



S prof.dr.sc. Draganom Primorcem, liječnikom i znanstvenikom, ali koji je i mnogo više od toga, razgovaramo o njegovim širokim interesima i doprinosu koje godinama neumorno daje na različitim područjima svojeg djelovanja te o tome kako svijet učiniti boljim mjestom za život.

Professor Dragan Primorac, M.D, Ph.D., a physician, and a scientist but who is also much more than that, in which he talks about his broader interests and contribution that he's tirelessly made over the years in various fields of his work, and about how to make the world a better place to live.

# DRAGAN PRIMORAC

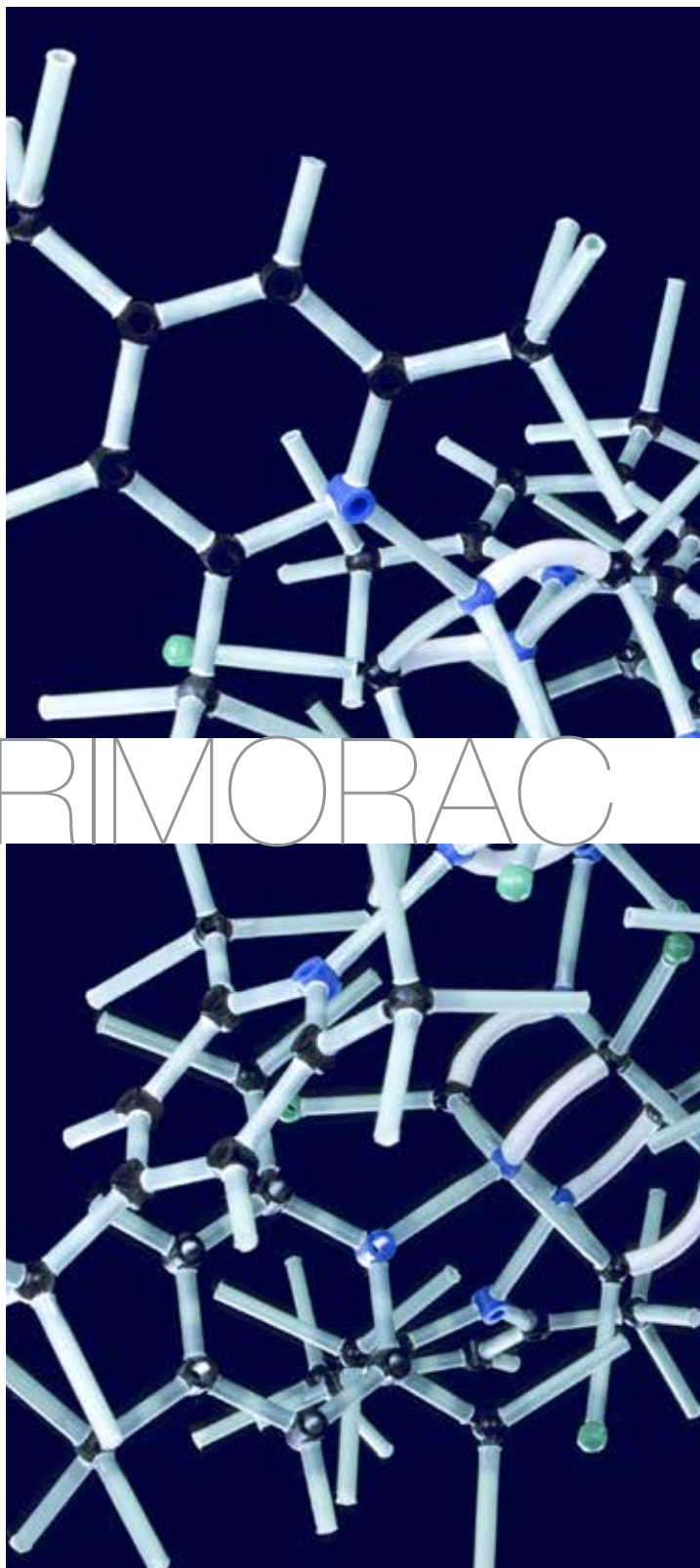
KAKO UČINITI SVIJET  
BOLJIM MJESTOM ZA ŽIVOT

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HOW TO MAKE THE WORLD  
A BETTER PLACE TO LIVE

PIŠE/BY \_ [Ksenija Žlof](#)

FOTOGRAFIJA/PHOTO \_ [Damir Fabijanić](#)



**Ž**ivimo u vremenu koje nam, možda više nego ikad, zorno pokazuje koliko je važno stvaranje mostova među ljudima. Nedavno je američki politički strateg i lider američke židovske zajednice Ari Mittleman u svojoj knjizi *Staze pravednika: priče o herojstvu, humanosti i nadi* hrvatskog liječnika i znanstvenika prof. dr. sc. Dragana Primorca uvrstio među devet osoba sa svih kontinenata koji su svojim radom pridonijeli izgradnji baš takvih mostova. Naslov te knjige kao da je vidovito najavio osobine koje nam najviše trebaju upravo sada, u ovom globalno izazovnom vremenu.

■ **Što za Vas znači uvrštavanje u spomenutu knjigu i kako ocjenjujete trenutak u kojem živimo?**

– Čast je biti u knjizi s iznimnim ljudima koji su tijekom svojeg života činili

dobro i, kako autor kaže, *hodali stazama pravednika*. Opisujući značenje pravedničke staze u *Knjizi izreka*, kralj Salomon kaže: *A pravednička je staza kao svjetlost svanuća, koja je sve jasnija do potpunog dana*. Ukratko, riječ je o ljudima koje senator Joseph Lieberman smatra ljudima koji s dobrom voljom djeluju zajedno i pobjeđuju netrpeljivost. Odgovornost svih nas jest usprotiviti se nepravdi i izboriti za prava onih najugroženijih. Knjigu *Staze pravednika* doživljam kao poziv na suradnju ljudi dobre volje kako bi zlo svake vrste, uključujući rasizam, ugrožavanje prava manjina te antisemitizam zauvijek nestali. Smatram da je bit svega sažeta u riječima Martina Luthera Kinga Jr.: *Najveća tragedija nije ugnjetavanje i okrutnost loših ljudi, već šutnja onih dobrih*.

veći se translacijskom medicinom, kojoj je svrha najnovije znanstvene spoznaje integrirati u kliničku praksu. Ako pogledate rangiranje najboljih svjetskih zdravstvenih institucija, prednjače one koje su u svakodnevni rad integrirale načela translacijske medicine. Osobno nikada nisam ostao vezan okovima postojećih znanja, nego je put kojim kročim konstantno traženje novoga. I tako više od 30 godina.

■ **Na čemu upravo najviše radite kad je riječ o medicinskoj praksi, a čemu ste se posvetili u znanstvenim istraživanjima?**

– Integracija koncepta personalizirane medicine u kliničku praksu trenutno je moj najveći prioritet. Personalizirana medicina temelji se na poznavanju i razumijevanju procesa na molekularnoj razini, što ima ključnu ulogu u pravodobnoj dijagnostici bolesti, no isto tako i u optimizaciji liječenja. Moj tim jednostavno živi personaliziranu medicinu, a kao odgovor na vaše pitanje istaknut ću samo dva segmenta našeg rada. Jedan od njih jest vezan uz rezultate naših petogodišnjih kliničkih istraživanja kojima smo po prvi put utvrdili molekularni mehanizam učinka autolognog mikrofragmentiranog masnog tkiva, koje sadrži mezenhimalne matične stanice, prilikom liječenja oštećenja zglobne hrskavice u oboljelih od osteoartritisa. Primijetili smo da takav oblik liječenja dovodi do značajnog porasta glikozaminoglikana (ključnih molekula hrskavičnog tkiva), što je za posljedicu imalo statistički značajno poboljšanje kliničkog statusa pacijenata u odnosu na početne rezultate. Drugi primjer vezan je uz kliničku aplikaciju farmakogenomike i tzv. genetičkih proaktivnih ili prediktivnih testova u kliničku praksu. Farmakogenomika pomaže razumijevanju zašto neke osobe odgovaraju na lijekove, a druge ne, zašto neke osobe trebaju više ili niže doze za postizanje optimalnoga terapijskog odgovora, a može upozoriti i na pacijente koji neće odgovoriti na terapiju, odnosno, na one u kojih se mogu pojaviti toksične nuspojave. S druge strane genetičke proaktivne ili prediktivne testove koristimo u svrhu prevencije nastanka bolesti i pravovremenog otkrivanja bolesti kao i u optimizaciji liječenja. Primjerice, nedavno smo u suradnji s američkim partnerima objavili rad u časopisu *Frontiers in Medicine*, a u objavljenom radu analizirali do sada najveći broj gena povezanih



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01 Dr. Primorac u svojem uredu u Specijalnoj bolnici sv. Katarina, koja je zasnovala partnerstvo s najvećom američkom zdravstvenom institucijom University of Pittsburgh Medical Center Prof. Primorac, M.D., Ph.D., in his office at St. Catherine Specialty Hospital, which has entered into a partnership with the largest medical institution in the US, the University of Pittsburgh Medical Center

02 Kao jedan od onih koji pridonose izgradnji mostova i tolerancije među ljudima, prof.dr.sc. Primorac uvršten je u knjigu Arija Mittlemana *Staze pravednika* Prof. Primorac, M.D., Ph.D., is included in Ari Mittleman's book *Paths of the Righteous* as someone who's contributed to building bridges between people

■ **Tijekom vaše bogate karijere jednako se uspješno posvećujete znanstvenom radu i liječničkoj praksi. Jedan od najvećih svjetskih izdavača znanstvene literature ELSEVIER BV objavio je popis na kojemu je i Vaše ime, a odnosi se na dva posto znanstvenika u svijetu s najvećim utjecajem citiranosti. Kako uspijevate uspostaviti ravnotežu između znanstvenog rada i njegove primjene u praksi? Koliko je važno povezivanje teorije s praksom?**

– Medicina je oduvijek bila moja ljubav, no znanost mi je bila i ostala trajna inspiracija u traženju novih znanja i novih istina. Jedno i drugo objedinio sam ba-

s nizom nasljednih kardioloških stanja koja dovode do iznenadne srčane smrti, točnije 294 gena.

■ **Vaša bolnica Sveta Katarina i Vi osobno dali ste velik doprinos u potrazi za uspješnim načinom suzbijanja i liječenja bolesti COVID-19, između ostaloga i mezenhimalnim matičnim stanicama. O čemu je riječ i nastavljate li i dalje istraživanja na tom području?**

– U časopisu *Vaccine* upravo smo objavili važne rezultate koji potvrđuju da je, za razliku od razine protutijela, razina stanične imunosti (koja je ključna u obrani od ponovne infekcije SARS-CoV-2) uglavnom konstantna u osoba koje su preboljele COVID-19 ili su cijepljene. Ti rezultati pridonose boljem uvidu u imunopatogenezu COVID-19, ali i javnozdravstvenom zbrinjavanju pandemije SARS-CoV-2. Istodobno, među prvima u svijetu uspješno smo primijenili liječenje mezenhimalnim matičnim stanicama pacijenta s teškom kliničkom slikom COVID-19. Mezenhimalne matične stanice koje su primijenjene u pacijenta s COVID-19 dobivene su iz koštane srži zdravog donora, potom selektirane i uzgajane u posebnim uvjetima. Ove su stanice posebne jer ne sadrže glavni sustav tkivne podudarnost (HLA-II), čime se sprečava imunosna reakcija organizma primatelja na stanice donora. Ključno je da prilikom sustavne primjene (putem cirkulacije) mezenhimalne matične stanice dolaze na mjesto upale ili oštećenog tkiva, pa tako i do plućnog tkiva te na tim mjestima sekrecijom oslobađaju brojne bioaktivne faktore koji imaju snažan protuupalni, imunomodulatorni, anti-apoptotični (sprečavanje smrti stanice), ali i regenerativni učinak. Kolege iz Izraela s kojima surađujemo također su pokazali sjajne rezultate, no još uvijek je riječ o malom broju pacijenata i za konačne prosudbe potrebno je napraviti velike kliničke studije. Na tragu svega, naš nedavno objavljeni pregledni članak u časopisu *Frontiers in Immunology* detaljno analizira odgovor imunskog sustava na infekciju uzrokovanom SARS-CoV-2.

■ **Bolnica Sveta Katarina ušla je u iznimno značajno partnerstvo s najvećom američkom znanstvenom institucijom University of Pittsburgh Medical Center (UPMC). Zamolila bih da nam približite značaj tog partnerstva.**

– UPMC je vrhunska zdravstvena institucija koja je ponos američkog zdravstva.

Osnovana je 1893. godine, a trenutno zapošljava 92.000 djelatnika, od toga 5.000 liječnika. Godišnji proračun bolnice jest 23 milijarde američkih dolara, a u lancu UPMC-a ukupno je 40 bolnica s 8400 kreveta. S druge strane, Specijalna bolnica Sv. Katarina stekla je svjetsku prepoznatljivost, koliko zbog sjajnih stručnjaka, toliko i zbog sustavnog integriranja najnovijih znanstvenih spoznaja iz personalizirane medicine u kliničku praksu. Naši su zajednički planovi brojni, a tu ponajprije mislim na znanstvenu i stručnu suradnju u području personalizirane medicine jer duboko vjerujemo da ona čini temelje za iskorak u medicini 21. stoljeća.

■ **Često ističete važnost farmakogenetike i implementacije personalizirane medicine u kliničkoj praksi. Također smatrate da bi se Hrvatska mogla pozicionirati kao jedan od lidera na tom području. Možete li to dodatno pojasniti?**

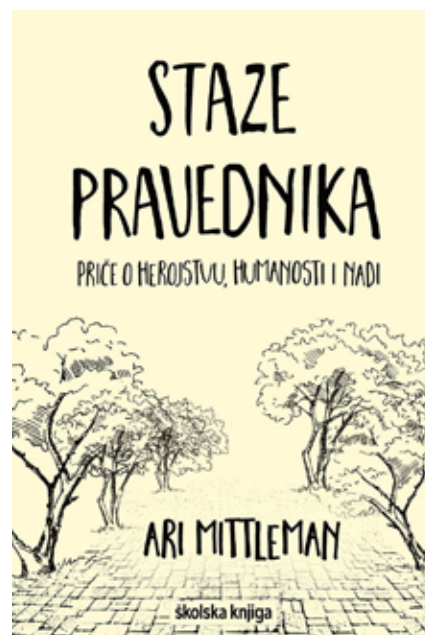
– Farmakogenetika između ostalog proučava vezu između genetičke predispozicije pojedinca i njegove sposobnosti metaboliziranja, transporta i distribucije određenog lijeka, kao i sposobnosti veza za određene molekularne mete poput receptora, enzima i drugih proteina. Ona pomaže razumijevanju zašto neke osobe nemaju željeni terapijski odgovor nakon primjene lijeka, zašto je za postizanje optimalnoga terapijskog odgovora kod nekih osoba potrebno primijeniti višu ili nižu dozu lijeka, a može uputiti i na one pacijente kod kojih će terapijski učinak izostati, odnosno na one u kojih se mogu pojaviti neželjeni učinci lijekova. Vodeći američki medicinski časopis *JAMA* prije niz godina objavio je članak o tome da samo u SAD-u u godišnje više od 2 milijuna hospitaliziranih bolesnika nakon uzimanja lijekova ima ozbiljne štetne učinke lijekova, dok njih 106.000 zbog štetnih učinaka lijekova umre. Danas su te brojke znatno veće. Zbog navedenoga, samo u SAD-u zdravstveni sustav izdvaja 30 milijardi dolara godišnje za liječenje komplikacija uzrokovanih štetnim učincima lijekova. S druge strane, nedavni podaci za Europu pokazuju da se 7 do 13 posto pacijenata prima u bolnicu zbog neželjenih reakcija na lijekove te da bi se korištenjem farmakogenetike većina tih učinaka mogla spriječiti. Specijalna bolnica Sv. Katarina, u suradnji s američkim partnerima iz poduzeća OneOme, čiji je

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**Integracija koncepta personalizirane medicine u kliničku praksu trenutno je moj najveći prioritet. Moj tim jednostavno živi personaliziranu medicinu.**

Integrating the concept of personalised medicine into clinical practice is at present my top priority. My team lives and breathes personalised medicine.

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suosnivač čuvena Mayo Clinic, u kliničku praksu uvela je do sada najsveobuhvatniji farmakogenetički test (analizira 27 gena i 111 pripadajućih polimorfizama odgovornih za metabolizam više od 300 lijekova). Knjiga koju smo objavili, *Farmakogenetika u kliničkoj praksi: iskustvo s 55 lijekova korištenih u kliničkoj praksi*, napisana je na engleskome, njemačkom i hrvatskom jeziku kako bi liječnici širom svijeta razumjeli važnost primjene farmakogenetike u kliničkoj praksi. Osim toga, ovih dana dovršavamo do sada najsveobuhvatniju knjigu iz farmakogenomike u izdanju Springer Naturea, jednog od najuglednijih svjetskih izdavača. Najvažniji cilj nam je

I ove godine u Dubrovniku u suradnji s Mayo Clinic, ISABS-om i bolnicom Sveta Katarina organizirate veliki kongres, koji obraduje teme iz forenzike i antropološke genetike i koji već postaje ne samo tradicionalan nego i legendaran jer je na njemu do sada sudjelovalo sedam dobitnika Nobelovih nagrada. Koje su teme ovogodišnjeg kongresa i na čemu će biti naglasak?

– Suradnja s Mayo Clinic izniman je privilegij. Posebno sam zahvalan vodstvu Mayo Clinic koje već gotovo dva desetljeća daje potporu zajedničkoj suradnji. Naš kongres okuplja vodeće svjetske liječnike i znanstvenike iz područja personalizirane medicine i jedan je od najznačajnijih svjetskih događaja iz ovog područja. U radu dosadašnjih kongresa sudjelovalo je sedam dobitnika Nobelove nagrade (prof. dr. Robert Huber, prof. dr. sc. Aaron Ciechanover, prof. dr. sc. Ada Yonath, prof. dr. sc. Paul Modrich, prof. dr. sc. Harald zur Hausen, prof. dr. sc. Avram Hershko, prof. dr. sc. Richard Roberts) te 5800 znanstvenika i petstotinjak pozvanih predavača, ukupno iz više od 70 država, što je Republiku Hrvatsku odredilo kao jednu od najznačajnijih destinacija iz područja znanosti, zdravstva, inovacija, ali i turizma. U radu ovogodišnjega, dvanaestog izdanja *ISABS Conference on Forensic and Anthropologic Genetics and Mayo Clinic Lectures in Individualized Medicine*, koja se u Dubrovniku održava od 22. do 27. lipnja 2022. godine uz više od 500 sudionika, sudjelovat će tri dobitnika Nobelove nagrade, prof. dr. sc. Richard Roberts, prof. dr. sc. Thomas Südhof i prof. dr. sc. Aaron Chechanover. Tijekom ovogodišnjeg kongresa naglasak će biti na epigenetici i njezinoj ulozi u nastanku bolesti, uključujući i nastanku karcinoma, farmakogenomici, genskoj i staničnoj terapiji, regenerativnoj medicini, ulozi strojnog učenja i umjetne inteligencije u liječenju karcinoma, prenatalnoj dijagnostici, forenzičkoj i antropološkoj genetici, ali i brojnim drugim inovativnim temama u medicini 21. stoljeća. Naša partnerska institucija tradicionalno je Američka akademija za forenzične znanosti.

In collaboration with the Mayo Clinic, the International Society for Applied Biological Sciences or ISABS, and St. Catherine Specialty Hospital, you're organising a big conference, which will again take place in Dubrovnik. This year's ISABS conference isn't the first you organised. ISABS conferences tackle topics in forensics and anthropologic genetics. What's more, seven Nobel Prize winners have participated in ISABS conferences so far, which makes it a par excellence event. What are the topics of this year's ISABS conference, and what will the conference focus on?

– Collaboration with the Mayo Clinic is an exceptional privilege. I'm extremely grateful to the management of the Mayo Clinic, which has been supporting this collaboration for nearly two decades already. Our conference brings together the world's leading physicians and scientists in the field of personalised medicine, and is one of the world's leading events in this field. Seven Nobel Prize winners have participated in the work of previous conferences, namely, Prof. Robert Huber, Prof. Aaron Ciechanover, Prof. Ada Yonath, Prof. Paul Modrich, Prof. Harald zur Hausen, Prof. Avram Hershko, Prof. Richard Roberts. Also, 5,800 scientists, and approximately five hundred invited lecturers from more than 70 countries from around the world have partook in the conferences so far. These facts have positioned the Republic of Croatia as one of the leading destinations in the fields of science, health, innovation, as well as tourism. In the work of this year's twelfth edition of the *ISABS Conference on Forensic and Anthropologic Genetics and Mayo Clinic Lectures in Individualized Medicine*, which is taking place in Dubrovnik between 22nd and 27th June, over 500 conference attendees will participate, including three Nobel Prize winners; namely, Prof. Richard Roberts, Prof. Thomas Südhof, and Prof. Aaron Ciechanover. This year's conference focuses on epigenetics, and its role in the development of disease including cancer, pharmacogenomics, gene and cell therapy, regenerative medicine, the role of machine learning and artificial intelligence in cancer treatment, prenatal diagnostics, forensic and anthropologic genetics, and a number of other innovative topics relating to 21st century medicine. Traditionally, our partner institution is the American Academy of Forensic Sciences.

omogućiti sustavno educiranje o važnosti farmakogenetike u kliničkoj praksi, čime bi se značajno smanjila pojavnost neželjenih učinaka lijekova kao i pojava smrtnosti uzrokovane lijekovima.

■ **Među vašim raznovrsnim interesima oduvijek je bilo i vaše posebno zanimanje za sport; član ste američke Kuće slavnih taekwondo, nedavno vam je uručen crni pojas 7 dan WTO organizacije i zlatna medalja Europske unije taekwondo; potpredsjednik ste Hrvatskog taekwondo saveza, član ste Vijeća Hrvatskog Olimpijskog odbora, a onedavno ste i član Zdravstvene i antidoping komisije Europskih olimpijskih odbora, najvišeg tijela svih olimpijskih odbora Europe. Čemu se želite najviše posvetiti na toj funkciji?**

– Sport je uz medicinu i znanost nedjeljiv dio moga života. Kao liječnik svim sportašima želim omogućiti pravovremenu dijagnostiku i najbolju moguću zdravstvenu skrb. Danas tu skrb temeljimo na individualiziranom pristupu, koja svakom sportašu optimizira dijagnostičke, terapijske i rehabilitacijske postupke. Upravo taj koncept svakodnevno provodimo u našoj bolnici Sv. Katarina, koja je službena bolnica Hrvatskog olimpijskog odbora i hrvatske nogometne reprezentacije.

■ **Nevjerojatno ste mnogo učinili na području suradnje Hrvatske i Izraela. Među zanimljivostima vezanima uz vaš život svakako je i prijateljstvo s Nobelovcem Shimonom Peresom te njegovom obitelji. Kako je došlo do tog prijateljstva?**

– Moj prvi susret s Shimonom Peresom dogodio se 2002. godine u njegovu jeruzalemskom uredu i tada je započelo naše prijateljstvo. Našem bliskom odnosu snažno je pridonio njegov sin i moj dragi prijatelj Chemi. Shimon Peres znao mi je govoriti: *Sanjaj veliko i to će ti se ostvariti*. Pred kraj života napisao je knjigu *Nema mjesta za male snove*, koju smo preveli i na hrvatski jezik. Sjajna autobiografska knjiga o životu iznimno mudrog čovjeka koji je obnašao gotovo sve ključne funkcije u Izraelu te na kraju postao predsjednik države i dobitnik Nobelove nagrade. Zsigurno je i jedan od najznačajnijih političara 20. stoljeća. Vjerovao je da političari i lideri nisu izabrani da demonstriraju silu i snagu, nego da služe svom narodu. U svojem predgovoru za njegovu knjigu *Nema mjesta za male snove: Hrabrost, imaginacija i stvaranje modernog Izraela*



**Farmakogenomika pomaže razumijevanju zašto neke osobe odgovaraju na lijekove, a druge ne, zašto neke osobe trebaju više ili niže doze za postizanje optimalnoga terapijskog odgovora.**

**Pharmacogenomics helps us understand why some people respond to medication and others don't, and why some people need higher and others lower medication doses to achieve optimal therapeutic effects.**

*napisao sam: Sebe je smatrao filozofom. Ja sam ga smatrao mentorom i prijateljem. Neki su ga smatrali liderom, a neki političarom. U mojim je očima bio i ostao sanjar, no jedan od malobrojnih sanjara kojemu su se gotovo svi snovi ostvarili.*

■ **Također, jedna od zanimljivosti jest i Vaše imenovanje prvim globalnim ambasadorom američkog sveučilišta Penn State, čime ste postali prva osoba u povijesti ovog sveučilišta osnovanog 1855. godine s tom titulom, a zanimljivo je i vaše imenovanje profesorom emeritusom na indijskom sveučilištu NFSU. Jesu li vas iznenadila ta imenovanja, koja su svakako veliko priznanje, ali i obvezuju.**

– Čast je biti imenovan prvim globalnim ambasadorom sveučilišta Penn State. Riječ je o sjajnom sveučilištu sa 24 kampusa na kojima studira više od 100.000 studenata iz više od 140 država širom svijeta. Penn State trenutno ima najveću mrežu aktivnih bivših studenata (Alumni) u SAD-u, njih više od 170.000, a čine je dobitnici Nobelovih nagrada, članovi američkog Senata i Kongresa, guverneri, suci Vrhovnog suda SAD-a te čelnici brojnih država. Moje imenovanje profesorom emeritusom na *National Forensic Sciences University* doživio sam kao priznanje za svoj rad i zahvalan sam vodstvu sveučilišta i svim institucijama Vlade Republike Indije koje su podržali moje imenovanje. Zajednički nam je cilj razvijati interdisciplinarnu forenzičke znanosti te znanost koristiti u borbi protiv organiziranog kriminala, terorizma, bioterorizma itd., a što će svijet učiniti boljim mjestom za život. ►

**W**e live in a time that clearly demonstrates, perhaps more than ever, just how important it is to build bridges between people. In his recent book, *Paths of the Righteous: Stories of Heroism, Humanity and Hope*, the American political strategist and American Jewish community leader Ari Mittleman ranked Croatian physician and scientist Professor Dragan Primorac, M.D., Ph.D., amongst the group of nine people from the four corners of the world who have contributed to building such bridges. Moreover, the title of Mittleman's book seems to have clairvoyantly

Suradnja i prijateljstvo dr. Primorac s najuglednijim svjetskim znanstvenicima, dobitnicima Nobelovih nagrada, liječnicima i najcjeljenijim svjetskim stručnjacima na raznim područjima ovjekovječena je na fotografijama koje krase police u njegovu uredu Prof. Primorac's collaboration and friendship with the world's greatest scientists, Nobel Prize winners, physicians, and the world's leading experts in different fields immortalised in photographs displayed on shelves in his office

listed the qualities that we need the most right now in this globally challenging time.

■ **What does being included in Mittleman's book mean to you, and how would you describe and assess the time in which we live?**

– It's an honour to be included in this book in the company of exceptional people who've done good in their lives, and who've walked the paths of the righteous, to paraphrase, as it were, Mittleman's title. Describing the meaning and significance of the righteous path, in the *Book of Proverbs*, King Solomon says: *The path of the righteous is like the morning sun, shining ever brighter till the full light of day.* In brief, these are people that Senator Joseph Lieberman considers to be individuals who work together in good faith to overcome intolerance. It is the responsibility of all of us to stand against injustice, and fight for the rights of the most vulnerable. I see Ari Mittleman's book *Paths of the Righteous* as a call for people of good will to collaborate, so that evil in all its forms, including racism, violations and denials of minority rights, and anti-Semitism, would forever disappear. I think that the essence of it all is best summed up by Martin Luther King Jr.'s quote: *The ultimate tragedy is not the oppression and cruelty by the bad people but the silence over that by the good people.*

■ **During your successful career, you have devoted yourself equally successfully to both scientific work and medical practice. One of the world's leading publishers of science and health information, ELSEVIER BV, has published a list with your name on it. This list is a list of the top two percent of the world's scientists with the highest citation impact. How do you find the right balance between conducting scientific work and its application in practice? How important is it to connect theory with practice?**

– Medicine has always been my love. But science has always been my endless source of inspiration in my search for new knowledge and new truths. I've combined the two in the field of translational medicine, which looks to integrate the latest scientific knowledge into clinical practice. If you look at the ranking of the world's best healthcare institutions, the ones at the very forefront are those that have integrated the principles of translational medicine into their daily work. I've always looked to be free of the shackles of existing knowledge, and the path I tread has always been characterised by a constant search for the new. And this has been so for more than 30 years.

■ **What have you been working on the most in terms of your medical practice, and what have you devoted yourself to in terms of scientific research?**

– Integrating the concept of personalised medicine into clinical practice is at present my top priority. Personalised medicine is based on knowing and understanding processes at the molecular level, which plays a key role in not only reaching timely diagnoses, but also in treatment optimisation. My team lives and breathes personalised medicine. In answer to your question, I'll highlight two segments of our work. One of these relates to the results of our five-year clinical trials which have established, for the first time, the molecular mechanism of action of autologous micro-fragmented adipose tissue containing mesenchymal stem cells in the treatment of articular cartilage damage in patients suffering from osteoarthritis. We've observed that this form of treatment leads to a significant increase in glycosaminoglycans – these are one type of cartilage tissue

molecules – which results in a statistically significant improvement in the clinical status of patients compared to their initial assessment. The other example pertains to the clinical application of pharmacogenomics, and proactive or predictive genetic tests in clinical practice. Pharmacogenomics helps us understand why some people respond to medication and others don't, why some people need higher and others lower medication doses to achieve optimal therapeutic effects, and it can also single out patients who won't respond to therapy, or those who may experience toxic side effects. Proactive or predictive genetic tests are used to prevent the onset of disease, to detect disease in a timely manner, and to optimise treatment.

For example, we've recently published a paper in the *Frontiers in Medicine* journal in collaboration with our American partner Invitae, in which we analyse the largest number of genes associated with a number of inherited heart conditions that lead to sudden cardiac death; 294 genes, to be exact.

■ **St. Catherine Specialty Hospital, a hospital that you founded, and you personally have contributed greatly to finding a way to control and treat COVID-19 disease. This included the application of mesenchymal stem cells. Could you tell us more about this, and whether you are continuing your research in this direction?**

– In the *Vaccine* journal, we have just published a set of important results. They confirm that, in people who have had COVID-19 or have been vaccinated against it, the level of cellular immunity is mainly constant, which is not the case with antibody levels. And one must bear in mind that cellular immunity is crucial in our body's defence against SARS-

CoV-2 reinfection. These results contribute to our understanding of the immuno-pathogenesis of COVID-19, as well as to the ways in which public health authorities manage the SARS-CoV-2 pandemic. It's worth pointing out that we were also amongst the first in the world to have successfully administered mesenchymal stem cell treatment to a patient suffering from a severe COVID-19 infection. The mesenchymal stem cells administered to the patient diagnosed with COVID-19 were obtained from the bone marrow of a healthy donor in partnership with Educell Ltd. The cells were then selected, and grown in special conditions. These cells are special because they don't contain human leukocyte antigens or HLA-II, a major histocompatibility complex (MHC). Given that these cells are HLA-II-free, if you like, that prevents the recipient's body from developing an adverse immune response to the donor cells. What is crucial here is that, during systemic administration via circulation, these mesenchymal stem cells reach the site of inflammation or damaged tissue, including lung tissue, and that they secrete, in these places, a number of bioactive factors that have strong anti-inflammatory, immuno-modulatory, anti-apoptotic (cell death prevention), and regenerative effects. Our colleagues from Israel that we work with have also arrived at great results. We have to bear in mind that the number of patients treated this way is still very small, and that large clinical studies are required for a definitive conclusion. In the wake of all this, our recently published review article in the *Frontiers in Immunology* journal analyses in great detail the immune system's response to an infection caused by SARS-CoV-2.

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**Odgovornost svih nas jest usprotiviti se nepravdi i izboriti za prava onih najugroženijih.**

**It is the responsibility of all of us to stand against injustice, and fight for the rights of the most vulnerable.**

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■ **St. Catherine Specialty Hospital has entered into an extremely important partnership with a leading academic medical institution in the US, the University of Pittsburgh Medical Center (UPMC). Could you explain in more detail why this partnership is important?**

– The UPMC is a top healthcare institution, the pride of American healthcare. It was founded in 1893, and currently employs 92,000 people, of whom 5,000 are physicians. The hospital's annual budget is \$23 billion, and the UPMC chain of partner hospitals encompasses a total of 40 hospitals with 8,400 beds. Similarly, St. Catherine Specialty Hospital has gained worldwide recognition, both because it employs great experts, and because it systematically integrates the latest scientific insight gained in the field of personalised medicine into clinical practice. Together, we have many plans, primarily focusing on scientific and professional collaboration in the field of personalised medicine, because we firmly believe that personalised medicine lays the foundations for medicine of the 21st century.

■ **You often highlight the importance of pharmacogenetics and the implementation of personalised medicine in clinical practice. You also believe that Croatia could position itself as one of the leaders in this field. Could you explain this in more detail?**

– Pharmacogenetics studies, amongst other things, the link between the genetic predisposition of an individual and their ability to metabolise, transport, and distribute a drug, and their ability to bind to certain molecular targets, such as receptors, enzymes, and other proteins. It helps us understand why some people respond to medication and others don't, why some people need higher and others lower medication doses to achieve optimal

therapeutic effects, and it can also single out patients who won't respond to therapy, or those who may experience toxic side effects. A number of years ago, a leading American medical journal, JAMA, published an article stating that more than two million hospitalised patients in the United States alone have serious adverse or unwanted drug reactions after taking medication, and that over 106,000 of them die as a result. Today, these numbers are even higher. Due to this, in the United States alone, the healthcare system spends \$30 billion a year to treat complications caused by adverse or unwanted drug reactions. Similarly, recent data collected in Europe show that 7 to 13 percent of patients are admitted to hospital due to adverse drug reactions, and that the application of pharmacogenetics could, in fact, prevent most of these effects. In collaboration with our American partners from OneOme, which was founded by the Mayo Clinic, St. Catherine Specialty Hospital has introduced the most comprehensive pharmacogenetic test to date into clinical practice, which analyses 27 genes and 111 associated polymorphisms responsible for the metabolism of more than 300 drugs.

The book we published under the title *Pharmacogenetics in Clinical Practice: Experience with 55 Commonly Used Drugs* was written in English, German, and Croatian with a view to helping physicians around the world understand the importance of the application of pharmacogenetics in clinical practice. Moreover, we're about to finish the most comprehensive book on pharmacogenomics to be published by Springer Nature, one of the world's leading publishers. Our most important goal is to provide a systematic education framework that educates about the importance of pharmacogenetics in clinical practice, which would significantly reduce the incidence of adverse drug reactions, and the incidence of mortality associated with the adverse effects of medical treatment.

■ **You have many different interests, amongst which your interest in sports has always stood out. You were inducted into the Taekwondo Hall of Fame, you recently gained your seventh-Dan black belt awarded by the World Taekwondo Organisation, you were awarded a gold medal by the European Taekwondo Union, you're the vicepresident of the Croatian Taekwondo Federation, you're a member of the Croatian Olympic**

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**Committee Council, and recently you became a member of the Medical and Anti-Doping Commission of the European Olympic Committee, the highest body of all Olympic committees in Europe. While serving in this capacity, what will you focus on the most?**

– Besides medicine and science, sport is an integral part of my life. As a physician, I want to be able to give all athletes timely diagnoses, and provide them with the best possible healthcare. Today, we base this care on an individualised approach, which helps us to optimise diagnostic, therapeutic, and rehabilitation procedures for all athletes. This is exactly what we've been implementing every day in St. Catherine Specialty Hospital, which is the official hospital of the Croatian Olympic Committee, and the Croatian National Football Team.

**■ You have invested a great deal in setting up collaboration between Croatia and Israel. A fascinating and curious fact about your life is your friendship with the Nobel laureate Shimon Peres and his family. How did that friendship form?**

– I first met Shimon Peres in 2002 in his Jerusalem office, and that's when our friendship began. His son and my dear friend Chemi contributed strongly to our developing a close relationship. Shimon Peres used to tell me: *What you dream will come true, so always dream big.* Towards the end of his life, he wrote the book *No Room for Small Dreams*, which was translated into Croatian. It's a great autobiographical book about the life of an extraordinarily wise man who held almost all key offices in Israel, and eventually became president of Israel, and who won the Nobel Peace Prize. He's unquestionably one of the key politicians of the 20th century. He firmly believed that politicians and leaders are not elected to show strength and demonstrate power, but to serve their people. In the preface to the Croatian edition of his book *No Room for Small Dreams: Courage, Imagination, and the Making of Modern Israel*, I wrote: *He considered himself a philosopher. I considered him a mentor and a friend. Some considered him a leader, and some a politician. In my eyes, he was and remains a dreamer, but one of only few dreamers whose dreams, almost all of them, came true.*

**■ Another fascinating fact about your life and career is that you were appointed as the first Global Ambassador of Penn State University, which was founded in 1855. Similarly, you were appointed the honorary title of professor emeritus by the National Forensic Sciences University in India. These appointments are given in recognition of your work and contribution, but they also imply duty and responsibility. Were you surprised by these appointments?**

– It's an honour to be named as the first Global Ambassador of Penn State University. It's a great university that boasts 24 campuses at which more than 100,000 students from more than 140 countries from around the world study. At present, Penn State University has the largest network of active alumni in the United States; more than 170,000, to be precise. And the university's alumni association consists of Nobel Prize winners, members of the US Senate and Congress, governors, US Supreme Court justices, and heads of state. I saw my appointment as professor emeritus at the National Forensic Sciences University in India as recognition for my work, and I am grateful to the university's leadership and all the institutions of the Government of the Republic of India who supported my appointment. Our common goal is to continue developing interdisciplinary forensic sciences, and to use science in the fight against organised crime, terrorism, bioterrorism, etc., which will make the world a better place to live. ■

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