

Summer 2017

TMU Spotlight+



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TAIPEI
MEDICAL
UNIVERSITY



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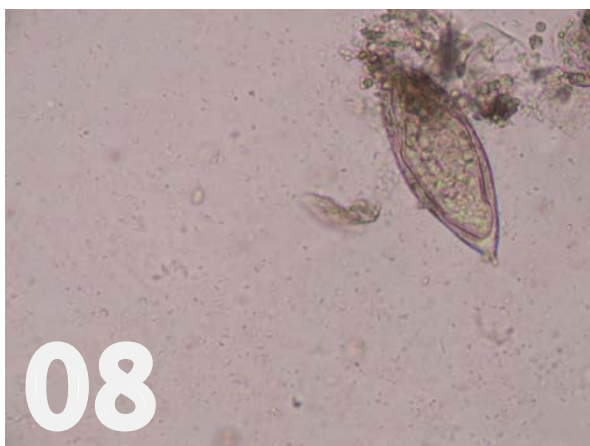
02



12



06



08

2 Dual-degree student triumphs with French research

6 New College of Nutrition takes research to higher level

8 Could common parasites cause neurodegenerative plagues?

Renowned TMU expert links man's best friend to mind's worst enemies

12 Homegrown TMU expert gives big data a human face

Alumnus joins faculty, leads team to "Top Geeks" Awards

16 TMU-NHRI researcher wins global awards for cancer breakthrough

Alumnus finds mechanism justifying daily oral chemotherapies

18 Cycles of progress

President Yen's farewell message reflects on lessons learned and the future

Dual-degree student triumphs with French research

Director Thierry Burnouf and Dr. Natalie Chou from TMU's Graduate Institute of Biomedical Materials and Tissue Engineering talked about their experiences in multinational collaborative research. Their neurological findings will soon be patented for treatment use.

Director Thierry Burnouf met Prof. David Devos, a neurologist specializing in Parkinson's and Alzheimer's disease clinical research, as a neighbor in France. But a Taiwanese student recently received not one but two doctorates there -- thanks to that chance link growing into a dual degree program between TMU and the Science University of Lille, a Nobel Prize-winning university. After they chatted about the TMU director's pioneering research into growth factor platelets, Burnouf presented his work at Lille 2 Hospital, the largest in France. The dual degree program recently yielded its first doctoral graduate, Natalie (Ming-Li) Chou. With a combination of weekly Skype meetings and travel between the two institutions, she conducted research that was roughly two-thirds at TMU, and spent a third of her study time in France.

Link grew across a garden fence

Director Burnouf recalls: "The beginning is a bit funny, because in Lille my neighbor used to be Prof. David Devos, who is a neuroscientist and a clinician following patients with neurodegenerative disorders, Parkinson's and amyotrophic lateral sclerosis [ALS, the "ice bucket challenge" disease]. And once when he was in his garden and I was in my garden, we started to chat over the fence.

"And I explained what I was doing in Taipei, working with growth factors, in particular with platelets ... looking for those having a protective role with neurons, probably as part of the repair mechanism provided by platelets when you injure yourself. ... And then we started to think about using these platelet growth factors for the treatment of people with neurodegenerative disorders [about five years ago]."

The idea of working together triggered a few

more rounds of discussion between representatives from both sides, involving those at the senior managerial level, and eventually evolved into a formal partnership linking TMU with Lille 2. The dual Ph.D. degree program was specifically designed to facilitate collaborative research between both parties through joint supervision of doctoral students, and Natalie Chou was the first TMU student embarking on this new project under the guidance of Prof. David Devos at Lille and Profs. Thierry Burnouf, Liang-Tzung Lin at TMU.

Learning different lab routines

Language differences were an issue, so Natalie started two weekly French classes in 2014 once she got to Lille. But despite the difficulties, she said, "This dual degree really opened a view of the field for me. So I know how they [European researchers] proceed with

their experiments.” Which turns out to be quite different from Taiwan’s laboratory norms.

Natalie explained: “I learned that the French collaborate very well! We would have weekly meetings, so people are talking about their results to each other. And if they would have problems or questions, they can answer to each other.

“So I think this is very good teamwork in France, which I think is different from Taiwan. They work with several supervisors and rely on each other -- where Taiwanese would tend to work independently in the laboratory. In France you share the results with each other and if you have questions, people can help you. So this is a really good aspect of what I learned there.” Besides closer teamwork on projects, Natalie also saw differences in individuals’ working routines and styles.

“Lab life is different there; they plan their work pretty much in advance. It’s a more efficient lab life there, where shorter working hours mean you’re more focused. You come in knowing what you’re going to be doing, instead of gearing up or having less-productive but longer hours.”

How she was selected

Natalie had been a stellar master’s degree student in TMU’s College of Medical Science researching candida albicans yeast. Then she worked as Research Assistant in Director Burnouf’s laboratory, and says that’s where she “started to learn more about blood, especially growth factors in blood.”

When Prof. Devos and Director Burnouf discussed using blood growth factors to heal Parkinson’s



Director Thierry Burnouf and Dr. Natalie Chou from TMU Graduate Institute of Biomedical Material and Tissue Engineering.

disease damage, Natalie was a logical candidate to pursue this research.

“Natalie had a good background in biological science when she started this degree program; she understood cell culture and she was already very well trained. The Parkinson’s cell line to be used was in Lille, so she went there to learn how to work with that,” Director Burnouf said.

He had already helped her to take a year to learn from a working visa in Germany. Since she had already

worked three months in a biotech company and six months in a blood center there, the prospect of crossing the planet alone didn’t faze her – or her family.

Patent, publication and Paris postdoc

Natalie pursued this research first using cells and then administered toxins to cause Parkinson’s-like damage in animals. The payoff was identifying a mixture of growth factors that showed healing effects.

So the partnership took off – with stellar results. “We got the patent report from the European patent office which is extremely favorable, so we are very optimistic that the patent will be granted ... we will start publishing after this spring.

As a next step after her dual Ph.D., Natalie will research immunity and neurodegeneration when she moves to Paris 6 University in March – this is the hallowed institution where Pierre and Marie Curie did their world-changing research into radioactivity. She will focus on Alzheimer’s disease in a postdoctoral fellowship with two years of funding from the Medical Research Foundation. Meanwhile Lille and TMU will carry forward their collaboration in pre-clinical and clinical work to treat ALS.



Dr. Natalie Chou with her supervisors Director Thierry Burnouf and Associate Prof. Liang-Tzung Lin.

Twice as nice in half the time?

Given the enormous demands of working in an unfamiliar language, one might expect this dual degree took longer than most doctorates. However, the opposite is the case because the French system rigorously limits doctoral studies to intensive three years research work – and because most French researchers are pretty good in English too.

Natalie recalls: “Initially I didn’t speak any French, and after I visited the first time in 2014, I realized there was a need to speak French to integrate well in their laboratory ... so now I can have some conversations in French.”

But Director Burnouf said language study is optional at Ph.D. level: “As Natalie said, [language fluency] is a matter of integration in the lab. Still, if you can’t speak French, you can still get by using English.”

The two systems differ greatly in how degree studies are organized. Natalie said French master’s students are expected to take 18 months of classes and then an exam – leaving them only six months in the lab as an internship that focuses on their chosen research topic. Then if interested in Ph.D. they have to defend their research proposal before a challenging board of examiners.

So students starting their Ph.D. programs are very focused – and the research must start immediately because time is limited, but without additional coursework. Students must present yearly progress reports, and requirements on publications and international presentations are the same.

In contrast, Taiwan Ph.D. students are expected to take two years of coursework: 18 credits of coursework and 12 thesis credits, a pattern she called “really heavy loading in the first two years.”

Weekly updates and a six-screen defense

TMU’s Graduate Institute of Biomedical Materials and Tissue Engineering now also requires Ph.D. progress reports every year, which Director Burnouf called “not a place where the professor should have their gun to shoot at the student [and fail them], but to give

advice, recommendations, perhaps suggest the student talk with other professors, in order to help the student to finish and publish. It's a committee that's supposed to help the student, not destroy the student. Students and professors should feel being on the same boat towards achievements and novelties!" Natalie concurred, saying "This helped me a lot to finish my Ph.D. in a short time."

They travelled to Lille in December 2016 for her defense, while three TMU committee members participated by video link – "three cameras and six screens" including the slides and speaker. But then the champagne was opened (this was in France, after all!)

Paying for this pioneering arrangement was complex. Natalie received a scholarship from TMU, and Lille paid for partial living and travel expenses. Director Burnouf said European studies are helped by a culture of benefits for students that extend far beyond the low tuition. "I think it's really beneficial to students: they can learn more, open their mind – and this does not involve a great deal more financial expense." Another TMU student, Yao-Ting Hsien, studied for a dual master's degree also at Lille. He received a scholarship from Taiwan's Ministry of Education, a CABRI grant from Lille University, as well as support from the French embassy, and did not need to pay tuition fees in Lille. He was paying only 250 Euros per month for dorm fees for en-suite facilities with his own kitchen, plus half of this dorm cost was reimbursed by French social welfare system that is open

to all foreigners as well as French citizens.

Natalie said multiple student discounts in Europe helped too, whether for local transport, student meals or movies: "I think France is the best for the student!"

Advice and rave reviews

"Taiwanese students are a bit shy about starting a dual degree program – which is a big mistake," Director Burnouf said.

Natalie encouraged students to pursue dual degrees, noting that "Language ability is pretty important," as is flexibility to deal with different freedoms and restrictions.

She faced a thesis defense and an oral defense, and in France she needed two external reviewers' approval before she could defend – not committee members from other institutions, but experts entirely unrelated to her research.

"I stayed there when there was a need, so I was traveling frequently back and forth," she said. "But there was also a weekly meeting through Skype, so Prof. Devos and Thierry could follow my work...I'm very happy to have this dual degree, so I can learn all these advantages from both sides."

There is now another TMU MS student, Ouada Nebie from Burkina Faso, continuing the work on traumatic brain injury and platelet growth factors. Dr. David Blum of Lille University, now a visiting professor at TMU, is on his MS committee, so the partnership that started over a garden fence will continue to bear fruit. 



Dr. Natalie Chou with members of her oral defense committee.

New College of Nutrition takes research to higher level

Expanded clinical and metabolic studies build industry ties to help Taiwan's foods become safer and healthier.



Dean Jane Chao has worn a lot of hats at TMU, but her latest appointment is her biggest challenge yet. As the College of Nutrition has branched off from decades of partnership with Public Health faculty, it is scrambling to meet public expectations that the nation's food supply should be safe and nourishing.

At the same time, her unit is expanding to embrace clinical studies with new physician professors, as well as partnering with industry to refine and market products that have been proven beneficial.

The college officially began operations in August 2016, but in January 2017 its new offices and conference room held its open house the same week as TMU's vast new Da-An Campus's on Keelung Road. The 6th-floor kitchens remain vital for student learning, but a new processing laboratory will teach students how food can be marketed. For example, they will be able to can or vacuum-seal new products and test them for purity. This equipment will be ready for new classes in the fall to contribute to the nurturing of a new generation of food safety experts.

A focus on food safety is perhaps the new col-

lege's most newsworthy achievement. In just the past few years, public confidence was shaken by food adulteration scandals involving plasticizers, unwholesome "gutter oil" and mislabeling of spurious "olive oil" tinted green.

The College of Nutrition has several new units, including the Food Safety programs. However, Dean Chao is also nurturing a School of Nutrition and Health Sciences and other units focusing on Metabolism and Obesity Sciences. In partnership with TMU's innovative programs that are helping to guide planning for the nation's long-term care initiative, a new research center will focus on Geriatric Nutrition, while another will partner with industry to focus on Nutritional Medicine and "to combine bench and clinical work."

TMU's partnerships with Japan's Tohoku University and Akita Nursing College have led to international delegations as well as grants from the nation's Health Promotion Administration on developing a nutritional screening tool for the elderly. This is much needed, as older bodies absorb foods less efficiently and need different standards for obesity, Dean Chao

explained.

TMU's Health Policy Research Center is another partner ensuring that the new college's research has impact in the world beyond the university. The public concern about food safety is reflected in the new School of Food Safety offering a master's degree program in that area. An Institute of Obesity and Geriatrics will perform clinical and basic research, and an expanded Food Sciences undergraduate program will maintain the college's traditional focus on nutrition. These new programs are different in their shift of focus from therapy to prevention. The college is recruiting physicians to join the faculty, and building fund-raising beyond grants to alumni donations and industrial partnerships.

As faculty members work with companies, these companies share their knowledge and facilities and often donate to expand TMU's capacities as well. As TMU scholars evaluate new health foods, they can show tangible effects on physiological functions that will help new supplements and other products find successful distribution in markets worldwide.

Dean Chao laughs as she explains that "We don't have factories" -- so such collaboration is the best path to development for her new Research Center for Nutritional Medicine. The supplements developed there can make nutrition problems of the elderly easier to treat, as many older adults have neither the time nor the appetite to eat a wide variety of nutrients in their low-potency natural forms.

She also mentioned the importance of TMU nutrition alumni, who not only donate to college fund-raising but also extend partnerships to their current employers. This kind of collaboration has made biotech the nation's fastest-growing industry, closely watched and extensively supported by Taiwan's government.

Dean Chao also said her college is proud of its international students. Its programs have welcomed English-speaking doctoral and master's degree students as well as Malaysians and other Chinese-fluent foreign enrollees for the undergraduate programs.

And the PhD students must publish to graduate, and so many moved on to work with government and academic institutions in their home countries. A Thai student has worked with the dark-colored rice favored across Southeast Asia, finding it has anti-inflammatory

properties from polyphenol compounds, and proving this with cooked and raw rice.

The Food Safety focus extends to the study of toxins and food science research, but also will embrace risk assessment and management issues that concern food producers and distributors.


"From farm to table, the whole process should be safe," Dean Chao explained. This will involve more registration and government involvement in managing the food supply, in order to evaluate potential risks. Her researchers also focus on determining cut-offs for "acceptable risks" -- for example, by setting limits for contaminants that cannot be entirely excluded.

She says that identifying risk sources in transportation, storage, cooking and packaging are equal in importance to ensuring pure ingredient sources. One current grant is examining pesticides in tea by seeking different biomarkers, because imported teas have different pesticides reflecting the different regulations in their countries of origin. Taiwan officials want to test the quality and authenticity of these products, even ensuring that their origin is what it is purported to be.

"We can use the fingerprints of the tea to certify the species," Dean Chao said, because some teas are marketed as mountain-grown but may not be. As her faculty grows by 50%, Dean Chao is looking for not only more food scientists and doctors, but also policy experts who are familiar with risk assessment, food legislation and government administration efforts.

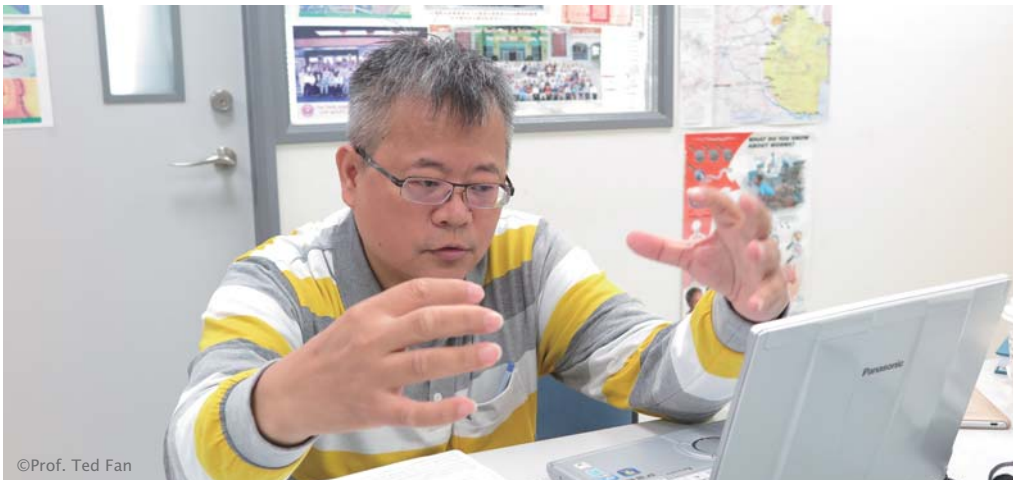
And as TMU expands with its new "glass building" next door to Health Sciences, this facility for public affairs and alumni outreach will have TMU nutrition alumni cooking up healthy snacks and fresh juices.

As President Yen Yun has observed that we can buy coffee from a handful of on-campus vendors already, this new enterprise will showcase best practices in nutrition promotion in a form that any student or faculty member can conveniently access in the planned "common area."

Dean Chao will be a few steps away, building her college to lead Taiwan to a new era of food safety and better nutritional knowledge -- because after all, we are what we eat. 

Could common parasites cause neurodegenerative plagues?

Renowned TMU expert links man's best friend to mind's worst enemies



Prof. Ted Fan is accustomed to his research being brushed off by health officials with the general consensus that “parasites won’t kill you.” Budgets are limited, they say, and they want to save lives, not address a complex set of problems that demand equally specific solutions.

But after working for years in TMU’s medical missions in Swaziland, the Marshall Islands and Sao Tome, he would beg to differ. In fact, even common roundworms can cause obstruction and death, especially in children and the elderly, who are the most likely victims and the least likely to be treated.

Prof. Fan disagrees with WHO’s “one pill” parasite treatment goal as ineffective. And recently he published a heavyweight paper in a major journal

linking roundworm in dogs to the neural damage that causes Parkinson’s and Alzheimer’s diseases.

So maybe parasites aren’t such a minor matter after all. Even in relatively advanced countries with wonderful health care, they may be much more widespread and undetected than most of us suspect – and causing neurodegenerative epidemics as populations shift toward the elderly.

Infections are common but silent

Most pregnant women are cautioned against cleaning cat boxes because feline toxoplasmosis can damage developing fetuses. A similar-sounding peril may transform our relations with dogs: *Toxocara canis* or

canine roundworm. These are common, but not widely tested for.

This will surely change if his finding that links these parasites to neurodegeneration and blindness is confirmed. A recent screening of 203 TMU students and 102 pregnant women found 8.3% and 33.3% of subjects carried canine toxocara, respectively.

Travelers as well as all who enjoy sushi risk infection with other parasites, Prof. Fan warned. He called pricey salmon a major culprit, noting that all raw fish are “hard to test” and therefore of questionable safety, even given the government’s recent emphasis on food safety.

Another threat comes home with those who do business in China, where schistosomiasis is spreading across that nation with global warming. WHO noted a dozen years ago that vast belts of land that used to freeze in winter no longer get cold enough to kill this parasite. It penetrates the skin whenever it touches contaminated water, whether from puddles splashed by pedestrians or farmers’ and vendors’ contact with damp soil. Female worms release eggs containing live miracidium which may dissolve blood vessels and burrow deep into the human liver and other organs, causing granulomas and even cancers.

While most cases are silent, they are also chronic, and the damage continues until treatment. The same is true of parasites many Taiwanese acquire on their travels, or from eating raw pig liver or seafood.

Malnutrition, anemia, organ failure

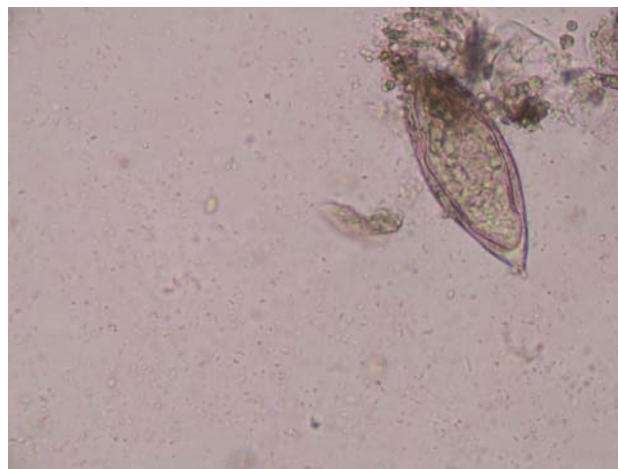
TMU’s museum in the United Medical Building has two tubes taller than a grown man that each holds a single tapeworm – some can grow to ten meters. These will lead to deficiency of vitamin B-12 and to severe anemia if untreated.

Another parasite Prof. Fan discussed was ascarid, or common roundworm: this can grow up to 30 cm in human guts, and children can have dozens in untreated cases, stealing their already insufficient nutrition and possibly causing obstructions, rectal collapse and death.

So while most people shrug off the seriousness of parasite infection, those who experience it do not. “People remember this forever!” he laughed, citing a certain sashimi-loving CEO he recalled having a tape-

worm of impressive proportions.

Treatment can be easy and quick – one tablet is 95% effective, and three days of treatment gives 100% success. But reinfection can continue endlessly; there’s no immunity to these pests.



Schistosoma haematobium ova found in a urine specimen from a Swazi child.

Patent pool provides nonprofit cures

Prof. Fan has another weapon against parasites since last summer. That’s when he received a law degree to better understand patents: “Otherwise you face lawsuits.” He hopes that a patent pool will provide a useful platform to address Africa’s neglected tropical diseases (NTDs) which most drug companies are unwilling to address for lack of profit potential.

And of the money that WHO spends on these NTDs (US\$90 million was the figure he cited), 77% goes to the “big three” diseases that include AIDS – and exclude parasites. Yet of WHO’s Tropical Disease Research priorities, 11 are parasites and 8 are zoonotic.

“There’s no business interest” in parasites, he said. The patent pool is expected to address this issue because countries will not be required to pay anything in before they can benefit from the resulting patented treatments.

Prof. Fan mentioned developing NTD drugs with TMU-Shuangho Hospital’s Dr. Yung-Ching Liu, who also offers a program of free exams for travelers. Yet the need exceeds the program’s size, with a half-million Taiwanese returning from work in China who face

no screening (although Southeast Asian laborers do). He said it's "ridiculous" not to check these people, and also was critical that screening of international students extends only to amoebas.

Two years ago he was given an award by the Ministry of Health and Welfare's chief of infectious diseases – and Prof. Fan used the opportunity to argue for testing of not only foreign students, but also the tens of thousands of Taiwan students who go on international service trips.

He sighed that their universities remain largely clueless about the health threats that these parasites pose – so most of the exposed students are still spreading this problem to their classmates and families.

Four threats at home, many more abroad

While he puts these four groups – returnees from China, foreign and domestic students, and travelers – at the top of Taiwan's parasite problem list, it is the poor who will sicken and die. "They think no one will die from parasites – but they fail to consider the economic losses" caused by such cases.

Prof. Fan said he himself had a bad encounter with cryptosporidium, which has no medications that effectively prevent or treat it. For a miserable week in the Marshall Islands he was visiting the bathroom up to thirty times a day, trying to stay hydrated as his body explosively expelled this invader.

This is the same parasite that large American cities (notably Milwaukee) found to be a fatal threat to HIV patients, since the tiny oocysts could not be screened out of water supplies until recently.

Such improvements are still years away from reaching Majuro and other low-resource water systems, he said. So the diarrhea-causing protozoa proliferate in the Marshallese tap water system and in rivers in Sao Tome and other African nations that supply water to most rural residents.

Most testing is vastly inadequate even where it is performed – looking for three or four species. Yet in Swaziland he found an average of 11 types of para-

sites in human samples, in Sao Tome 13, and in the Marshall Islands, 9 species.

Clean, cheap, clever testing kits

At this point he brought out a testing kit that he helped develop that costs only NT45 (US\$1.40) per compact tube. It offers a sealed, stable and low-cost alternative to the messy, smelly and less-effective "one-drop smear" method used to this point.

The kits have the further advantages of being storable indefinitely for re-checking of samples, and using two liquid preservatives that any hospital has on hand.

He worries about his older countrywomen who increasingly travel to exotic places. "Rich ladies like Africa" he said, recalling meeting dozens of Taiwanese in a South African airport recently.

As humans age, our immunity goes down – but anyone with runny bowels or a fever should see a doctor immediately. Prof. Fan said a urine specimen, a blood draw and a urinary screening are all cheap and useful tests, and showed a clever slide with multiple windows to test for more threats than past slides.



1 / *Paragonimus westermani*-like eggs (arrows) deposited in the tissue section of colonic mucosa.
2 / Oral part of *Ancylostoma ceylanicum* showing two different sized teeth.



©Prof. Ted Fan



©Prof. Ted Fan



©Prof. Ted Fan



Toxocara canis larvae in culture medium.

A higher profile for parasites and screening Prof. Fan grew solemn as he mentioned lives lost that simple and inexpensive solutions could save. He estimated that 60% of Swazis are HIV-positive, but antiretroviral drugs are unaffordable for many. Similarly, Pap smears could save thousands of women who present with early-stage cervical cancer – but the whole nation has only two technicians who screen for this.

Training, funding and upsizing of programs could address these killers, he said, but parasites get shoved to the bottom of the list of public health priorities. Prof. Fan has written a NT\$ 1 million grant so TMU can promote parasite testing in Swaziland by training technicians, and they in turn can train others. As this awaits approvals, he said the lab processing

procedure is easy -- but identification of different species takes expertise.

This renowned TMU scholar is making waves globally as well as locally. In a recent issue of the Clinical Microbiology Review (a major journal with an impact factor of 17), he linked *T. canis* to the beta amyloid and A β plaque formations that cause neurodegenerative disease via cerebral toxocariasis.

His next two projects continue this work, which five reviewers in his field have already sought to advance as a research priority with great promise. Prof. Fan may deal with parasites, but clearly this threat is not a minor matter – it is very big news indeed.



Homegrown TMU expert gives big data a human face

Alumnus joins faculty, leads team to “top geeks” award



Dr. Iqbal (right) with Dr. Shabbir Syed-Abdul and their team.

Usman Iqbal arrived at TMU from Pakistan in 2010 expecting to get a master's degree. Instead he got two degrees, important roles editing three scholarly journals, more than fifty scholarly publications in six years – and now a tenure-track position with the Global Health and Development program.

But this story isn't about what TMU has done for Dr. Iqbal; it's about what he's doing for TMU's global reputation with his research.

On 4 and 5 March 2017, his team took top honors at the University of Melbourne's Datathon, a short-term but high-pressure competition that start-

ed at the Massachusetts Institute of Technology (MIT). This Australian award was based on finding promising patterns in a given data set, and TMU's six were competing in a field of 120 participants.

But what makes such studies qualify as big data? "Velocity" was the word he chose, using the examples of Twitter (daily volume: 90 million tweets) and Facebook (30 billion posts per day). Dr. Iqbal then offered some analogies: "How would you go about building a fire engine out of Lego toy blocks?" His answer is that you would study a variety of different information sources to try to approximate the truck's

Dr. Iqbal arrived at TMU in 2010 on a scholarship for master's degree studies in Health Care Administration. He hadn't planned to stay for his Ph.D. studies, and quite nearly went to Sydney instead.

"I liked the environment here," Dr. Iqbal recalled. In his final semester he had gotten involved with Dean (of the College of Medical Science and Technology) Jack Li's Biomedical Informatics lab and played a role in the SANA project – a global health informatics initiative – so he decided to stay.

"There's more variety and range of things to do here," he said. Studies elsewhere seemed narrow by contrast, as students arrive with a thesis proposal and are told to "stay within that fence." Here he became involved with a variety of research leading to dozens of publications, as well as with scholarly journal publishing.

"Here I can taste all the flavors," he said with a smile. So despite offers with better pay (one was from Spain), Dr. Iqbal stayed after his Ph.D. to take a faculty position last August. He said part of the reason was gratitude.



©Dr. Usman Iqbal

"Taiwan is open to international students; it's friendly and safe. The world knows Taiwan is good at research, so graduates are highly employable around the globe. There's good accommodation for foreigners at TMU too."

This opportunity comes at a price – the infamous Taiwan work ethic. "In other countries you aren't expected to work after business hours, but in Taiwan the popular social media apps mean that business communication never stops. It helps that I don't mind long hours and am pretty focused on my work."

As a first-year doctoral student, his paper on benzodiazapines and pneumonia was published in BMJ Thorax, a leading journal with an 8+ impact factor. This is the kind of opportunity that made a TMU education into a life at TMU – and both sides are grateful that Dr. Iqbal chose to continue his work here.

various functions.

“How would you extrapolate a coloring book’s content if you had only one page, or design a puzzle if you had only one piece to work from?” You would look for patterns – and that’s exactly what big-data studies focus on. Not causes or theories, just promising correlations.

Cheaper, faster, better results

If this sounds superficial, consider his sobering prediction that managers will soon be replaced by such reports noting metrics and inefficiencies. Computers will replace many other job categories as human expertise becomes too expensive, too slow and less reliable – witness the rise of computerized accounting and legal services.

But TMU’s business is health care. Here too, apps are proving irresistible because they cut costs while ensuring consistent quality.

Dr. Iqbal noted that Taiwan’s single-payer system is second only to Denmark’s in providing efficient, high-quality universal health services. But another of its virtues is the information that it provides through various databases.

In particular, each reimbursement claim lists the recipient’s address, diagnosis, medications, age, coexisting conditions, length of hospital stay, mortality, even income level. Other databases can interlink to compare various categories, for example relating these doctor’s office visits to information on air quality on various days, or noting spending patterns in the casualties and services after catastrophic events such as earthquakes.

That is why he said datathons are as demanding and exciting as hackathons (which Dr. Iqbal also excels in). His team of two staff and four students had two days to compete with other groups to find the most interesting and useful patterns in the data presented to them by contest organizers.

“They give the data, we find the questions: ‘Is it important? Is it doable?’” Dr. Iqbal explained. In Mel-

bourne, they took electrocardiogram data and looked for heart rate variations that could predict cardiac arrest. Such information allows better preventive care by identifying higher-risk patients for individualized treatments.

“We were going to try to predict intensive care unit infections” based on the same data, he said. Many of the 120 participants will meet again at upcoming datathons planned in Malaysia and, later this year, at TMU.


Big data shakes up the drug world

Taipei Medical University has years of collaboration with MIT on M-health – health applications involving mobile phones. Dr. Iqbal clarified that these tend to be service- and practice-oriented, rather than research-oriented as datathons are.

One productive research area is long-term risks of various medications. The entire medical world has heard echoes of TMU’s findings regarding benzodiazepines, a common family of medications used for sleep. TMU found that those who took these drugs long-term had higher cancer rates.

Finding reasons is not as easy as finding correlations, Dr. Iqbal cautioned. He noted that the news about some drugs is good: aspirin use is associated with lowered rates of pancreatic cancer, for example.

“Drug research generally stops when medications hit the market,” he said. With this termination of evaluation, it is difficult to track long-term effects of new drugs, especially regarding cancers and other risks. Big data makes it easy and cheap to find this information – without worrying about human subjects and ethics board clearance.

“You have to design the methodology very carefully,” Dr. Iqbal said. But in translational medicine, it’s helpful in finding useful combinations of factors or drugs. And it’s very efficient, he said: “Big data reduces the time and money needed for the same [research] results.” 



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TMU-NHRI researcher wins global awards for cancer breakthrough

Alumnus finds mechanism justifying daily oral chemotherapies



©Dr. Kevin Tsai

Dr. Kelvin Tsai is used to acclaim – a press release about his most recent paper inspired some twenty news stories published around the world, and he recently returned from accepting the Breast Journal Award from WISE Blackwell publishers at a Florida ceremony.

Yet he's sorry that by his reckoning it took so long for the medical world to see the light. Some two decades after low-dose "metronomic" oral cancer medications were first found effective, less unpleasant and potentially much cheaper than injected chemotherapy agents, they're finally being taken seriously -- because Dr. Tsai discovered the "why" of their greater effectiveness.

TMU is where he received his medical training, but Dr. Tsai took a long road through Harvard and the University of California before returning to establish a

joint TMU cancer lab that cooperates with his National Health Research Institutes (NHRI) team in Hsinchu.

In December's *Journal of Experimental Medicine*, his team's findings showed the previously unknown role of the stroma that surrounds and supports tumors. Dr. Tsai said this is often fibrotic tissue, like the lumps women check for in breast self-exams.

Such inflammation can be a sign of cancer – but since, as he said, "you can't palpate a pancreas," other diagnostic imaging can be used to reveal this larger "ecosystem of cancer" beyond the tumor itself.

Five years ago, he began researching stromatic changes in mice, studying cancer stem cells and immune cells during conventional "maximum tolerated dose" (MTD) chemotherapy. He watched the dramatic expansion of cancer stem cells as macrophages become immunosuppressive between treatments, and levels of protective T cells (familiar as an index of HIV/AIDS progression) also fell between conventionally timed treatments as a result of "stromatic activation."

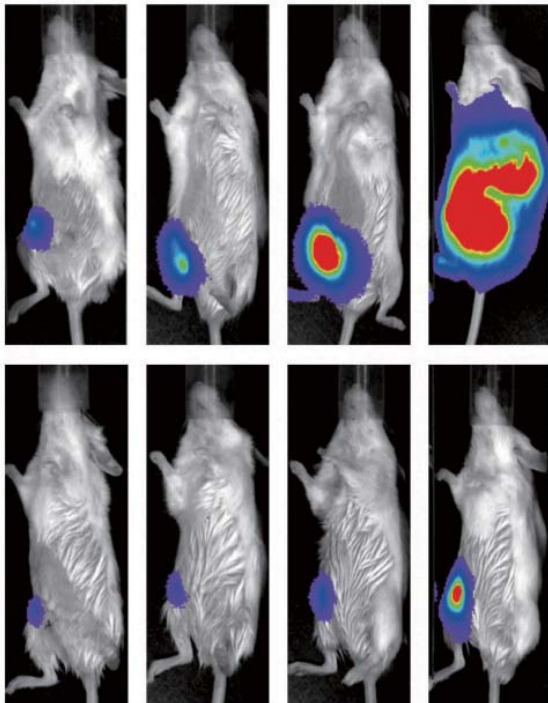
These problems were reduced by low-dose metronomic treatments, with less resistance between cycles. Such oral medicines not only prolong lives and cut costs, but also are tolerated more easily by patients, who no longer have the prospect of debilitating reactions after intravenously infused medications at longer intervals – because the "maximum tolerated dose" is frequently unpleasant or even dangerous for patients.

Dr. Tsai was quite candid about the "conservative" bias of the pharmacological establishment keep-

ing this alternative out of reach for twenty years after metronomic treatment was proposed. After all, the conventional patents they hold are big money-makers, so for that reason they prefer injectable drugs. As a result, he said, most oral medications are being developed in Asia, not by the Big Pharma companies of the West.

His colleague Dr. Nicholas Andre from Marseille in France calls this an “equity issue” and has founded a global initiative to promote these alternatives. Dr. Tsai was invited to serve as an ambassador for this effort, but said that because “this [advocacy] is not science,” he prefers to continue to promote the metronomic concept with research instead.

Also on his TMU team is Dr Jorge Tze-Sian Chan, a Wanfang Hospital GI oncologist, and three laboratory researchers. Meanwhile, his ten-year collaboration with the University of California–San Francisco continues to yield important research, such as a paper on stem cells three years ago -- and one that he said “is going to be huge” later this year.



Mice with breast cancer or pancreatic ductal adenocarcinoma responded better to low-dose metronomic chemotherapy.



Dr. Tsai with his National Health Research Institutes (NHRI) team.

After returning to his alma mater, Dr. Tsai continues working with his longtime lab in Hsinchu, and his team on campus Skypes regularly with both San Francisco and Zhunan, where a larger team manages his studies that involve animals and different equipment. Plans are ready for TMU to build a new state-of-the-art Cancer Research Center, which in due course will better support Dr. Tsai’s ambition in combating cancer.

Dr. Tsai received his medical degree at TMU before completing his clinical training at Veterans General Hospital in 1993, then went further toward research with a Harvard five-year Ph.D. scholarship and postdoc research in San Francisco. Dr. Tsai most recently ran a lab and clinical trials at the National Health Research Institutes in southern Taiwan, but his desire to give his own son the best educational choices ultimately convinced him to move back to Taipei.

Now that the mechanism supporting metronomic chemotherapy has been found, his next task is to demonstrate its efficacy, or how much better it works.

A huge multicenter clinical trial will be led by TMU to study an oral drug from a Taiwan company that can be used for a new metronomic chemotherapy regimen in the treatment of various types of solid cancers. And eventually, millions of cancer patients around the world can look forward to an affordable pill daily, instead of agonizing weekly infusions of a “maximum tolerable dose” of less-effective cancer drugs.





Cycles of progress

President Yen's farewell message reflects on lessons learned and the future

Two months from the end of his six-year term, Dr. Yun Yen shares some of the accomplishments and challenges he experienced during his leadership of TMU's USD \$ 700 million operations.

When I first started my term as TMU's president in 2011, I felt a strong sense of mission to transform our university into a truly international institution. While I recognized that TMU had a history of success based on past performance, I was particularly drawn to the challenge of ensuring our university could reach its full potential.

One of our first priorities was reorganizing leadership roles at the institutional and college levels. Creating a vision, setting goals and clarifying expectations ensured accountability and promoted continuing improvement across the entire campus.

Building on TMU's successes in clinical care, we also invested tremendous efforts and resources to develop our core facilities. We placed particular focus on enhancing research facilities and upgrading translational medicine research. Thanks to constant staff support and dedication, our research programs stimulate increasing interaction between basic scientists and clinical professionals. Working together, our research experts channel their findings to clinicians and vice versa, creating synergies and finding answers to some of the world's most significant health challenges.



the challenge of managing a complex operation of 6,000 students and 10,000 employees. But six years later, I can look back at what we have achieved together with some level of satisfaction and give myself a B+ grade. I think I passed my test.

This job also re-sharpened some of my soft skills. Being able to quickly process information and come up with a reasonably good conclusion is never easy. Quite often, I was expected to make difficult decisions, sometimes with high-stakes outcomes, at the end of a five-minute conversation. This used to be unthinkable for me, but now it's becoming a norm, and I think I am doing okay without letting personal preferences get in the way.


If I were to give one word for my successor to keep in mind, it would be fairness. Being able to resist pressures that come your way will be a significant part of your job, and at times this will require a bit of compromise between operational needs and personal bias. It is easy to overlook the amount of time and effort that people have put in behind the scenes before their propositions are set in front of you. But it is important to bear in mind the need to play fair and be prudent in ensuring the best possible outcomes for

all parties, because every decision we make involves someone's life, career or deeply-held beliefs.

I have worked with a wide range of professionals, and I had a great staff when I worked in the States, but I never saw a cohort that matched TMU's perseverance and integrity. Our people are very hard-working and faithful to their mission. I consider myself lucky to work with amazing individuals whose commitment to TMU goes far beyond expectations. It is such a great honor and responsibility to serve as president, and having had the pleasure of working with such devoted people, I want to make sure they are not taken for granted.

Now that I am approaching the end of this journey, I look forward to going back to my routine as a professor, a role that I thoroughly enjoy. Having spent six years taking care of many other people's interests, I am ready to go back to my lab and focus on research, ready to teach younger professionals, and ready to serve patients again.

There are things I gave up over these six years that I look forward to enjoying again, such as enjoying family life. After countless occasions and duties that kept me from returning home for dinner and spending time at home, I will be able to put these commitments back on track. I hope that in a year's time I can also get rid of the 15 pounds that I gained during this job!

In conclusion, I leave one final message for everyone at TMU before my departure. In the end, what really counts is not one's title, money or fame, but the most basic principle in life: being a good person. That is all that matters. 

A stylized, handwritten signature of Dr. Yun Yen in black ink.

Dr. Yun Yen
President
Taipei Medical University



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