming in here doing a PhD with the group which has a focus in more translational research. So that's how I decided to move to London in 2005 to do a PhD at the school of pharmacy.

PARASTOU: So am I right in understanding then that your sort of application was funded for a scholarship but the field of research was very much whatever was offered to you by those institutions. Is that how it worked?

MIRAZ: During the application process you have to indicate what is the broad field of research you'd like to do and you have to indicate which universities and supervisors you have contacted already. So I could have gone to any of the three but then I have to make a decision and inform the Commonwealth Commission okay I am putting a school of pharmacy as my preferred choice.

PARASTOU: Am I right that by that time you sort of narrowed it down to medicinal chemistry?

MIRAZ: Initially I worked with GMP implementation and then moved into the research and development as a formulation scientist so later part of my industrial time was working as

a formulation scientist and then when I was doing research at the University I was working in natural product chemistry. I wanted to do some semi-synthesis, but we didn't have the right infrastructure there to do some semi-synthesis. So I just felt that medicinal chemistry is something which I should get trained and start this proper research in synthetic medicinal chemistry or semi-synthesis in back-end tech university so that was the goal at that time. So I kind of had exposure to everything except clinical pharmacy because I must say that clinical pharmacy research has now developed in Bangladesh at that time there wasn't much clinical pharmacy research going on.

INTERVAL

PARASTOU: That was going to be my question how you came to want to focus on medicinal chemistry so if we wind forward a little bit then you arrive in the UK to undertake your PhD and I understand you had a young family at the time. Now how did you make it all work, Miraz?

MIRAZ: So I came to the UK, I was married at that time with two young kids. My son was just three years old and my daughter was nine months old and my wife was also a pharmacist just did her DPharm degree from the university and she was a very good student as well. So I didn't have any family members. I had one or two friends here. So childcare was the biggest problem because we as an immigrant and a student we didn't have access to any public funds so the amount of money a commonwealth was paying as a stipend was very difficult to even just maintain a livelihood here with renting a flat commuting and then if we decided to use the childcare then almost all the money will be gone for the childcare. So it was tough, so I had to kind of take on additional jobs. I was a very good tutor when I was back in Bangladesh. I used to take a handsome amount of money for tutoring for one day a week or sometimes two day a week. So I thought okay why don't I try to see whether I can do something like this and I was lucky that I managed to secure few tutoring jobs in different parts of London. So I used to drive to those places in the evening or weekend so we can now do many sessions. Then I was earning sufficient amount to make sure that my kids could go into these good nurseries. It was fun time I must say. Children probably suffered a bit but I was very close to my kids. At home the kids department was always mine and it still is mine so I used to whenever I had anything anytime I used to spend with the kids.

PARASTOU: I'm interested, Miraz, what were you tutoring in? What was the field? Was it chemistry? Was it general tutoring?

MIRAZ: So I was mainly doing a level so I would be doing chemistry and biology. I had a student who were close to who was going to a school of pharmacy in Medway. So I started tutoring him for some pharmacy when I was doing my PhD. I used to do different types of tutoring. It's essentially whatever opportunity was available. I was up for it.

PARASTOU: And in the month all of this you were of course doing your PhD and leading on your own research. Could you tell us a little bit about your PhD and what your main findings were?

MIRAZ: I was doing a PhD in DNA targeted drug discovery so one of the main challenges that we faced at that time. The DNA is interesting. You have got only four base pairs, ADGC, and then you have, I should say four bases, ADGC, but you have to kind of direct compounds that can recognize some specific sequences so that you can target cancer cells and spare the healthy cells. Now most of the important transcription factors in the promoter regions we see there are lots of GC rich, so guanine and cytosin rich region, but there are no real building blocks available that can direct them to guanine and cytosines. Most of the natural polyamides like distamicin, the tropicin, those were the bases for designing different drugs. They were all going to prefer these adenine and thymine 80 sequences. So my PhD was to try to identify polyamides starting with smaller building blocks that can recognize GC sequences because David watched in a field called pyrrolobenzodiazepines which are DNA minor binding drugs, but covalent binders. So you need some non-covalent components which can direct the covalent component to a specific sequence. So I synthesized hundreds of different compounds with a new type of building blocks which were by a real type of building blocks. This biolumines they were linked directly carbon-carbon. So very different compared to traditional imidazole pyrrol [?] type of building block that you find in the nature. And we were able to identify a new building block which we called MPB, the methyl phenylbenzinamine [?] which were able to tolerate the GC sequences much better compared to any other building blocks. And we synthesized compounds with that MPB building blocks which showed exquisite potency. So it's like femtomolar [?] to pico-molar activity against cancer cell lines, particularly triple-negative first cancer and pancreatic cancer cell lines. And then moving into in vivo they showed excellent activity as well. So the PhD project, the original research objective that was hugely successful and everyone was very excited, which meant it was decided that it will be patented. So we were trying to get some additional data with other collaborators so that we can file a patent.

PARASTOU: So it sounds very successful and what's happened to that work, Meraz? Did you get the patents?

MIRAZ: It was patented and then it was assigned to Astrogenica and Astrogenica used that patent and some of the previous patent that came from Davis Lab to former company and then that acquired Astrogen. So those patents helped really the shape these antibody drug conjugate landscape containing the PBDs. So the Astrogenica, when they acquired spirogens [?] , that patent became a part of their portfolio. I'm aware that there has been modifications to the classes of drug that utilized the findings of my PhD research. And also we used some part of that in designing new generation compounds, which helped me to set up a spin-out company with David King's, which was called femtogenics [?] at that time, which has been now relaunched as a few therapeutics after a six to seven million funding round. So the findings that I managed to get from my PhD was very helpful.

PARASTOU: So Miraz, we are going to zoom forward a little bit more now because I think that you've very impressively led the development of new antimicrobial compounds as well as having led the field in terms of anti-cancer agents. So I just wondered if you could tell us how did you apply your existing skills to a completely new area?

MIRAZ: I was originally trained as a cancer chemist. I have heard that during my PhD. So when I secured my first academic position at King's in 2012, at the time the head of the institute was Professor Peter Highlands. And Professor Clyde Page was my mentor. So there was a push to develop antimicrobial research at King's because King's had a very strong virology department where it was doing really well. But there was not really a chemistry focused research area of discovery and and medicinal chemistry where insular pharmaceutical science wanted to take the next step. There was very little going on at the time. So one of the main focus for me was to establish my independent research group in antimicrobial research or antimicrobial development. I started with my cancer focus when I started at King's but then gradually started to develop collaborations with different organizations to work in the antimicrobial research area. But I must say it was extremely difficult because there was no one at King's who was doing bacterial research or antimicrobial research per se. So I had to kind of call the email, lots of colleagues in different universities to find out whether they would be willing to screen compounds against these priority pathogens which has been identified by WHO which we call the escaped pathogens. So there are mainly two gram positives and entervocas [?] and stuffhylapocas [?] , and then you have got these gram negatives like pseudomonas, clepsalas [?] , and the bacteria. It was quite difficult because I was not finding tractions and was not finding someone who would be able to evaluate the compounds because as medical chemists we were able to design synthesized compounds against different bacterial targets but you need someone to actually test to see whether these compounds are active. So in 2014 we had a kind of a chance encounter with UK health security agency. At that time it was public health inland and their gram negative group leader Dr. Mark Sutton. So they agreed to test some of our compounds, and it was kind of a real breakthrough because the compounds that we sent were highly active and that meant they were interested in our research. We signed an umbrella agreement which covered IP, which covered revenue, which covered these research infrastructure and since then we have had huge success in developing new generation antifungal agents, antibiotics, there has been 23 joint projects between King's College London and UK health security agency and they have now become a strategic partner of King's College London in developing antimicrobials.

PARASTOU: Well great to hear for humanity. Are you hopeful that we can create new antimicrobials and bring us back from the age of doom?

MIRAZ: I think we can and we are developing antimicrobials but there is a problem that needs to be addressed otherwise this new antimicrobials, the academics, and small startups are developing will never see the market. We are gently need new antimicrobials but the market is broken. So what happens is you are developing new antimicrobials but they cannot generate the sufficient amount of funds or revenue once they are marketed. So it's a scenario which is commercially not attractive that these doom that we are facing

that there is a huge rise in antimicrobial resistance and by 2050 it is projected that 10 million people will be dying here. The farmer is not actually investing in antimicrobials whether leaving the field because the infection is an accurate indication. You take an antipsychotic for seven days maximum and you feel better, you get well, you will have no footprint for the rest of your life. So the amount of time you are buying that medicine is relatively a short window, and then we have got quite a number of generics which are very cheap which is still do work against say 80% cases which means companies which are developing antibiotics in some cases are getting going bankrupt after they get the approval. One example is archaeogen [?] which got bankrupt after they got the antibiotic approved by FDA. So unless these market dynamics change I feel that we are at the edge of a cliff and millions of people will die needlessly because the commercial world is not considering antibiotics as a lucrative business. What they are missing is the antibiotics underpin the modern medicine the way we know it. You can think about any surgery anything minor to major starting from child part to very critical say neurosurgery you need an antibiotic post-surgery to avoid infection. Any minor injury trauma you need an antibiotic along with the treatment that you are giving. So everything will probably lead to just the pre-antibiotic era where we had no antibiotic to combat infectious disease so even minor as class we could kill people.

PARASTOU: Yeah it certainly is a potentially scary future scenario but I guess it's reassuring to know that somebody with your drive, Miraz, is working in this area. Do you think that you can encapsulate what it is that underpins your drive or rather what advice you would give others either based here in the UK or internationally to go on and pursue their own dreams?

MIRAZ: Sometimes the drive comes from your passion. You'd like to do something which can create a meaningful impact to the lives of people. So when I started with my cancer drug discovery work I think one of the goal was, and it still is that I would like to see that the drugs that I'm developing are helping to cure people. So the fear and therapeutics which is now taking drugs to clinical trials and I would like to be the bedside of the patient who is receiving the first drug. So I think that's the same passion that you have for antimicrobial so where you understand the difficulties that's globally we are facing and then perhaps growing up in a country like Bangladesh in the subcontinent where there's lots of poverty, and you see people sometimes do not have access to medications and there are a number of infectious diseases there where people are dying because sometimes they're not sufficient antibiotics or antibiotic with the right activity they can access to. So we'd like to make the world a slightly better place in terms of access to medications, in terms of getting drugs that can possibly help them to cure people but it can also come from many different ways, sometimes from the family the values that you grow up with sometimes what you really enjoy. So, I think everyone probably complains that I work too hard including my wife and and sometimes I just feel that I'm not working hard enough. I probably enjoy what I do and that's the most important thing to do what you enjoy because then it doesn't feel like a chore it feels like that you are enjoying your life at the same time doing something meaningful which might have an impact in other people's lives.

PARASTOU: That's fantastic to hear, Maras and I know your passion is infected almost nopon intended of course in that students educated by yourself are very appreciative of what you're able to teach them within your field and I understand that you've been nominated for numerous teaching awards. What do you think about the education of the next generation of scientists?

MIRAZ: I feel that as an academic that's really important because if we want to make any meaningful impact that will be probably through the next generation so it's important to instil those values to give them that opportunity, give them the right education. So I'm probably one of those researchers who is a passionate as the teaching as well so I don't know which one I would be putting fast or second, so I very much enjoy my teaching and I love that interaction with the students and sometimes I get a clap at the end of the lecture I feel like that's probably the best moment of the day and I feel that the students appreciate and engage with the lecturers where they feel that they are trying to make them understand and make them feel valued so that has been my motto that where whenever I'm taking on any course I try to give my best in teaching I just don't do teaching because I have to do it.

PARASTOU: That's wonderful to hear. Miraz, your passion that you've clearly got a huge commitment both to your work but also to the people around you, you've shown incredible resilience and great leadership skills you've used your confidence and you haven't been afraid to challenge those in authority where your values and what you believe is right has driven you forward. It's been a real pleasure to speak with you, Miraz, and I want to say thank you very much.

MIRAZ: The pleasure is mine thank you very much it's been lovely to to recall some of those life moments and speak to you about my journey.

PARASTOU: Thank you, Miraz.

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