

## Ana Alfirević Interview



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### 1. Where did you grow up?

I was born and grew up in Zagreb. My mum and dad were both from Zagreb and my dad's mother's family are proper 'Agramers' named Frelich of Austro-Hungarian ancestry. That's where my strong Zagreb accent comes from. Every now and then I am told that I speak archaic Croatian.

### 2. What do you remember from your elementary school and high school days?

I attended 'classical' primary school with Latin and ancient Greek being taught from year 5-8. I still have many good friends from that time. Quite a few of us went to Zagreb Medical School together, strengthening our friendship further. First two years of my secondary education were at the Mathematical grammar school in Jordanovac. This school was phenomenal in terms of maths and physics education. Those two years provided me with an excellent foundation for my future scientific career. To this day I remain convinced that maths is particularly important for modern medical education given the big data availability not only in epidemiology, but also in any branch of medicine. For the last 2 years of my secondary education, I went back to the Classical Grammar school, where emphasis was on social sciences and languages. Changing schools gave me a great opportunity to meet very nice and interesting people with diverse interests. Some of them are internationally acclaimed musicians, artists, medics, philosophers, linguists etc.

### 3. How did you decide to study medicine?

I was toying with the idea of following my mum's career – she has a PhD in chemistry, and two of her sisters who graduated in chemistry were very successful businesswomen and scientists. Another option was history of arts, but I was persuaded to sit the entrance exam for medicine by my sister and her friend who were finishing their 3rd year of undergraduate medical studies. I passed the exam and that was it.

### 4. Did you enjoy your medical student days in Zagreb?

Medical school education was the best time ever! We worked hard and played hard. We studied a lot, but had a lot of fun, particularly popular was the Youth Club at the Medical School „KOMA“, which we attended frequently. We also enjoyed skiing. In those 'pre-climate-change' days we would go to Sljeme to do a few runs after our morning lectures and workshops. Tennis was also popular after-hours activity. Sports Club SD "Medicinar" had just acquired access to one tennis court (dvanajstica) at the nearby Šalata where both, students and staff members could book time to play. We used to play together and that's when I had the opportunity to play tennis not only with my friends and colleagues, but also with professors. Our professor of pathology, late Prof Oberman was one of my tennis partners. At the court next to ours, Josip Palada, the European zone Davis Cup winner in 1939 was often giving tennis lessons. He was kind enough to give me some useful tips on how to improve my backhand shots – with mixed results I have to say.

I still enjoy playing sports and keeping fit.



Figure 1. Graduation ceremony at Zagreb Medical School in 1986 with Prof Mijo Rudar

**5. What were your favourite subjects during the first three years at the School of Medicine?**

Pharmacology, of course. As soon as I passed the exam, I became a student „demonstrator“, helping younger colleagues with practical sessions. That was a paid duty, which was appreciated, but much more important was the insight into the experimental pharmacology for both, *in vivo* and *in vitro* approaches. I attended my first medical student conference in Tuzla, where I presented my work on skin biopsies in foetuses suffering from epidermolysis bullosa. Interestingly, many years later as a scientist I was investigating drug-induced toxic epidermal necrolysis (TEN) so my undergraduate experience was a great foundation for this work.

**6. Which basic science professors do you still remember?**

I remember many professors and lecturers fondly, some of them were at the start of their successful careers. I think that our pre-clinical teaching at Medical School was very good. We grasped the important concepts in biochemistry, physics, anatomy, microbiology etc. It may not have been obvious to us at the time how important all these preclinical subjects would be to all who are interested in experimental pre-clinical and clinical research, and to those who wish to pursue an academic career.

**7. Did you ever think that one day you might become a pharmacologist or devote yourself to one of the basic medical sciences?**

I was interested in both, pre-clinical and clinical Pharmacology very early on. When I was working at the Department of Oncol-



Figure 2. Masters Degree - MSc in Pharmacology at the University of Liverpool in 1997

ogy and Nuclear Medicine at the University Hospital Sisters of Mercy (Vinogradska cesta) in Zagreb, I was both, a clinician and research associate. We were investigating innovative radiotherapy techniques such as brachytherapy that were being introduced in our hospital. Therefore, in my mind research whether it is clinical or basic science was exciting. Therefore, my transition from clinical work to basic science research was smooth and enjoyable.

**8. Did you find the clinical subjects more interesting than the preclinical subjects?**

We were all very pleased when we started attending clinical teaching sessions at med school as we were becoming „real“ doctors. But I was always asking why? Why is this symptom and that sign happening? What is the mechanism of this and that? Why is this drug working for a specific disease and not for others? Why is this person responding to treatment and others are not? Our teachers were very often impressed by our group because we asked so many relevant questions, we were inquisitive, curious

and thirsty for knowledge, but sometimes pain in the neck as not all the answers could be given and explained. That inquisitive approach inspired me to start with some clinical research during my medical school at the Department of Dermatology looking at foetal skin biopsies.

**9. Are there any stories from your clinical studies that you still like to tell?**

I was very interested in Primary care. During our fifth year in Medical School we attended Public Health training in Zagorje. Our day started early and my friend Jasna and I were given a task to measure blood pressure in remote villages around Zlatar and Belec to population, who did not like going to health centres, particularly for prevention and screening. We were visiting locals in their small houses or sometimes in their small vineyards. From early in the morning they would offer us a welcome drink „Doktorice bute si spili kupicu“. We refused many times and offended many people as that metal cup with their local wine was the only way they felt they could show us how welcome we were in their home. Anyway, I learned that despite my better judgment and in order to show my respect to those extremely poor local people I had to have a sip „iz kupice“. From that moment, almost without exception their compliance was exemplary. That experience helped me to appreciate the importance of good rapport and communication with my patients.

**10. Which clinician or clinical teams impressed you the most? Did you have role models?**

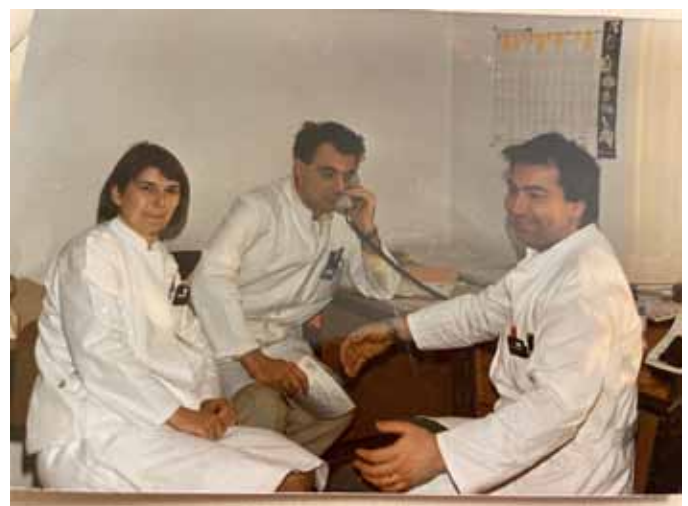
There were many brilliant medics, young and old, who inspired me to study more, to strive continuously to be a better doctor, but I must give a special mention to Prof Šime Spaventi. He was a visionary manager who lead the Department of Oncology and Nuclear Medicine at the Sisters of Mercy Hospital as successful business with the best medical equipment and Apple Mackintosh computers when others in Croatia and in the UK were using inferior platforms. Later on in my career when I was in the UK, I recognised the excellence of his innovative approach, the importance of strong links with industry and his recruitment strategy. This was hugely important for me when I became Head of Department of Pharmacology and Therapeutics in Liverpool..

**11. From your CV I see that you first worked in oncology and nuclear medicine in Zagreb, but then moved to United Kingdom. How come?**

I enjoyed working at Oncology and Nuclear Medicine Department under the leadership of Prof Šime Spaventi and later on, Prof Zvonko Kusić. I recognised that our department was one of the centres of excellence in former Yugoslavia, where many patients from far away were attending with thyroid gland problems,

and various malignances including melanoma, breast, colon or gynae cancers. Nuclear Medicine was fast developing at that time with novel technologies being developed and research as an integrated part of the specialty.

When in 1989, my husband Žarko received a British Council scholarship to complete his PhD in Obstetric MRI in Liverpool, I joined him in 1990 as a visiting Doctor in the Department of Nuclear Medicine. As I was a Nuclear Medicine specialty trainee in Zagreb, that time in the UK was very valuable for me and I learned a lot. Our plan was to stay only for a short period. However, Zarko was very well regarded not just for his clinical work but also at the University of Liverpool, so we decided to extend our stay in the UK. I had a difficult choice to make. Should I continue training in Nuclear Medicine which in the UK was a subspecialty of Radiology? This path would have taken me approximately ten years in order to become a trained Nuclear Medicine specialist with a heavy clinical commitment, on-call duties and long hospital working hours. With my husband already a clinician with a heavy workload, two small children and no extended family support, I decided to take a career break of 6 years to raise our two children. Once they started school, clinical work was not a path I wanted to pursue anymore. Science was the obvious choice. And what subject did I select? Pharmacology, of course. Immediately after completing my MSc course, I was offered a job and accepted on a PhD programme. My two PhD supervisors, Prof B Kevin Park and Prof Sir Munir Pirmohamed, were the most successful basic and Clinical Pharmacologists in the UK at the time, it was a real privilege to be part of their team. In Liverpool, my clinical training and basic Pharmacology knowledge meant that I was the important link between medics and lab scientists.



*Figure 3. Doctors office in the Department of Oncology and Nuclear Medicine with colleagues Prof Tomica Bolanča and Prof Boris Pokrajac*

**12. How long did it take to adjust to the life in the United Kingdom?**

Not long at all. We were so well accepted at work and among our many friends and neighbours. British people are generally kind, polite, pleasant, willing to accept and integrate foreigners. We've lived longer in the UK, than in Croatia, and I can proudly say that I feel that both countries are our home.

**13. Did you feel that professionally you were falling behind your husband, or you accepted it stoically as a fact of life, thinking that „my time will come“?**

I never wanted to compete with Žarko and certainly I did not think that I could or should try to match his C.V. I am well aware that very few women are so lucky not just to be able to afford not to work, but also, at the time of their choosing, go back to their career and achieve so much in a relatively short time. I feel very privileged to have been able to support my young family when they needed me most. There is a saying that behind every great man there is an exhausted woman, but to support my husband was a very easy task as he was doing so well professionally. It was my job to find the best place to live, best nurseries and schools for our children. I wanted to integrate fully our family into the British society and build our history and lasting friendships for our kids and for us. Žarko's salary provided us with comfortable living in a big house with a beautiful garden, where we had many, many unforgettable celebrations with extended family and friends, children's parties with bouncing castles, magicians, trampolines, etc. However, as soon as Ema started school at the age of four years, I knew the time had come for me to go back into science and medicine.

**14. You entered the Department of Pharmacology and Therapeutics as a Master student and ultimately became a Chair of that Department. Could you briefly outline the key events that happened during that professional trajectory of yours?**

I worked very hard, as most other people in the Department, but my two mentors Profs Pirmohamed and Park were on another level altogether. There was no weekend or an evening when they would not be at their computers. Work-life balance was not in their dictionary. That said, it was truly inspiring to witness continuous excellence over those 25 years I worked with them. Because of all the internationally renowned researchers and clinicians in the Department, we were successful in attracting many huge grants which funded excellent research. We even received a prize from Her Majesty the Queen Elizabeth II (photo). In addition, two former Heads of Department were knighted for their contribution to Medicine. Such working environment was incredibly motivating and offered me fantastic opportunities



*Figure 4. In 2015, I received an award from the British Pharmacological Society (BPS) and the Australasian Society of Clinical and Experimental Pharmacologists and Toxicologists (ASCEPT) and spent 2 weeks lecturing in Australia- Hobbard (Tasmania), Melbourne, Adelaide. With Prof Peter Molenaar, President of ASPECT, and Prof Dominic Geraghty, President-elect*

to contribute to international research. For example, my first conference talk as a PhD student was at the Cold Spring Harbor Laboratory Conference in Long Island, New York. That lab was famous for sequencing human genome, but also as James Watson of Watson and Crick DNA fame, lived there. My claim to fame is that James Watson gave a 10 minute talk to a full auditorium which bears his name, and immediately after him was Ana Alfirevic delivering a 20 minute presentation on her work. How scary was that?

International excellence was the norm at our Department, not just in research, but also in teaching and administrative duties. Therefore, I became a Governor on the Board of the Liverpool Women's Hospital, elected Trustee at the British Pharmacologi-

cal Society, Chair of the Pharmacogenomics Research Network at the European Federation of Pharmaceutical Sciences, etc. I completely subscribe to the view that talent gives you 10% chance of being successful, but 90% is hard work. It is also true that I needed self-confidence, sense of gender equality and emotional intelligence to be recognised as a leader. I was the first woman in the long history of the Department of Pharmacology in Liverpool who became Professor and later Head of Department. I am sure that none of these would have been possible if I thought that there was a glass ceiling for academic progression of women.

**15. What were the initial challenges that you encountered as Head of Department and how did you overcome them?**

The main issue was that there were many excellent researchers in the Department that did not want to work together. I am talking about 5 or 6 big players who were extremely successful in getting funding for research, about £20-30 million per project. But we had also a few junior researchers who were really struggling to get funding, and therefore were overloaded with teaching. We started a formal mentorship programme and put a lot of emphasis on staff meetings with a dedicated time to talk about ongoing research projects with frank discussions on how they can be improved and how can people contribute. That approach would generate not just useful comments, but also new collaborations and networking ideas. At least one massive grant application was successful as a direct consequence of these interactions. People started to generate ideas that highlighted long recognised research strengths in the department such as pharmacogenomics, drug safety, nanomedicines, antiretrovirals and drug-drug interactions, neuropharmacology, pharmacokinetics and pharmacodynamics in infectious diseases.



*Figure 5. EU Commission FP7 grant meeting with collaborators in Tallinn- Colin Palmer, Mia Wadelius, Alun McCarthy, Ana Alfirevic, Anu Aaspollu, Katarzyna Bloch, Cyrielle Maroteau, Moneeza Siddiqui, Joseph Fahy*

Far more rewarding than attracting funding for me as HoD, was when my younger female colleagues saw me as their role model. For many years I was the only female academic member of department and certainly the only female lecturer. When I was leaving, several women, two of them were newly appointed professors, said to me that I inspired them to take on Clinical Pharmacology. They thought that I maintained my good nature and humane characteristics with grace and dignity throughout my career in a man's world of Pharmacology! I was chuffed but also convinced it was a two way street, because I learned a lot from all my students. They came from all over the world, and when they returned back to their countries they were very successful professionals indeed.

**16. Early in your career you entered a new field of pharmacology named either pharmacogenetics or pharmacogenomics. Sorry, but I do not know the difference between these two disciplines. Maybe you could enlighten us since you have written several articles about this aspect of pharmacology.**

The two terms, pharmacogenetics and pharmacogenomics, are often used interchangeably. Both describe a discipline that investigates how do human genes influence response to medications in terms of both, efficacy and safety. Although strictly speaking the former term was coined when the discipline was dealing with a single gene at one time, while the latter includes testing all the genes in the genome. Today, our capability to sequence the whole genome in many research laboratories globally has increased the pool of information and our knowledge dramatically. Big data handling, artificial intelligence and machine learning have all been part of my research and my PhD students have mastered many skills that are now very much in demand.



*Figure 6. As Head of Department of Pharmacology and Therapeutics I took part in the Graduation Procession when my mentor Prof Kevin Park received an Honorary Fellowship at the University of Liverpool. Here together with a few of Kevin's former PhD students.*

**17. Genes seem to play a major role in predisposing people to adverse drug reactions. Genetics of which drug reactions did you study in greatest detail?**

We were interested mainly in serious and lifethreatening adverse drug reactions (ADRs). Initially, because of our good working relationship with neurologists interested in refractory epilepsy, we started with antiepileptic drugs, especially carbamazepine which causes hypersensitivity reactions. Meanwhile, several epidemiological studies demonstrated that 6.5% of all hospital admissions in England were caused by ADRs. In paediatrics, the percentage was even higher (>14%). We focused on drugs that most commonly cause severe ADRs. Anticoagulants, warfarin in particular, was the top culprit. Interestingly, it took approximately 17 years from the discovery of genetic factors that influence warfarin dose requirements to the implementation of point-of-care genetic testing for dose optimization. I am very proud to have been an active participant in the journey from the discovery of genetic associations to implementation of pharmacogenetic testing in the UK National Health Service. The process included training for clinicians on how to interpret genetic results and how to adapt the dose in an individual patient. We have developed a clinical decision support system aimed for bed side use by busy clinical staff. We investigated also statin-induced muscle toxicity, clozapine-induced agranu-

locytosis, drug-induced liver toxicity, misoprostol-induced hyperpyrexia in South American women with postpartum haemorrhage, and many others.

**18. Genomics of adverse drug reactions is one of your major interests. Hence these two questions for you: Do most adverse drug reactions occur in people who have a genetic predisposition to such reactions? How much progress has been made in defining the genetic basis of drug reactions in various human populations?**

Warfarin, antiplatelet agents and opioid analgesics are good examples of drugs associated with severe adverse drug reactions that require hospitalisation. The aetiology of these adverse drug reactions and inter-individual variability to drug response is very complex. There are multiple factors at play, such as individual patient characteristics (age, sex, body mass index), clinical factors (renal or hepatic impairment; co-medications), environmental exposures (smoking) and genetics. There is no question that safety of prescribing can be improved with pharmacogenetics and evidence based guideline recommendations are now available. However, implementation has been limited to a relatively few academic hospital centres. The key next step is to tackle prescribing in primary care. Only then we will be able to see the real benefits on the population level.



*Figure 7. Global Pharmacogenomics Network Meeting in London in 2019- Attendees: Ana Alfirevic, Jonathan Bruun, Wasun Chantratita, Ann Daly, Collet Dandara, Marie-Pierre Dubé, Andrea Gaedigk, Kathy Giacomini, Henk-Jan Guchelaar, Dyfrig Hughes, Magnus Ingelman-Sundberg, Stefania Koutsilieri, Ron Krauss, Lawrence Lin, Christine McNamee, George Patrinos, Ewan Pearson, Minoli Perera, Munir Pirmohamed, Krishna Prasad, Mark Ratain, Mary Relling, Dan Roden, Matthias Schwab, Chonlaphat Sukasem, Ron van Schaik*

Your question about different populations raises an extremely important point that has been one of the key drivers of my research. Pharmacogenomic testing can lead to even more health inequalities despite the concerted international efforts to include as many diverse populations from all continents into pharmacogenomic research and implementation. I contributed to the H3 Africa project where we developed specific gene chips for diverse tribes in Africa to enable genome wide association studies in that population. Genetic testing in South American population is even more complex. This population is a true genetic melting pot of indigenous population, Europeans, Japanese, and other immigrants.

**19. Your official title is Professor Emerita of Pharmacology and Personalised Medicine at the University of Liverpool. To me this indicates that pharmacogenomics is very important for personalised medicine. How important is it?**

Pharmacogenomics (PGx) is the study of how genetic variation affects drug response. PGx aims to move away from the standard empirical trial and error prescribing approach and transition towards a more stratified and precise prescribing paradigm. Personalised medicine, or precision medicine as it is known in the US, is an innovative approach that uses information about an individual's genomic, environmental and lifestyle information to guide decisions related to their medical management. I am a bit biased, I think that the concept of personalised medicine has developed through pharmacogenomics. Admittedly, we medics have been trying to adapt therapy to individual patients ever since pharmacology existed. In fact Paracelsus, a German-Swiss physician in the 16<sup>th</sup> century thought us that "All things are poison and nothing is without poison; only the dose makes a thing not a poison».

**20. You have extensively collaborated with practicing clinicians and industry. How productive were these collaborative research projects?**

I regard very highly research that goes on in pharma industry. I have learned a lot from them about regulatory science and drug safety reporting. We also benefited from their expertise in statistical genetics. That said, we need more pre-competitive collaborations. Our most exciting work came from collaborations with competing pharma companies. They had to agree to join forces to develop a solution for a problem that they all share, and from which none of them would gain a competitive advantage. One such example in the biggest collaborative project that I contributed to, funded by the Innovative Medicines Initiative (IMI) an EU grant giving body. The aim of the project was to improve tests for liver toxicity in early drug development. Twelve big pharma companies, four small to medium-size enterprises (SMEs) and ten EU universities were partners in this £32 million project.



*Figure 8. The Department of Pharmacology received the Queens Anniversary Prize for Higher and Further Education (2018-2022), the prize, which is the highest accolade for any academic institution*

I also collaborated with SMEs to develop a simple and cheap genetic test for determining a panel of HLA alleles implicated in immune-mediated ADRs. We validated that test in our DNA archive from patients who experienced serious ADRs, and developed a clinical decision support system, which is now used in several PGx centres in EU and US.

In my final few years, I led several pharmacology and systems biology projects in reproductive medicine and pregnancy, including the multiomic approach to preterm birth within the Harris Centre for Preterm Birth. That was an opportunity to work with my husband and we jointly supervised 3 PhD students. You can imagine how stressful it was for our students to have Alfirevic & Alfirevic as their supervisors!

**21. You have been very active in several British and European pharmacological and genetic societies. In retrospective was this time and effort well spent or is it too early to say if it was worthwhile?**

I am Elected Trustee of the British Pharmacological Society with responsibility for Senior Academic Leadership, which is very enjoyable for several reasons. This role gave me the opportunity to network with more than 5,000 members worldwide. This role is also an unique platform to implement new ideas and visions in keeping with the BPS high standing in pharmacology research and education communities, not just in the UK but also internationally; I am determined to develop the spirit of inclusion, to promote pharmacology as a science that unites clinical and basic science knowledge, skills and expertise for the benefit of patients, research communities and students.

As a Member of the Genomics England Clinical Interpretation Partnership (GeCIP) and the lead for PGx data interpretation I was involved in the 100,000 Human Genomes project. That was Genomics England's very first initiative to sequence 100,000 whole genomes from around 85,000 NHS patients affected by rare diseases or cancer. This was particularly worthwhile as such huge genetic datasets allowed detailed analysis of PGx relevant information. Big data are full of blind alleys so careful interpretation is essential. This project provided me with the opportunity to design a Masters programme to train the NHS staff about the role of genomics in healthcare – another very worthwhile initiative.

**22. You have published more than 160 peer-reviewed papers, many of them in high impact journals, but also served on editorial boards or as editor of medical journals. Do you still hold some of those editorial functions?**

I am Senior Editor of the British Journal of Clinical Pharmacology and I serve on the editorial board of two other journals - Pharmacogenomics and Journal of Personalised Medicine. There are many invitations to join different editorial boards and I select these roles very carefully as editorial duties require a lot of work and dedication. If you want to do editor's job properly, by which I mean being fair to all hard-working researchers that submit papers to your journal, you need to have time and make an effort. I have had many rejected papers in my career, and I am fully aware of the impact this may have, particularly on young researchers. This is the reason why I expect such high standards from myself and my fellow editors. We are all genuinely interested in great research, and we want to see it published as soon as possible.



*Figure 9. Liverpool in 2023 after I retired from the University*



*Figure 10. My former students and colleagues Prof Catriona Wait, Dr Amy Chadwick and Dr Lauren Walker*



*Figure 11. British Journal of Clinical Pharmacology Senior Editor's Meeting- Serge Cremers, Andrew Webb, Oscar Della Pasqua, Geert Jan Groeneveld, Robert Likić, Ana Alfirevic, Robert Bies, Ann Daly, Charles Whalley, Chris Ackroyd, Anya Aujla-Jones*



**23. What is your most often cited paper and what is your h-index?**

My „Oscar“ goes to the NEJM paper that stemmed from my PhD on antiepileptic drug-induced immune mediated skin reactions that are on occasions life threatening. We found an association between a human leukocyte antigen (HLA-A\*31:01) gene and carbamazepine induced -hypersensitivity reaction in Caucasian population. We introduced the concept of probability calculations in order to help clinical interpretation of our results. This is now fairly common in PGX research. I was the corresponding author for that paper. Working on that paper with the best medical journal editorial team in the world was a real eye-opener. I wish we could provide such experience to all authors who submit papers for publication. My second „Oscar“ for highly cited papers goes to the paper we published in the journal „Nucleic Acid Research“ based on HLA allelefrequencynet database. One of my PhD students worked with bioinformaticians and data scientists to log all the HLA alleles that have been associated with diverse adverse drug reactions, which was an addition to the HLA allele frequency database. We summarized all published information to guide everyone who deals with drugs that may cause immune-mediated adverse drug reactions.

Google science	
Citations	7750
h-index	44
i10-index	89

**24. Which one is your favourite paper?**

It will have to be one of the first papers that I wrote at the University of Liverpool. It was a small ‘negative results’ paper, published in Pharmacogenomics, which showed that there was no association with HLA-B\*15:02 and carbamazepine-induced SJS/TEN in Caucasian population. Although published in a relatively low impact factor journal, the paper made a huge clinical impact and was included in the Summary of Product Characteristics in the Product Information leaflet of several Drug Regulatory Agencies such as MHRA, European Medicines Agency (EMA), FDA etc.

**25. I see that you hold a British PG certificate in Teaching and Learning? Is this certificate required from all professionals entering British medical education? How much time did you spend teaching medical students and clinical residents?**

It was necessary to attend formal education for undergraduate teaching at the University of Liverpool for all academic staff members. Every Lecturer had to demonstrate that they acquired theoretical pedagogical knowledge and to have several formal



Figure 12. Keeping fit in the Health Club Esplanade, Zagreb

observed lectures to undergraduates, where detailed feedback was provided on what was done well and what could be improved in further teaching sessions. I opted for a 2 years part-time course that was required for promotion to Senior Lecturer. I must say that was my most difficult degree. I was working full time, had to teach students, had to attract funding for my research and then attend half day sessions at the University Education Centre, write essay assignments during the night and pass 5 modules to achieve the certificate. I was exhausted, but very pleased when I achieved a Merit.

I had to do a lot of teaching for medical students and science degree students, however, as a senior academic I enjoyed more developing curricula for students. As I was working on the syllabus for Personalised Medicine and Genetics Theme, I visited the Medical Education Department at Stanford Medical School and discussed my ideas with the Dean for Medical Education and the Curriculum Lead for Pharmacology, Prof Brian Kobilka who happened to be the winner of the Nobel prize in Chemistry in 2012 for studies of G-protein-coupled receptors. Our goal as educators is to prepare a new generation of health and science professionals and physicians to work in a world that will evolve over their 30+ years career. Emerging concepts in Pharmacology have to be seamlessly integrated with enduring basic and clinical science concepts. The theme I developed, included lectures and workshops about pharmacogenomics, but they were much broader and clinical geneticists, genetic counsellors, ethicists and statistical experts contributed to teaching. I worked with Communication Skills Tutors to develop scenarios that students had to read and discuss among themselves before coming to the teaching session. One of the very successful scenarios was on BRCA gene and the probability of breast and ovarian cancer in families that carry risk alleles. Supervised by genetic counsellors,



Figure 12. With family skiing

our students had to communicate the risks to their patients and their siblings. We used actors instead of real patients which was great fun. The teaching on risk and probabilities was done in collaboration with the Harvard University and Massachusetts General Hospital Clinician Training leads. Our key learning outcomes were ability to synthesise complexity, uncertainty and risk to facilitate shared decision making with patients focusing on acute medical care.

For the NHS staff, I developed the Pharmacogenomics and Stratified Medicine module within Genomics Education Programme. I found that teaching in groups of diverse student populations, (medics, chemistry, pharmacology, pharmacy) was the most inspiring and rewarding, as they all contribute their expertise for the benefit of all.

Common to all my academic endeavours is the opportunity and joy of working with diverse multidisciplinary and multinational teams with mutual understanding and respect for equality and diversity.

## 26. What are you most proud of in your professional life?

My students! Liverpool Uni is truly multinational and multicultural. I taught many British students that were brilliant, but my big inspiration were foreign students, starting on their PhD journey with rather poor knowledge of English and education, and prior knowledge that doesn't match that of their UK counterparts. Seeing them how they blossom, often ending up with distinction at the end of their degree, would give me a great sense of pride.

One of my former PhD students who worked in my lab on statin-induced muscle toxicity, developed an *in vitro* model of muscle bundles derived from human primary myocyte, which could contract in a 96 well plate. She used that model in her

postdoctoral work to monitor how the muscle tissue responds to microgravity and accelerated aging processes in space. She was funded by the European Space Agency and she prepared her experiment which was taken to the International Space Station. You can see the experiment being unpacked by one of the astronauts in the Space Station (<https://youtu.be/eUdCth7ycYo>). Several students who acquired highly sophisticated programming skills, bioinformatic skills, whole genome sequencing data analysis, machine learning and artificial intelligence to integrate multi-omic data in diverse clinical areas, did very well. They became lecturers in Oxford, Cambridge and Manchester University immediately after they completed their PhD studies. At international conferences I usually meet some of my former students, who are now very well regarded researchers and/or clinicians in the UK or in their home countries; Germany, France, Sweden, Italy, Jordan, United Arab Emirates, Saudi Arabia, Libya, Uganda, Egypt, Mexico, Malawi, etc.

## 27. Since you retired and spend more time in Croatia, do you have plans for some collaborative projects with Croatian scientists?

I am open to discuss education and research collaboration. However, I strongly believe that university education at the undergraduate and particularly, at the postgraduate level has to be research-informed and research-led. I am no good in giving lectures that have to be done just because they are part of a syllabus. At this stage of my career my value is in giving lectures based on topics that I am an internationally recognised expert for. I heard many times that my lectures inspired students to select Pharmacology later in their medical or research career. Therefore, my window of opportunity to collaborate with Croatian scientists and educators remains limited. Given the exponential growth of entire medical knowledge that doubles every few months, it is important to equip students and junior doctors with tools and skills how to find and importantly, how to interpret relevant information and knowledge that is of benefit to their patients. I think that communication skills and confidence to say „I don't know“ are important attributes for doctors that we are training now. They will be working in the ever changing medical environment for many decades to come.

## 28. Any message for our younger colleagues considering to follow in your footsteps?

My message to them is that a journey is much more important than the final destination. Everything is possible, absolutely everything as long as you put your heart, your effort and your talent into your journey. And enjoy it, despite all 'negativity', junior doctors strike actions and the rest, we are a very privileged profession given the opportunity to do great research and treat patients.