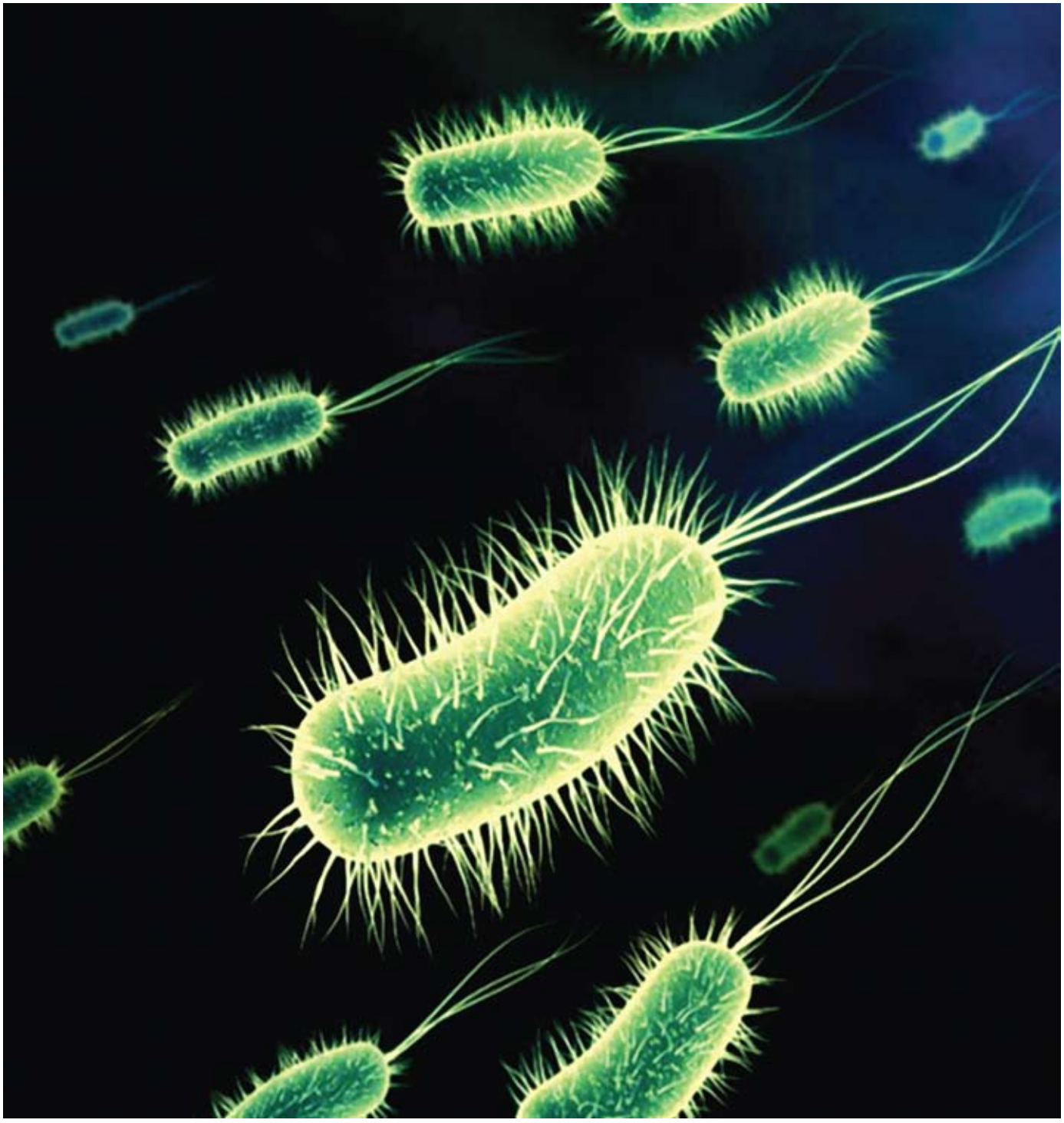


RAZGOVOR: IGOR ŠTAGLJAR

Piše/By **Anđelka Mustapić**

USPJEH

U ZNANOSTI, USPJEH JE TIMA

Fotografije/Photos **Petar Strmečki**

INTERVIEW: IGOR ŠTAGLJAR

SUCCESSES IN SCIENCE ARE SUCCESSES OF A WHOLE TEAM

Jedan od najperspektivnijih hrvatskih znanstvenika, koji već sada tvori elitu svjetske znanosti, Igor Štagljar (42), angažiran je višestruko: redoviti je profesor na Medicinskom fakultetu Sveučilišta u Torontu u Kanadi, voditelj Laboratorija za molekularnu genetiku u sveučilišnom Centru za istraživanje života, uspješni istraživač i suosnivač biotehnološke kompanije Dualsystems Biotech Inc iz Švicarske.

Igor Štagljar (42), one of the most promising Croatian scientists who is already part of the world science elite, has multiple duties: he is a professor at the Faculty of Medicine at the University of Toronto, Canada, head of the Molecular Genetics Laboratory at the Life Research Centre, a successful researcher and co-founder of the Swiss-based biotechnological company Dualsystems Biotech Inc.

Kao molekularni biolog prije deset godina Igor Štagljar počeo je - na glasovitome Švicarskome nacionalnom tehnološkom institutu ETH-u, gdje je doktorirao i poslije bio jedan od najmlađih profesora - razvijati sa svojim znanstvenim timom originalnu biotehnološku metodu za identifikaciju novih proteina uključenih u nastanak raka. Ta mu je metoda otvorila putove u proučavanju teških genetskih bolesti, osobito cistične fibroze, a za njezino je liječenje, zahvaljujući upravo prof. Štagljaru, potreban, kako se vjeruje, još samo jedan korak.

■ **Razvili ste sa suradnicima, i patentirali, tehnologiju membranskoga dualnog sustava (MYTH). Najjednostavnije objašnjeno, o kakvoj je tehnologiji riječ i zašto je ona tako epohalna, kako je ocijenjena u svjetskim znanstvenim krugovima? Primjerice, utjecajni znanstveni časopis *The Scientist* uvrstio ju je među sedam tehnologija u području istraživanja života, koje će u idućem desetljeću obilježiti biomedicinske znanosti. Zbog nje ste, na posljetku, nagrađeni najuglednijim kanadskim priznanjem za inovaciju... Što Vaša tehnologija znači za samo istraživanje i, možda, jednoga dana za liječenje genetskih bolesti?**

- Tehnologija MYTH jest molekularno-biološka metoda kojom se mogu pratiti *kontakti među proteinima* ili tzv. *proteinske interakcije*. Što to, jednostavno rečeno, znači? Proteini su važne makromolekule u svim organizmima, gdje obavljaju mnogo esencijalnih funkcija. Prilikom obavljanja tih funkcija proteini nikad ne djeluju sami, nego kontaktiraju druge proteine. Mnoge ljudske bolesti posljedica su ili prekida normalnih ili nastanka novih proteinskih interakcija. Zato je vrlo važno biti kadar pratiti i detektirati proteinske interakcije preko molekularno-bioloških metoda, jer tako možemo spoznati kako razviti nove terapije protiv brojnih ljudskih bolesti. Sve te navedene proteinske interakcije možemo pratiti MYTH tehnologijom, a njezina najveća prednost pred ostalim tehnologijama kojima se danas koristi u molekularnoj biologiji jest činjenica da je to zasad jedina metoda koja se uspješno može primijeniti na velikom broju proteina što se nalaze na samoj periferiji stanice. Primjerice, ljudski proteini koji su uključeni u nastanak cistične fibroze, Alzheimerove bolesti, shizo-frenije, Parkinsonove bolesti, tumora mozga, pluća i dojke, kao i brojnih drugih bolesti mogu se izravno analizirati našom MYTH metodom. Na taj je način, MYTH tehnologija prvi korak u procesu razvitka novih lijekova (eng. *drug discovery*) jer s pomoću nje možemo otkriti nove ciljne molekule (tzv. *drug targets*), koje ćemo poslije pokušati ili uništiti ili popraviti dotičnim lijekom.

■ **Vaše je znanstveno područje proteomika. Kakva je to zapravo medicinska disciplina?**

- Proteomika (engl. *Proteomics*) jest vrlo mlada subdisciplina molekularne biologije (rođena u početku ovog stoljeća) čiji je zadatak dekodirati funkciju svih proteina u ljudskom organizmu. Proteom je stručni naziv za skup svih proteina u određenom organizmu. Primjerice, iako sve ljudske stanice sadržavaju otprilike 26.000 gena, ljudski proteom ima otprilike deset puta više proteina, dakle otprilike oko 260.000. Od tih 260.000 proteina samo je njih petsotinjak, po našim sadašnjim spoznajama, izravno uključeno u nastanak ljudskih bolesti. Zanimljivo je spomenuti kako znanstvenici pretpostavljaju da sveukupno postoji oko 3000 proteina u našem organizmu, koji su uključeni u nastanak različitih bolesti, što znači da još moramo pronaći preostalih 2.500 proteina (tzv. *drug targeta*) i njihovu egzaktnu vezu s navedenim bolestima...

■ **Možete li objasniti Vaša nedavna znanstvena otkrića vezana uz cističnu fibrozu, neizlječivu i najčešće nasljednu bolest? Koja je tajna te bolesti i kad bi Vaše otkriće moglo rezultirati lijekom za tu bolest?**

- Cisticna fibroza (CF) opaka je nasljedna bolest uzrokovana promjenama u ljudskom CFTR genu, a u prosjeku pogađa jedno od 2500 novorođene djece. Kod oboljelih začepljeni su dišni putovi i gušterača, a bolest također pogađa i znojne žlijezde, kao i reproduktivni sustav. MYTH tehnologija idealna je za proučavanje proteina kao što je CFTR, jer CFTR nalazi se na periferiji (membrani) ljudskih stanica, gdje pomaže transportu kloridnih iona u unutrašnjost i izvan stanice. Upravo zbog te izravne veze CFTR-a s cističnom fibrozom, odlučili smo da MYTH tehnologiju najprije testiramo na CFTR proteinu i nedavno prvi put identificirali šest novih proteina koji komuniciraju sa CFTR-om. No, ono što je najvažnije jest otkriće da jedan od tih šest navedenih proteina, pod imenom TUS1, znatno pomaže CFTR-u prilikom obavljanja njegove funkcije. Drugim riječima, na molekularnoj razini otkrili smo potpuno novi način na koji funkcionira CFTR, i to se otkriće pokazalo važnim za razvoj novih terapija protiv cistične fibroze.

■ **Hoće li to Vaše novo otkriće uskoro rezultirati proizvodnjom lijeka za cističnu fibrozu?**

- Što se tiče našeg otkrića i razvitka novog lijeka protiv CF-a, put je još dug te će nam za to još trebati razdoblje od otprilike 7-8 godina. No htio bih spomenuti da je američka tvrtka Vertex Pharmaceuticals iz Bostona nedavno razvila novi lijek pod imenom VX-770, koji bi vrlo uskoro mogao znatno popraviti

kvalitetu života pacijenata oboljelih od CF-a. Spomenuti lijek radi na principu da korigira funkciju promijenjenog CFTR proteina te se na američkom tržištu očekuje do kraja godine.

■ **Za proizvodnju jednog novoga lijeka potrebno je prosječno oko 800,000.000 američkih dolara. Je li to glavni razlog zašto se tako dugo, pošto znanstvenici daju smjernice, čeka lijek?**

- Glavni razlog zbog čega je proces pronalaska lijekova tako skup jest to da od bazičnih laboratorijskih otkrića, dakle otkrića tzv. ciljne molekule koju treba uništiti ili popraviti s lijekom, do upotrebe lijekova u klinici, protekne u prosjeku 10 do 15 godina. Vidite i sami da je riječ o dugotrajnom procesu u kojemu dotični lijek mora proći kroz četiri različite faze istraživanja koje su, kao što se može zapaziti iz navedene novčane svote, veoma skupe. Možda će zvučati zapanjujuće, ali tek svaki peti lijek koji se pojavi na tržištu financijski vrati ulaganje od njegove prodaje, što znači da je cjelokupni proces otkrivanja lijekova još i danas prilično neučinkovit. Upravo zato suvremena medicina i molekularna biologija ulažu golema sredstva u razvitak novih tehnologija koje će navedene neuspjehe svesti na minimum. I upravo su zato u procesu otkrivanja lijekova uključeni stručnjaci iz različitih disciplina kao što su liječnici, molekularni biolozi, kemičari, ali i informatički specijalisti.

■ **Bavite se molekularno-biološkim istraživanjem genetskih bolesti, što je danas top znanost od koje se očekuje, među ostalim, spasonosno rješenje za borbu protiv karcinoma. Sada diljem svijeta mnogo znanstvenih timova razvija nove terapije i postoji nada da će netko od njih, danas-sutra dati revolucionarno otkriće, tj. lijek. Ali, Vi niste tako optimistični.**

- Da, imate pravo kad kažete da je to jedan od najvažnijih zadataka današnje molekularne biologije i medicine. No kao znanstvenik koji se bavi tim istraživanjima želim, prije svega, odaslati iskrenu poruku javnosti da mi nikad nećemo biti kadri stvoriti jedan jedini univerzalni lijek protiv svih karcinoma. Zašto? Zato što na temelju današnjih opširnih molekularnih, imunoloških, histopatoloških i drugih spoznaja o tumorima možemo govoriti o postojanju dvjestotinjak različitih tumora u ljudskom organizmu. Gotovo svaki od tih tumora jedinstven je jer uzrokuju ga molekularne promjene u različitim genima i njihovim proteinskim produktima. Glavni cilj suvremene molekularne biologije prije svega je razumjeti svaki od tih dvjesto tumora kao jedinku za sebe, tj. shvatiti koje promjene u genima i njihovim proteinskim produktima dovode do pojave tih tumora - to je jedini način na koji ćemo moći kreirati nove, pametne lijekove što će biti efikasni u suzbijanju tumora. Htio bih još spomenuti da su molekularna biologija i medicina u posljednjih deset godina postigli zapaženi napredak u stvaranju nekoliko takvih pametnih lijekova kao sto su to npr. *Herceptin*, monoklonalno protutijelo što se primjenjuje u liječenju metastaza dojke, zatim *Gleevec*, kojim se koristi u liječenju mijeloične leukemije, te *Sutent*, koji se primjenjuje u liječenju tumora bubrega i gastrointesticijskih tumora želuca. Uza spomenute lijekove, u kliničkim pokusima u visokorazvijenim zemljama, danas se testira pedestak novih pametnih lijekova protiv različitih vrsta tumora.

■ **Lani ste otkrili kemijske supstancije koje blokiraju djelovanje opasne bakterije Pseudomonas aeruginosa? Možete li objasniti to otkriće, prevesti ga s jezika znanosti na govorni jezik?**

- Naša posljednja istraživanja probudila su nadu u razvoj novih terapija u liječenju pseudomonalnih infekcija koje su, među ostalim, glavni uzročnik smrti oboljelih od cistične fibroze, osoba oslabljena imuniteta kao i osoba oboljelih od side. Jednostavno rečeno, razvili smo novi znanstveni pristup s pomoću kojega se mogu pronalaziti lijekovi koji neutra-liziraju infekcije izazvane patogenom bakterijom Pseudomonas aeruginosa. Taj je naš pristup osobit u tome Tako smo pronašli novi lijek (nazvali smo ga *Exosin*) koji uvelike reducira infekcije prouzročene dotičnom bakterijom. Osim toga, razjasnili smo mehanizam na samoj razini molekula u ljudskim stanicama preko kojega djeluje Exosin i tako postavili temelje za novi lijek protiv pseudomonalnih infekcija.

■ **Kakve emocije u Vama pobuđuju Vaša otkrića?**

- Otkako sam se preselio u Toronto, često kontaktiram s pacijentima oboljelima od cistične fibroze, kao i njihovim obiteljima. Moram priznati da ti susreti u meni izazivaju dvojake osjećaje: s jedne me strane uvijek uvelike rastuže, jer ispred sebe vidite bolesnu djecu koja se svakim danom bude u pet sati ujutro da bi provela gotovo šest sati dnevno na respiratorima što im omogućuju da prežive. Njihovi roditelji u vama vide veliku nadu, slamku spasa, jer nadaju se da ćete im vi i vaš znanstveni tim moći pomoći. Eto, baš to je razlog što sam s druge strane i sretan, jer vidim da naša istraživanja idu u dobrom smjeru i daju nam nadu da će jednog dana ista djeca imati koliko-toliko normalan život, koji zacijelo zaslužuju. Nema ljepšeg osjećaja od onoga kad vidite da se vaša znanstvena vizija i trud cijelog laboratorija pretvara u stvarnost koja će vrlo vjerojatno donijeti dobrobit čovječanstvu.

■ **Što je imalo odlučujuću ulogu u Vašim uspjesima?**

- Odlučujuću ulogu za uspjeh u mojoj znanstvenoj karijeri imali su moji roditelji, koji su mi uvijek bili velika podrška u životu, kao i to što sam se školovao na najboljim svjetskim sveučilištima. Dakako, zato su zaslužni i moji mentori, koji su me tijekom studija i specijalizacije motivirali da počnem obožavati znanost te da o znanosti razmišljam otvoreno, ali u prvom redu kritično i racionalno. Nadalje, dosad sam za svoj znanstveni tim uvijek odabirao izrazito nadarene, marljive i inteligentne suradnike, koji su uvelike zaslužni za naš uspjeh. Želio bih naglasiti da danas uspjeh u znanosti znači uspjeh tima, nikako pojedinaca, jer da biste danas publicirali jedan rad u renomiranome znanstvenom časopisu, morate imati izrazito jak znanstveni tim u kojemu sve funkcionira kao u najboljemu švicarskom satu.

■ **Možemo li danas govoriti o znanstvenoj sreći u smislu u kojemu se ona tumačila u vrijeme, recimo, otkrića penicilina, tj. kad je znanstvenik istraživao 10, 20, 30 godina i onda, kao najedanput, slučajno, nešto otkrio?**

- Mislim da sreća ima određenu ulogu za uspjeh u životu, no, budimo realni, za uspjeh u znanosti ipak morate biti radoholik, inteligentni, morate biti izvrstan menadžer, koji će znati prodati projekt znanstvenim fondacijama i časopisima, i, na kraju, morate biti vrlo hrabri i ustrajni, no morate se i znati nositi s porazima. Imate li sve te spomenute osobine, uvjeren sam da ćete gotovo uvijek moći isprovocirati vašu sreću koja će vas pratiti ne samo u znanosti, nego i u životu općenito...

■ **Ima li u znanosti talenata ili je tu riječ samo o inteligenciji, egzaktnosti, educiranosti, upornosti, beskrajnoj ljubavi...?**

- Moje mi dosadašnje iskustvo govori da najveći znanstveni talenti nikako nisu tzv. štreberski ili *ziheraški* tipovi. Zašto? Pa upravo zato što neki štreber nikad neće biti spreman riskirati i upustiti se u projekt za koji su izgledi da uspije vrlo mali. A upravo takva, manje očita znanstvena otkrića rezultiraju epohalnim otkrićima koja onda budu publicirana u najboljim znanstvenim časopisima. Dakle, morate biti, dakako, skloni riziku, uporni, načitni, educiran i privrženi znanosti, ali, također, i tvrdoglavi (u pozitivnom smislu), morate imati viziju koja je unikatna i s kojom ćete uspjeti zavesti cijeli znanstveni svijet.

■ **Za engleskog književnika, slikara i grafičara Williama Blakea, nadahnuće je:**

Vidjeti svijet u zrnu pijeska,
i nebo u divljem cvijetu,
nositi beskraj na dlanu,
i vječnost u trenutku!

I znanstvenik, nedvojbeno, ima zanosa, ali što je za nj nadahnuće?

- Ha ha, mislim da biste na ovo pitanje dobili potpuno različite odgovore od različitih znanstvenika. Nedvojbeno je da mi znanstvenici poimamo znanost kao veliku strast koja nas ispunjava slično kao i najstrastvenija ljubav. Za mene osobno nadahnuće u znanosti znači traženje nečega što još nitko nije pronašao, traženje nove tehnologije ili shvaćanje važnoga staničnog procesa koji će rezultirati objavom izvrsnog rada te, dao Bog, poboljšanjem kvalitete ljudskih života na potpuno nov i inovativan način, nešto za što će ljudi reći *hej, pa ovo je stvarno cool!.*

Biblijsko gledanje na svijet zapravo je jezgrovita slika na kojoj se nadmeću Božja moć i ljudska zloća. Toga, u konkretnom značenju dobra i zla, danas ima gotovo do nepodnošljivosti, odnosno, sve nas više iznenađuje dobro, a loše situacije, loša raspoloženja... postaju naša stanja, stvarnost. Kako Vi, kao znanstvenik, percipirate svijet i ljudsku sudbinu?

- Po prirodi sam prilično emotivan, ali veoma pozitivna osoba. Kao i mnogi drugi ljudi, nekoliko sam se puta veoma razočarao u životu, no uvijek pokušavam racionalizirati i zaboraviti te loše situacije i misliti na ono što me raduje u životu, a to su moja djeca, moje slobodne aktivnosti, sport i znanost. Mislim da bi naš planet Zemlja bio mnogo bolje mjesto za život kad bi ljudi mislili pozitivno, kad ne bi bilo zavisti, kad bi svi imali pravo na edukaciju i kad razlika između siromašnih i bogatih ne bi bila takva kakva je danas.

Kako ste posložili svoje životne prioritete?

- Najvažniji su mi prioritet moje djevojčice Lara (12) i Leja (9). Želim im omogućiti vrhunsku edukaciju, usaditi im pozitivan ali i kritičan stav prema životu te da nauče koristiti se svojim potencijalima i objektivnim mogućnostima. Dakako, i dalje želim da moj znanstveni tim maksimalnim trudom i zalaganjem postigne što zapaženije rezultate. No unatoč tomu što katkad radim i po 14 sati na dan, veoma mi je važno da mogu uživati u drugim stvarima u životu, koje me usrećuju. Kad to kažem, onda prije svega mislim na slušanje glazbe, obožavam *contemporary jazz,* sviranje na gitari i svakodnevno bavljenje športom, koje me najviše opušta. Prilikom bavljenja športom dosad su mi uvijek padale na um najzanimljivije znanstvene ideje.

Kao rođeni Zagrepčanin, od 22. godine živite u inozemstvu. Radili ste na glasovitom Švicarskome nacionalnome tehnološkom institutu (ETH), poznatome i po tome što je dao 23 nobelovca, među kojima su bili i hrvatski znanstvenici, nobelovci Lavoslav Ružička i Vladimir Prelog, radili ste na University of Washington u Seattleu, sada u Torontu, dakle u vrhunskim znanstvenim sredinama. Jeste li se kao mlad čovjek, i stranac, morali naprezati dva-tri puta više od ostalih kolega da biste se mogli dokazati i, što još više treba naglasiti - iskoračiti?

- Moj odgovor definitivno je potvrdan. No da budem iskren, nisam nikad previše razmišljao o tome jesam li kao stranac bolji od ostalih, pogotovo ne u SAD-u i ovdje u Kanadi, jer to su zemlje u kojima ima vrlo malo domorodaca i u kojima su emigranti svakako dobro došli te zbog toga imaju zapažene uloge u svim strukturama njihova društva. Moj je životni moto uvijek bio da pokušam dati svoj maksimum i da, prije svega, na otvoren, pošten i nearogantan način ostvarim svoje ciljeve. Uz malo sreće o kojoj smo govorili, uz mnogo odricanja i spremnosti na rizik te s timom izvrsnih i pouzdanih suradnika, uspjeh će gotovo uvijek doći po sebi.

Ten years ago, Igor Štagljar as a molecular biologist at the famous Swiss Federal Institute of Tehnology ETH - where he received his Ph.D. and went on to become one of the youngest professors - he and his team of scientists began developing an original biological method for the identification of new proteins involved in the development of cancer. This method paved the way for the research of grave genetic diseases, particularly cystic fibrosis. Thanks to professor Štagljar, it is now believed that we are only a step away from finding a cure for this disease.

With your associates you have developed and patented the membrane dual system technology (MYTH). Could you briefly explain the theory and the technology and tell us why the international scientific community hailed it as a groundbreaking development? The major scientific magazine *The Scientist*, for example, added it to the seven life research technologies that would dominate biomedical science in the next decade. This technology has also earned you the most prestigious Canadian innovation grant... What does your technology mean for research itself and, perhaps one day, for the treatment of genetic diseases?

- MYTH technology is a molecular biological method which enables us to monitor *contact between proteins* or the so-called *protein interactions*. Now, what does this mean in simple terms? Proteins are important macromolecules in all organisms, in which they perform many essential functions. In the performance of these functions, proteins never act on their own, but rather contact other proteins. Many human diseases develop as the consequence either of an interruption of normal protein interactions or of the occurrence of new ones. This is why it is very important to be able to monitor and detect protein interactions through molecular biological methods, because it can help us understand how to develop new therapies for various human diseases. We can monitor all of these protein interactions with MYTH technology, and its greatest advantage, in comparison to other technologies used in molecular biology today, lies in the fact that this is currently the only method that can be successfully applied to a great number of proteins situated on the very perimeter of the cell. For example, human proteins involved in the development of cystic fibrosis, Alzheimer's disease, schizophrenia, Parkinson's disease, tumours of the brain, lungs, breasts, and many other diseases can be directly analyzed using our MYTH method. In this way, MYTH technology is the first step in the drug discovery process because it can help us discover new target molecules (drug targets) which we will then try to destroy or improve with the drug.

Your area of science is called proteomics. What is this medical discipline like?

- Proteomics is a very young sub-discipline of molecular biology (born at the very beginning of this century) with the task of decoding the function of all proteins in the human organism. Proteome is the term used to describe a set of all proteins in an organism. For example, even though all human cells contain approximately 26,000 genes, the human proteome consists of approximately ten times more proteins, around 260,000. Of the 260,000 proteins only some five hundred, according to our current findings, are directly involved in the development of human diseases. I should mention that scientists assume that there are some 3000 proteins in our organism involved in the development of different diseases, which means that we still have to find the remaining 2500 proteins (drug targets) and their exact connection with the corresponding diseases...

Can you tell us more about your recent scientific discoveries on cystic fibrosis, an incurable and most commonly hereditary disease? What is the secret to this disease and when could we expect your discovery to result in the cure for the disease?

- Cystic fibrosis is a vicious hereditary disease caused by modifications to the human CFTR gene, and is found in approximately one in 2500 newborn children. Patients experience clogging of the airways and of the pancreas and the disease also affects the sweat glands

and the reproductive system. MYTH technology is ideal for conducting research on proteins such as CFTR, because CFTR is located on the periphery (membrane) of human cells, where it helps to transport chloride ions in and out of the cell. It is precisely because of this direct connection of CFTR with cystic fibrosis that we have decided to test MYTH technology on CFTR protein first and recently we were able to identify for the first time six new proteins that communicate with CFTR. But the most important part of our discovery was that one of the six proteins, TUS1, has an important role in helping CFTR renew its function. In other words, we have discovered an entirely new way that CFTR functions at the molecular level and this discovery has proved to be significant for the development of new therapies for the treatment of cystic fibrosis.

■ **Is your new discovery going to result in the cure for cystic fibrosis any time soon?**

- When it comes to our discovery and the development of a new drug for CF, we still have a long way to go; it will take some 7-8 years. But I would like to say that the Boston-based American company Vertex Pharmaceuticals recently developed a new drug called VX-770 which could significantly improve the quality of life of CF patients very soon. This drug functions by correcting the function of the modified CFTR protein and is expected to be available in the US market by the end of this year.

■ **The production of a new drug costs approximately 800,000,000 US dollars. Is this the main reason why so much time has to pass between the initial scientific discovery and the production of a drug?**

- The main reason for the high cost of drug development is the fact that it takes an average of 10 to 15 years from the time of basic laboratory discoveries, to the discovery of the target molecule to be destroyed or improved with the drug, to the clinical use of drugs. As you can see, this is a lengthy process in which the drug in question has to pass through four different research phases which, as you can see by the amounts cited, are very expensive. This may surprise you, but only every fifth drug on the market can assure a return of the funds invested in its development, meaning that the entire drug development process is still quite inefficient. This is why modern medicine and molecular biology are now investing great amounts of money in the development of new technologies which would reduce the failure rate to a minimum. And this is also why drug development processes involve experts from different fields such as doctors, molecular biologists, chemists, but also IT specialists.

■ **You work on molecular biological research of genetic diseases, which is the leading branch of science today, and it is expected to yield, among other things, a solution for the fight against cancer. Numerous scientific teams around the world are developing new therapies as we speak and there is hope that one of them will produce a revolutionary solution any day now, a cure. But you are not that optimistic.**

- Yes, you are right when you say this is one of the most important tasks of molecular biology and medicine today. But as a scientist involved in this type of research, I would like to be frank and tell the general public that we will never be able to create a single universal cure for all types of cancer. Why is this so? Because, based on elaborate molecular, immunological, histopathological and other data on tumours that we have today, we can identify around two hundred different types of tumours in the human organism. Almost each of these tumours is unique because it is caused by molecular modifications in different genes and their protein products. The main goal of modern molecular biology is primarily to understand each of the two hundred tumours as an individual unit, that is, to understand the changes in the genes and their protein products that result in these tumours - this is the only way in which we will be able to create new, smart drugs, efficient in fighting tumours. I would also like to say that in the last ten years molecular biology and medicine have made significant progress in creating several smart drugs, such as *Herceptin*, a monoclonal antibody applied in the treatment of breast cancer metastasis, then *Gleevec*, used in the treatment of myeloid leukaemia, and *Sutent*, used in the treatment of kidney tumours and gastrointestinal stomach tumours. Along with these drugs, some fifty new smart drugs against different types of tumours are being clinically tested in leading developed countries.

■ **Last year you discovered chemical substances that block the activity of the dangerous bacteria Pseudomonas aeruginosa. Can you tell us more about this discovery and translate it for us from the scientific to everyday language?**

- Our latest research has kindled hope in the development of new therapy for the treatment of pseudomonas infections which are one of the main causes of death in cystic fibrosis patients, persons with weakened immunity and AIDS patients. Basically, we have developed a new scientific approach to the development of drugs that neutralize infections caused by the pathogenic bacteria Pseudomonas aeruginosa. Our approach is unique in that the entire drug screening process takes place in brewer's yeast. This is how we found a new drug (we called it *Exosin*) which greatly reduces infections caused by the said bacteria. Also, we shed light on the mechanism at the molecular level in human cells through which Exosin acts and thus we set the foundations for a new drug for pseudomonas infections.

■ **What emotions do your discoveries evoke for you personally?**

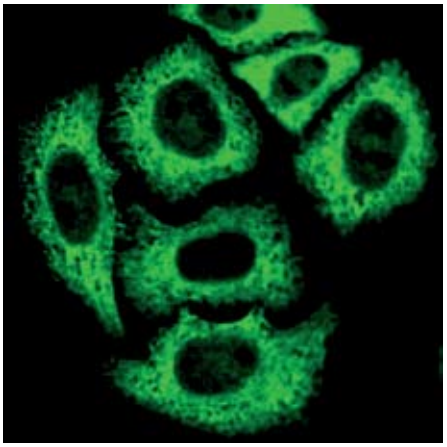
- Since I have moved to Toronto I have been in touch with cystic fibrosis patients and their families. I have to admit that these encounters evoke conflicting feelings: on the one hand, it always saddens me to see sick children who have to wake up at five in the morning every day to undergo almost six hours of respiratory treatment a day in order to survive. Their parents see you as their great hope, their last straw, hoping that you and your team will be able to help. But this, on the other hand, makes me feel glad, because I can see that our research has a good perspective, giving us hope that these children will someday be able to lead a more or less normal life, which they certainly deserve. It is the most beautiful feeling in the world to see your scientific vision, the effort you and your lab have invested, is turning into reality which will most probably be beneficial to mankind.

■ **What has played a crucial role in your success?**

- My parents were crucial in the success of my scientific career, they have always been greatly supportive, and also there was the fact that I attended the best universities in the world. Of course, I owe a lot to my mentors, who motivated me during my studies and specialization to adore science and to embrace it with an open mind but, most of all, in a critical and rational manner. Furthermore, I have always chosen extremely talented, hardworking and intelligent associates for my scientific team and they have greatly contributed to our success. I would like to stress that success in science today always means the success of the team, never the individual, because in order to publish a paper in a renowned scientific magazine today you have to have an extremely strong team functioning in synch like the best of Swiss watches.

■ **Can we, in our day and age, speak of scientific luck in the sense in which it was seen, for example, in the times when penicillin was discovered, when a scientist would search for 10, 20, 30 years and then suddenly, as if by coincidence, discover something?**

- I think luck does play a certain part in one's success in life but, let's face it, in order to



succeed in science you primarily have to be a workaholic, intelligent, an excellent manager who knows how to sell a project to scientific foundations and magazines and, finally, you have to be very brave and persistent but you also must know how to handle defeat. If you have all these qualities, I am certain that you will almost always be able to provoke your luck, which will then accompany you not only in science but in life in general...

Does science require talent or is it just about intelligence, accuracy, education, persistence, immense love for the work...?

- From my own experience I can say that the greatest talents in science are never the so-called geeky or unadventurous types. Why is this so? It is because a geek would never be prepared to take a risk and embark on a project that is unlikely to succeed. But it is these, less obvious, scientific research that result in revolutionary discoveries that get published in the best scientific magazines. So you have to, of course, be prepared to take a risk, be persistent, well-read, educated and dedicated to science, but you also have to be stubborn (in the positive sense of the word), you have to have a vision that is unique and that will manage to seduce the entire scientific community.

For the English poet, painter and printmaker William Blake, inspiration is:
To see a World in a Grain of Sand
And a Heaven in a Wild Flower,
Hold Infinity in the palm of your hand
And Eternity in an hour.
Scientists are undoubtedly passionate, but what do they see as their inspiration?

- Ha, ha! I think different scientists would give you completely different answers to this question. We scientists definitely see science as a great passion that fulfils us just like the most passionate love. For me, inspiration in science means to search for something no one else has ever found, search for a new technology or the understanding of an important cellular process that will result in the publication of an excellent paper and, with God's help, in the improvement of the quality of human life in a new and innovative way, something that people will be able to see and say: *Hey, this is really cool!*

The Biblical vision of the world is in fact an image of competing divine power and human wickedness, in a nutshell. Today we witness this, in the form of good and evil, practically more than we can take, that is, we frequently find ourselves surprised by the good whereas the bad situations, bad feelings... have become our reality. How do you, as a scientist, see the world and the fate of humankind?

- I usually respond to things pretty emotionally, but I am a very positive person. Like many others, I have had several grave disappointments in my life but I always try to rationalize and forget the bad situations and think about what makes me happy, my children, my hobbies, sports and science. I think our planet Earth would be a much better place to live in if people were more positive, if there was no envy, if everyone had the right to education and if there was not such a great gap between the rich and the poor.

What are your priorities in life?

- My major priorities are my daughters Lara (12) and Leja (9). I want to provide them with top education, endow them with a positive but critical attitude towards life and teach them how to use their potential and objective possibilities. Of course, I still want my scientific team to yield the best results possible through maximum engagement and dedication. But, in spite of the fact that I sometimes work 14 hours a day, I find it very important to enjoy other things in life that make me happy. By this I primarily mean listening to music, I love contemporary jazz, playing the guitar and my daily sports activities, which I find the most relaxing. The most interesting scientific ideas that I have had have occurred to me while doing sports.

You were born in Zagreb and have been living abroad for 22 years now. You worked at the renowned Swiss Federal Institute of Technology (ETH), famous for having given the world 23 Nobel Prize winners, including Croatian scientists Lavoslav Ružička and Vladimir Prelog, you worked at the University of Washington in Seattle, now you work in Toronto, all cutting edge scientific environments. As a young man and a foreigner, did you have to work twice as hard than your colleagues in order to prove yourself and, even more importantly - to set yourself apart?

- My answer is definitely yes. But to be honest, I have never given too much thought to whether I, as a foreigner, was any better than the others, especially not in the USA and here in Canada. These are the countries with very few homegrown people, immigrants are definitely welcome, which is why they have important roles in all segments of their societies. My motto has always been to try to give my best and, most of all, to try to realize my goals in an open, honest and modest way. With a little luck, as we already discussed, with a lot of sacrifice and risk taking and with a team of excellent and reliable associates, success will almost always inevitably ensue. ■