Global Challenges Report

Sharing Innovation and Building Capacity to Fight Neglected Tropical Diseases:

A Selection of WIPO Re:Search Fellowship Stories

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WIPO
WORLD
INTELLECTUAL PROPERTY
ORGANIZATION

Abstract

Four years after the creation of WIPO Re:Search, a consortium launched by the World Intellectual Property Organization (WIPO) and BIO Ventures for Global Health (BVGH) as well as pharmaceutical companies and public sector research institutions, the initiative is thriving and has been making substantial progress in contributing to the global efforts to fight neglected tropical diseases (NTDs), malaria, and tuberculosis (TB). To date, over a hundred research collaboration agreements under WIPO Re:Search have been facilitated by BVGH. And, thanks to sponsorship by the Government of Australia, a fellowship program was started in 2013 that enables developing country scientists to spend one to 12 months in corporate and university research and development (R&D) labs.

This Report documents the experiences of the six scientists who participated in the fellowship program, which was renewed with a doubling of resources for the period 2016-2018.

Foreword

Neglected Tropical Diseases (NTDs), including malaria and tuberculosis (TB), disproportionately affect populations in developing countries. In addition, it is often the most economically disadvantaged within developing countries that suffer the most from NTDs, malaria and TB, yet, and because NTDs are largely 'diseases of poverty', there is a lack of economic incentive for private industry to invest in the development of new medicines. Moreover, while there is great human capital in developing countries, local institutions are limited in their capacity to engage in basic pharmaceutical research and product development.

In order to address this issue (i.e., high disease burden but lack of institutional capacity to tackle the challenges), Australia, as part of our support to the World Intellectual Property Organization (WIPO) has since 2013 earmarked significant financial contributions to WIPO Re:Search under the Australia WIPO Funds-in-Trust Program. Our funding has enabled developing country scientists to be placed in world class laboratories at pharmaceutical companies and universities, allowing the scientists to improve their research skills, advance their research programs, develop a strong network of collaborators, and—importantly—raise their profile within the global R&D and health innovation ecosystem.

For the fellows from Cameroon, Egypt, Ghana, Nigeria, and South Africa participating in the program, their time in research institutions in the United States of America, India and Switzerland (the latter two with global pharmaceutical companies) gave them access to intellectual property assets, equipment and technology, and expertise to support their research of the health conditions directly relevant to their home countries. The fellows who have taken part in the program to date are skilled scientists in their own right, equipped with the local knowledge which allows them to offer a unique perspective and insight into these diseases.

The partnership stories in this report demonstrate the real benefits of this program, not only from the scientific advancements and medical discoveries, but in the establishment of a "WIPO Re:Search network", linking the developed and developing world, prime laboratories, and people, and encouraging an ongoing culture of sharing innovation to tackle these diseases.

I am delighted that the Australian Government has committed additional funding through the Funds-in-Trust program to WIPO and continues to support the placements in this important initiative over the next three years. I have no doubt that these collaborations will follow the precedent set by our previous fellows and continue the momentum on this important cause.

Patricia Kelly
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Section 1:
WIPO Re:Search

WIPO Re:Search is a novel consortium, through which public and private sector organizations share their valuable intellectual property (IP), compounds, facilities, expertise, and know-how with the global research community working on new drugs, vaccines, and diagnostics to treat NTDs, malaria, and tuberculosis (please find a detailed explanation in Box 1). WIPO Re:Search plays an increasingly active role in connecting a variety of actors – it fosters collaborations not only between pharmaceutical companies and academic researchers but also between pharmaceutical companies and biotech start-ups, between academic institutions as well as industry-industry alliances.

WIPO Re:Search came into existence through the initiative of two organizations, WIPO and BVGH, in collaboration with a number of pharmaceutical companies and other public and academic research institutions. WIPO staff serve as the Secretariat, managing the WIPO Re:Search database of IP assets contributed by Members, coordinating communications between organizations and Members, and organizing the meetings of Members. As the Partnership Hub Administrator, BVGH performs the crucial role of facilitating connections and collaborations between Members, as well as other activities. To this end, BVGH proactively examines scientists' current NTDs-related research and proposes collaboration opportunities with other Members. The organization also manages requests from researchers, identifies Member organizations able to fulfill these requests, and helps forge mutually beneficial collaborations. BVGH works closely with WIPO to recruit new Members, and to communicate the Consortium's activities and achievements. Over time, as the Consortium's success has been recognized, the Government of Australia has contributed Funds-in-Trust (FIT) to support WIPO Re:Search in achieving its mission.

The report documents how the partnerships act as an investment in human and institutional capacity building and can be a strategic contribution to establishing robust platforms for research and clinical trials in NTDs in regions where such diseases are prevalent.

The active participation of some of the world's largest pharmaceutical companies and top universities is one of the key factors of the project's success. Indeed, the combination of private and public actors allows cross-sectoral connecting and leveraging of IP assets and

Box 1:

Neglected Tropical Diseases (NTDs) are a diverse group of mainly infectious diseases[1] that prevail in tropical and subtropical conditions and disproportionately burden impoverished populations in the developing world.[2]

NTDs can also be found among the extreme poor living in wealthy countries.[3] More than a billion people – i.e. one-sixth of the world's population – are infected with one or more NTDs, an additional two billion are at risk each year, over half a million people die as a result.[4]

NTDs coexist with poverty because they thrive where access to clean water and sanitation is limited, and people live without protection from disease vectors.[5] They are also recognized as a contributor to poverty since they can impair intellectual development in children, reduce school enrolment, and hinder economic productivity by limiting the ability of infected individuals to work.[6]

Until recently, NTDs received limited attention from the global community. Their classification as "neglected" denotes the dearth of drugs available to effectively and safely prevent, diagnose, and treat them. However, remarkable progress has been made in tackling NTDs since the announcement of the London Declaration on NTDs in 2012 - a partnership which includes the United Kingdom, the United States of America, the Bill & Melinda Gates Foundation, 13 pharma companies, and many others.[7] For example, in 2013, more than 1.35 billion treatments were supplied by pharmaceutical companies alone, and by the end of 2014, more than 70 endemic countries had developed multi-year integrated NTD control plans (nearly a 50% increase since 2012).[8]

access to state-of-the-art laboratories and equipment for academic or non-profit researchers from low- and middle-income countries. Both groups have the same goal in mind – to develop new drugs, vaccines, and diagnostics for NTDs, malaria, and tuberculosis. And WIPO Re:Search exists to catalyse connections, and initiate long-lasting collaborations and institutional relationships, as we discover in Box 2.

BVGH works closely with WIPO to recruit new Members, and to communicate the Consortium's activities and achievements.

This Report presents a selection of stories about the sabbaticals undertaken through the WIPO Re:Search fellowship program. They will be centered around the insights of one Arab scientist and five African scientists. The focus is on how the experiences enabled both the fellows and the hosts to open new avenues for cooperation, networking, and other long-term benefits. The report documents how the partnerships act as an investment in human and institutional capacity building, and can be a strategic contribution to establishing robust platforms for research and clinical trials in NTDs in regions where such diseases are prevalent. It also sheds some light on why developed country research institutes and companies collaborate with scientists from low- and middle-income countries. All sabbaticals were made possible as a result of Funds-in-Trust contribution to WIPO from the Australian Government.

This approach taken by WIPO Re:Search founders and Members demonstrates that intellectual property does not constitute a barrier to research for NTDs, malaria and TB. The companies and other research institutes participating in WIPO Re:Search believe there are opportunities to manage IP innovatively to encourage research and development of health solutions that are particularly needed by the world's poorest populations.

1 Infectious diseases are caused by pathogens, which include bacteria, fungi, protozoa, worms, viruses, and even infectious proteins called prions. See 'Introduction to Pathogens', in Molecular Biology of the Cell, by Bruce Alberts et al., 4th ed. (New York: Garland Science, 2002), http://www.ncbi.nlm.nih.gov/books/NBK26917/.

2 'Neglected Tropical Diseases', WHO, accessed 30 November 2015, http://www.who.int/neglected_diseases/diseases/en/.

3 Peter J. Hotez, The Continuing Threat of Neglected Tropical Diseases, 2015, http://docs.house.gov/meetings/FA/FA16/20150415/103323/HHRG-114-FA16-Wstate-HotezP-20150415.pdf

4 'Investing to Overcome the Global Impact of Neglected Tropical Diseases. Third WHO Report on Neglected Tropical Diseases' (Geneva, Switzerland: WHO, 2015), http://apps.who.int/iris/bitstream/10665/152781/1/9789241564861_eng.pdf.

5 About the NTD Program', USAID's Neglected Tropical Disease Program, accessed 30 November 2015, http://www.neglecteddiseases.gov/about/index.html.

6 Ibid.

7 Hotez, The Continuing Threat of Neglected Tropical Diseases.

8 Ibid.

Box 2:

WIPO RE:SEARCH AND INTELLECTUAL PROPERTY

One of the components of WIPO Re:Search is the database which provides information on the intellectual property (IP) assets available for licensing. These IP assets include compounds, enabling technologies, know-how, and other valuable data. Through the database, researchers have the possibility to search for data that can be potentially useful for their studies. If they identify data sets that could help accelerate their research, they can contact BVGH who will connect the interested party with the company or institution that holds IP rights, to explore access.

Beyond the database, WIPO Re:Search Members pledge to provide royalty-free licenses for R&D relating to NTDs, malaria, and tuberculosis. Moreover, any product developed through WIPO Re:Search must be licensed royalty-free for use and sale in least developed countries (LDCs).

Section 2:

WIPO Re:Search Fellows

DR. FIDELIS CHO-NGWA, UNIVERSITY OF BUEA, CAMEROON

Dr. Fidelis Cho-Ngwa, Head of the Pan-African ANDI Centre of Excellence and Associate Professor of Biochemistry and Molecular Biology at the University of Buea in Cameroon, works on onchocerciasis (river blindness). He was one of the first researchers to have benefited from the WIPO Re:Search fellowship programme. Please find further information and details of this disease in Box 3.

Fidelis developed interest in onchocerciasis research when he was doing his Master's degree at the University of Buea. "We are talking about a disease that affects 25 to 40% of Cameroonians and when you look around you see relatives, friends, brothers, sisters who are infected and suffering, but there is no cure," he said, "if you are living in a highly endemic area, then it is likely you are going to have onchocerciasis until you die *as there is no cure*." In the study of this disease, he aims at identifying natural products active against *Onchocerca* worms. He firmly believes that natural products can be a rich source of novel drug leads.[9]

Dr. Fidelis Cho-Ngwa

In 2013, Fidelis was invited to spend three months at Novartis facilities in Basel, Switzerland. Having extensive experience in onchocerciasis, he went there with clear goals in mind. Fidelis wanted to acquire in-depth knowledge and skills required to use high-performance liquid chromatography (HPLC) and mass spectrometry (MS) techniques in order to, among other things, extract, purify, and identify active natural product compounds for filarial diseases. Novartis' state-of-the-art equipment combined with the host's strong support made Fidelis' plan possible. Read more on HPLC in Box 4.

In addition, he was able to benefit from working in the company's Natural Products Unit – an experience

Box 3:

ONCHOCERCIASIS (RIVER BLINDNESS)

Onchocerciasis (River Blindness) is a parasitic disease caused by the filarial worm *O. volvulus* transmitted by the bite of an infected blackfly. There is no vaccine or medication to prevent infection with *O. volvulus*.[10]

Onchocerciasis is the world's second leading infectious cause of blindness and occurs mainly in tropical areas. Over 37 million people are infected and about 169 million are at risk of being infected.[11] More than 99% of infected people live in 31 African countries.[12] It is a disease of the poorest of the poor and it is found mostly in rural areas.

Currently, ivermectin is the only recommended drug to treat infected people.[13] It kills only the juvenile worms (*microfilariae*) and is ineffective against the microfilariae-producing adult worms.[14] To eliminate the parasite, patients must take this medicine over the life span of the adult worm – up to 14 years. Mass drug administration (MDA) of ivermectin has eliminated or significantly reduced the burden of the disease in many endemic areas. Unfortunately, concomitant killing of the microfilariae of *Loa loa* by ivermectin can cause adverse consequences. Due to this, its MDA was halted in co-endemic communities, most notably in West and Central Africa, causing the urgency for a new drug in this region.[15]

Box 4:

LIQUID CHROMATOGRAPHY–MASS SPECTROMETRY

Liquid Chromatography–Mass Spectrometry (HPLC-MS, or alternatively LC-MS) is a powerful analytical technique, which has many useful applications and has very high sensitivity. It combines the separating power of liquid chromatography (HPLC) with the detection specificity of mass spectrometry (MS).[16] HPLC-MS is widely used in every stage of drug development: drug discovery, preclinical development, clinical development, and manufacturing.[17]

which reinforced his belief in the potential of natural products, especially medicinal plants, in drug discovery. "We have to go back to natural products to increase our repertoire," he said smiling, "you do not know where the 'magic' will come from." Fidelis continued to explain, "Around 99% of microorganisms have not yet been cultured," and added, "microorganisms are always at war with each other, they fight for their territory[18], they know how to produce something, therefore they can constitute a cure!" In his opinion, pharmaceutical companies should continue and/or reinvest in the development of new therapeutics based on natural products. Fidelis was therefore excited that Novartis maintains a special unit dedicated to this field of research.

> Within only two years of working with WIPO Re:Search, we have been able to achieve what some of our predecessors who worked without the platform could not achieve in a decade.

Fidelis' work at Novartis was a two-way street. He described it as a win-win situation; for companies such as Novartis, scientists from endemic countries add unique perspectives and skills to their research. "We can make them aware of our problems," he asserted. The exchanges he had with his colleagues at Novartis paved the way to a solid, trusting network, "Our friends at Novartis promised to help whenever needed."

After returning to Cameroon at the end of his fellowship, Fidelis was not only determined to transfer his skills and knowledge to his students and colleagues but also to upgrade his laboratory. He knew that an analytical HPLC machine would help to find potential drug candidates and complement the phenotypic screens[19] used in his lab. He reached out to BVGH to explore how BVGH could help him secure the much-needed HPLC machine. "Combining this technology with the very rich biodiversity, along with the excellent assays we have on the ground, we believe that it would not be long before high quality drug candidates to treat onchocerciasis start coming out," he commented, "now it takes us months to isolate a single molecule whose purity remains very doubtful."

BVGH had already initiated an equipment donation program, which complemented the goals of WIPO Re:Search. MSD (known as Merck & Co., Inc. in the United States and Canada) agreed to donate six HPLC systems to BVGH for placement at African research institutes. BVGH also partnered with Agilent Technologies to gain access to the software needed to run the machine and analyse data. Agilent also provided Fidelis' laboratory with a set of consumables and spare parts, as well as technical support. Fidelis was proud of this achievement, "receiving this machine really helped in so many ways!"

On top of this, some of the best scientists came to his university to teach students and staff how to use the new equipment. The visits were coordinated by BVGH as part of Merck (MSD) Fellowship for Global Health collaboration with BVGH. "We are able to move the research forward thanks to all these things," Fidelis observed.

Beyond drug discovery, the sabbatical inspired Fidelis to engage on the issue of counterfeit, falsely labelled, and spurious drugs. He plans to use the HPLC machine to implement this plan: "This type of quality control is possible thanks to my sabbatical – it is an ongoing benefit." As Fidelis explained there are currently insufficient technologies in Cameroon to detect counterfeit drugs. One of his graduate students is writing a thesis on the proportion of fake drugs in the Cameroonian market. "It will be the first time a formal study on this subject has been conducted in my country," Fidelis said.

At the time of writing this report, Fidelis' work to develop a cure for onchocerciasis is still in the discovery phase but, thanks to various spillovers from the

sabbatical, there has been substantial progress. One particularly valuable achievement that accelerates the process even further was obtaining a Grand Challenges Explorations grant from the Bill & Melinda Gates Foundation, by Fidelis and his research team. It was awarded to pursue a project entitled "Toward the Development of Safe Onchocerca Macrofilaricides." Thanks to this grant, the researchers at University of Buea are able to develop a small animal model to test the safety of candidate drugs for treating onchocerciasis in people who are co-infected with the *Loa loa* parasite.[20]

Moreover, various new WIPO Re:Search collaborations have emerged after Fidelis's experience at Novartis. For example, Merck KGaA, based in Darmstadt, Germany, will share with Fidelis a subset of highly potent molecules to screen against *Onchocerca*.[21] The best leads will be later advanced by the University of Buea and Merck KGaA and potentially other partners. Through BVGH FundFinder, the BVGH team recommended Fidelis and Merck KGaA jointly apply for the Wellcome Trust Pathfinder Award. They were successful and Fidelis' laboratory was awarded funding to support the collaboration with Merck KGaA.

Fidelis is engaged in another important collaboration. He identified several natural products with activity against both microfilariae and adult *Onchocerca* and in order to move his screening hits forward, BVGH connected him with Dr. Raymond Andersen, an organic chemist at University of British Columbia (UBC). Dr. Andersen has the essential technologies, expertise, and experience needed to fractionate and identify active compounds from natural product extracts. Together they will perform activity-guided fractionation to isolate and characterize the extracts' active compounds.

"Within only two years of working with WIPO Re:Search, we [at the University of Buea] have been able to achieve what some of our predecessors who worked without the platform could not achieve in a decade."[22] Fidelis pointed out. He added that he was not aware of other organisations that are as concerned with discovery of drugs as is WIPO Re:Search. "There are about a hundred collaborations now," he continued, "and many of them are done in partnerships with pharmaceutical companies - where things really happen - this is the fastest way to bring the product into being." Fidelis summed up his experience with WIPO Re:Search by saying, "I pray that the initiative continues because it is one very powerful way of empowering neglected diseases endemic country scientists to contribute to finding remedies for the neglected ailments. Because they live with the problems, they are passionate about finding their solutions."

When asked about his reaction to the 2015 Nobel Prize in Physiology or Medicine, Fidelis replied that he welcomed it with excitement. The prize was granted to Dr. William C. Campbell, Dr. Satoshi Ōmura, and Dr. Youyou Tu for their research and contribution to the development of novel therapies for filarial diseases (avermectin) and malaria (artemisinin). "This is wonderful, our area of research has been recognized," he commented. Moreover, the therapies that were rewarded are based on natural products, which is additionally motivating to Fidelis. Find out more on avermectin in Box 5.

Box 5:

DR. CAMPBELL AND DR. ŌMURA'S AVERMECTIN

Dr. Campbell and Dr. Ōmura developed avermectin, the parent of ivermectin (later named Mectizan), a drug that has radically lowered the incidence of river blindness and lymphatic filariasis. In 1987, MSD (known as Merck & Co., Inc. in the USA and Canada), the manufacturer of Mectizan, declared that it would donate the medicine free of charge - as much as needed for as long as needed.[23]

Even though ivermectin has been tremendously successful, there are a few serious disadvantages in using it. Firstly, ivermectin targets only a larva (microfilaria), i.e., it does not kill the adult worms. Secondly, ivermectin can cause severe adverse reactions in the treatment of patients who have a high intensity of *Loa loa* (eye worm) infection.[24] Moreover, low response rates and resistance to ivermectin have been also reported.[25] Fidelis, on the other hand, studies the adult parasite and attempts to address the issues related to co-infection with loiasis. Considering all this, it is clear there is still a lot of work ahead regarding onchocerciasis.

DR. WELLINGTON OYIBO, UNIVERSITY OF LAGOS, NIGERIA

Dr. Wellington Oyibo, Director of Research and Innovation, University of Lagos, Nigeria, is a medical parasitologist. Wellington previously worked on onchocerciasis; however, in the past ten years he has focused on malaria.

Nigeria is the country with the highest number of malaria casualties worldwide,[26] representing a quarter of Africa's entire malaria burden.[27] "It is an endemic area, so the interest is to see how medicines, but especially diagnosis, could be made available. If you have malaria and can detect it early, then you can treat it," Wellington explained.[28] An expanded explanation of Malaria and the regions affected by it can be found in Box 6, and the diagnostic problems related to it in Box 7.

"We have been using the gains from the fellowship, for example, best practices to develop our clinical research capacity..."

Wellington's rich experience in malarial diagnostics include his participation in a World Health Organization (WHO) platform focusing on the use of malaria rapid diagnostic tests (RDTs), together with quality assurance of these tests. RDTs are recommended for use in areas where good-quality microscopy is not available such as rural health centres and community-based case management programmes.[29] "In developing countries

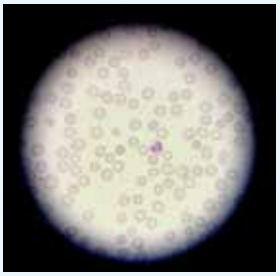
Dr. Wellington Oyibo

where we have infrastructure problems, rapid point-of-care tests can facilitate diagnosis rather than using clinical symptoms alone," he explained. Working in this landscape and merging his interests in diagnosis and quality assurance, Wellington also became interested in the use of biomarkers in drug R&D.

When the opportunity for a sabbatical at the Novartis site in Basel, Switzerland, came, he had three interests in mind. Firstly, Wellington wanted to see the developments in malaria R&D by the industry to guide his research. He indicated interest to work on malaria because, at the time, Novartis had two molecules that were in clinical Phase II on top of the marketed anti-malarial medicine. Secondly, "I wanted to look at opportunities where I could have engagements with Novartis and other groups for the development of a platform in malaria diagnostics," he noted. Finally, he

Box 6:

MALARIA



Malaria is caused by parasites that are transmitted to people through the bites of infected female mosquitoes. If not treated, malaria can quickly become life threatening by disrupting the blood supply to vital organs. In many parts of the world, the parasites have developed resistance to a number of malaria medicines.

About 3.2 billion people are at risk of malaria. Sub-Saharan Africa carries a disproportionately high share of the global malaria burden. In 2015, the region was home to 89% of malaria cases and 91% of malaria deaths.

Malaria is a preventable and treatable disease. Early and accurate diagnosis is essential for effective disease management and malaria surveillance. High-quality malaria diagnosis is important in all settings as misdiagnosis can result in significant morbidity and mortality.

Source [30]

wished to obtain skills that would enable him to build a clinical trials platform in Africa where new diagnostics, medicines, and vaccines for NTDs could be tested.

Wellington joined the program already inspired about the possibility to merge his diagnosis-oriented approach and Novartis' expertise in drug development. "They are producing medicines, but you have to be able to test a patient before the treatment," he remarked. "I wanted to explore if - as a pharma company - they had an interest to get into diagnosis." Then he elaborated, "Novartis has strong best practices and they manage clinical trials on an ongoing basis. In contrast, the clinical trial platform in Africa is quite poor." All this inspired Wellington to ask the question: "How to set up clinical trials for diagnostics in antimalarial medicine trials?"[31]

During his three-month sabbatical at Novartis, Wellington concentrated largely on identifying malaria and non-malaria fever biomarkers, and developing diagnostics for complicated and uncomplicated malaria. Working alongside Novartis researchers, he also gained exposure to product pipeline development processes and management, as well as insights into clinical trial conduct, and the governance of knowledge and intellectual property.[32]

In Novartis's labs, Wellington was excited about the opportunity of using high-tech tools – from DNA extraction to sequencing, as well as assaying antimalarial compounds from blood samples and dry blood spots (DBS).[33] "Though these machines are expensive and therefore difficult to maintain in a university environment, it underscores the usefulness of collaborations that will fast-track exploratory research for malaria biomarker targets in the parasite," he noted. According to Wellington, "this is linked to knowledge transfer, which is an important aspect of robust skills development."

During his fellowship at Novartis, Wellington succeeded in building networks with researchers in various labs. He collaborated with the immunological profiling group, the profiling group on malaria (focusing on severe malaria) as well as the biomarker development group (BMD). The BMD expressed interest in a joint project with the objective of "looking at malaria in different processes, in different patients to develop some protocols that will enable the use of DBS for large-scale parasite genomic profiling." Unfortunately, due to time constraints, Wellington was unable to pursue all his projects in detail. He is nevertheless optimistic about Novartis' interest in biomarkers for malaria and believes that it opens up the opportunity to provide solutions not just for treatment, but also for proper diagnosis. "This will contribute immensely to the effective case management of malaria in endemic countries," he believes.

When asked how researchers at Novartis could benefit from this collaboration, Wellington replied: "I am in the malaria landscape and they find that useful because I work both from the bench and the bedside, and I am involved in program implementation as well, so my research is interesting for them. It is a win-win."

Another valuable skill Wellington gained at Novartis was research design and management, including the ability to ask the "right questions." "In academia you have opportunities to think broadly, but if you put energy in focusing on specific problem-solving, then you can see what comes out by redefining and refining your questions and your queries," he remarked.

In addition, Wellington was impressed with the management of the company's biobank, specifically its sample storage system. "This is a good lesson on how to manage my research platform," he said, and added that this will help him to successfully apply his observations to his own biobank in Lagos. Wellington highlighted that this type of lesson has many applications, "You can expand the same skill to other diseases and conditions."

Box 7:

THE EFFECTS OF MALARIA MISDIAGNOSIS AND OVER-DIAGNOSIS

Misdiagnosis and subsequent wrong treatment (or lack thereof) may have many consequences. Firstly, incorrect treatment may have serious ramifications on health, including death. Moreover, there is a high economic cost for societies linked to the wasting of antimalarial drugs. Finally, if antimalarial medicine is used inappropriately, the risk of resistance to malaria to parasites is enhanced.

Source [34]

After his return, Wellington has been transferring his new skills to his students at University of Lagos and actively leveraging the initial collaboration. Rotations through several labs at Novartis prepared him not just for his research but also new leadership roles. Soon after his sabbatical, Wellington was appointed Director, Research and Innovation of the University of Lagos and a full professor. In this new role, he brings the experiences obtained during the sabbatical to, among other things, direct industry-university linkages, and manage IP.

Wellington has also been exploiting additional opportunities with Novartis. One of the key follow-up projects was SMS for Life in Nigeria, "It is a platform which is meant to facilitate the tracking of stock levels of medicines and ensure that they are available," Wellington explained. His host at Novartis, Dr. Dominic Ehrismann, assessed Wellington's contribution as invaluable: "Wellington was very helpful in making the right connection with the people in the government to discuss an extension of the SMS for Life program to Nigeria."

Another ongoing project focuses on dried blood spots (DBS) analysis. "We developed a very simple method – Wellington would sample malarial patients in Nigeria and all he has to do is take blood samples and put them on a filter paper. This filter paper can be shipped to Switzerland by post and we then deploy whole genome sequencing," Dominic added, "so we bring all our advanced technological capabilities into the game and sequence for the presence of resistance genes in malaria." He highlighted this initiative is an example of Novartis' efforts to teach the visiting researchers skills that can be easily transferred to all settings.

"What WIPO Re:Search decided to do, which is a game changer, is getting people together to see where they can tap into their strength and where their weaknesses can be overcome,"

Wellington was happy to announce significant progress in building the clinical trials site. Wellington's university was visited by a vice-president of Novartis. "We have been using the gains from the fellowship, for example, best practices to develop our clinical research capacity," he highlighted, "there is an ongoing communication on how Novartis can guide this process."

Only three years after his sabbatical, the ANDI Centre of Excellence in Malaria Diagnosis, University of Lagos successfully conducted a Phase III trial on a urine-based malaria diagnostic test that has been registered for malaria diagnosis in Nigeria. Moreover, the platform passed two External Quality Assurance (EQA) assessments commissioned by the WHO and the Foundation for Innovative New Diagnostics (FIND) within just one year. Given the positive outcomes, the Centre can now conduct clinical performance evaluation trials for malaria diagnostics.

Wellington believes that the collaboration with Novartis can continue to thrive. "Opportunities exist in the areas where we can define our own strategic interests – you needed some match-making between the agenda of the University of Lagos and Novartis," he pointed out.

"This process is a continuum and there are several branches to it," Wellington noted. In addition to his sabbatical experience at Novartis, BVGH coordinated placements and funding for two of his students at some of the world's best research institutions. Wellington is proud that two of his students (Uche Igbasi visited the National Institute of Parasitic Diseases (NIPD), Chinese Centre for Disease Control, Shanghai, China, and Chika Okangba went to Stanford University, USA) were invited to participate in similar programs. Wellington referred to these experiences as "very explosive - two years' work was done in just a few months."

When asked about the significance of WIPO Re:Search in the NTD landscape, Wellington commended the consortium for involving companies and focusing on knowledge-sharing and trust-building. "Addressing these issues and drawing on the expertise in developing countries is generally not supported enough, and WIPO's platform allows scientists in developing countries to access this knowledge, the materials, and thus benefit from technology transfer," he explained. "For every collaboration, especially when it has to do with products and IP, the best place to be is WIPO Re:Search," he emphasised.

Wellington is extremely positive about WIPO Re:Search's contribution in the NTD landscape, "What WIPO Re:Search decided to do, which is a game changer, it is about getting people together to see where they can tap into their strength and where their weaknesses can be overcome," he stated. "For instance, you could be doing good research, you have products, molecules, and candidates either for medicines or diagnostics or for vaccines but you cannot move it forward,"[35] Wellington elaborated. "WIPO Re:Search has helped us be more efficient while maintaining high quality research. We could do things in just a few weeks' time – this has to do with knowledge sharing." He added that WIPO Re:Search's value is not exhibited in "just in one product, but this can galvanize action and move to create other things."

Looking to the future, Wellington hopes to obtain a malaria antibody that is able to dislodge or disrupt the interaction in which malarial parasites attach to the

Box 8:

CHIKA OKANGBA

Chika Okangba, during her stay in Dr. Ben Pinsky's laboratory at Stanford, learned how to collect and process patient samples, how to perform the Stanford multiplexed RT-PCR assay for dengue, malaria, and leptospirosis, and how to analyse the results. She used the multiplex assay to screen Wellington's sample collection. While few cases of dengue or leptospirosis were identified, Chika confirmed the diagnosis of malaria in a significant number of patients that tested negative by microscopy. One paper describing an aspect of the findings of this research has been published in the Journal of Clinical Microbiology.[36] This exploratory research will pave the way for further optimization and expansion to include the detection of other aetiologies responsible for non-malarial fevers that form the larger proportion of fevers than are seen currently to ensure that febrile illnesses in developing countries are addressed as countries target the pre-elimination phase of malaria.

Source [37]

Box 9:

UCHE IGBASI

Uche Igbasi was awarded a two month-long fellowship at Dr. Jun-Hu Chen's laboratory at the National Institute of Parasitic Diseases (NIPD), Chinese Centre for Disease Control, Shanghai, China. Her key goal was to acquire skills in the recent molecular based procedures in malaria research. The initial stage of her research, which is focused on antimalarial resistance, included collecting dried blood spots from malaria positive patients from 7 health facilities and 20 communities in different areas of Lagos State, Nigeria. The malaria screening for these samples was done in Wellington's laboratory at the ANDI Centre of Excellence for malaria diagnosis, College of Medicine, University of Lagos.

The molecular aspect of the research, meanwhile, was completed at NIPD. "The study showed some novel findings like mutation in the Kelch 13 (K13) propeller gene at A578S, which has recently been associated with slow parasite clearance rate in a Ugandan study, and some new haplotypes of Pf-Chloroquine resistance transporter gene (Pfcrt) that have not been reported in Nigeria," Uche elaborated.

"It was a fulfilling program. The skills I acquired during my fellowship are being used in the implementation of my research activities in my institute, and also passed on to students under my tutelage," she highlighted. About four academic publications are expected from this partnership.

blood vessels. Then, “the parasite would not have an opportunity to attack, to go into blood vessels, and we can move that product forward and commence real trials in humans,” he remarked. “This would be phenomenal if you could dislodge parasites and have a vaccine, for example,” Wellington hopes.

DR. OLFAT HAMMAM, THEODOR BILHARZ RESEARCH INSTITUTE, EGYPT

Dr. Olfat Hammam is a pathologist who specializes in schistosomiasis pathology (See Box 10 for details). She works at the Theodor Bilharz Research Institute (TBRI), Giza, Egypt and has academic training in Egypt and Germany.

Dr. Olfat Hammam

Olfat’s research addresses early diagnostic, prognosis, and early treatment, as well as complications of schistosomiasis. “Currently, I mainly work on complications diagnosis,” Olfat specified, “and my research focuses on urinary bladder carcinomas associated with schistosomiasis.” She explained that urinary schistosomiasis (*Schistosoma haematobium*) touches many people in Egypt, and this type of bladder cancer is a common disease in this country. “Many get infected during their work in the fields, especially if they do not protect themselves properly. The infection can lead to bladder cancer,” Olfat added, “and this, unfortunately, is a very serious disease, especially if the squamous cell carcinoma type is diagnosed.”

WIPO Re:Search supported Olfat in obtaining her sabbatical at Stanford University, Palo Alto, California. Her choice was a result of a careful investigation and preparatory work by BVGH, and Olfat saw the Stanford lab as a perfect match. Dr. Michael Hsieh, with whom she was invited to work, has an extraordinary expertise in schistosomiasis and other neglected tropical diseases. In addition, he specializes in animal models for research – something that Olfat wanted to explore in depth.

Box 10:

SCHISTOSOMIASIS

Schistosomiasis, also known as bilharzia, is a chronic disease caused by parasitic worms that live in certain types of freshwater snails. People get infected during routine agricultural, domestic, occupational, and recreational activities which expose them to infested water.[38] Depending on the species of parasite, schistosomiasis causes renal and bladder dysfunction or liver and intestinal disease, and contributes to anaemia and growth retardation in children.[39]

Schistosomiasis affects almost 240 million people worldwide.[40] It is considered second only to malaria as the most devastating parasitic disease in tropical countries.[41] The geographic distribution of the various species of schistosomes is dependent on the distribution of the species of their intermediate freshwater snail hosts. The disease can be found in 74 tropical countries in Africa, the Caribbean, South America, East Asia, and the Middle East, with 62% of the burden occurring in 10 countries in Africa.[42]

Schistosomiasis control focuses on reducing disease through periodic, large-scale population treatment with praziquantel, which is the recommended treatment against all forms of schistosomiasis.[43]

When she came to Palo Alto her key goal was to study the various mechanisms responsible for the association between urogenital schistosomiasis and bladder cancer. “We need to know what are the factors that contribute to an increased risk of bladder cancer in Egyptian patients with schistosomiasis,” she explained. Moreover, Olfat wanted to investigate the differences in squamous cell carcinomas of the bladder in Europe, USA, and Egypt in order to better understand the links between schistosomiasis and these cancers.

One of Olfat’s most valued assignments was working on an experimental schistosomal mouse model. “Based on this model, I am generating new ideas to help find early diagnosis of schistosoma infection or bladder cancer and the genetic changes taking place in schistosomal bladder cancer,” she stated.

Olfat was constantly motivated to learn new skills, going beyond her expertise, “I asked Dr. Hsieh whether I could go to another lab because there were new techniques that I wanted to see and learn,” she explained. Olfat appreciated the opportunity of being in such a stimulating environment, “If you are in a place where everything is available, you can finish your work and do whatever you want within the limit of these labs.” When questioned on which new techniques she was especially proud of, she replied, “Tissue microarray – it is very hard but I have learned it during this fellowship. I would never have known it otherwise,” she stated. After mastering tissue microarrays techniques, she applied them to human schistosomal bladder cancer specimens. Olfat also worked on laser capture microdissection, “It is only at Stanford. For a pathologist, it is a very important skill,” she emphasised. “These two skills, I would never have learned without WIPO Re:Search programme,” she explained.

From the very beginning, Olfat was determined to share her skills and knowledge with researchers working in Michael’s lab. She found it especially exciting that
she was able to teach other researchers pathology. “Most departments had no pathologist so when I went there I found many projects and people came to me to help them,” Olfat reported. “Dr. Michael allowed me to work with everyone so I was very happy.” She also supervised some of the students and colleagues there, “I taught them relevant pathologic procedures, we made protocols together, revised them, and I could also teach them some pathology tricks.” Olfat gladly announced that after the students learned the relevant techniques, there was no need to commission this type of work to external labs.

Her hard work did not stop in the lab. Olfat also co-authored four peer-reviewed articles with Michael, published in PLoS Neglected Tropical Diseases, Trends in Parasitology, Experimental Parasitology, and the FASEB Journal. She also co-wrote a paper on kidney pathology with Dr. Linda M. Dairiki Shortliffe (who was Chair of the Department of Urology at Stanford at the time).

Olfat spoke enthusiastically about the people she worked with at Stanford. “Dr. Michael is very experienced, cooperative, and helpful. Anything I asked him for, he would help me out,” she commented, “sometimes we would have different ideas, for example on bladder cancer, but as long as there were no financial restraints, he facilitated my work.”

> And I will pass my message to them: go and see the world, open your mind and eyes to the world.

In addition, Olfat feels that her interpersonal skills improved because of the sabbatical at Stanford. “You have a different social life there – it is very different than in Egypt. I learned to share knowledge with other doctors, with other friends. I can see another way of life now,” she explained. As a female scientist, Olfat felt that the sabbatical made her stronger, and now she can serve as an example, “I will share my wonderful experiences and encourage other women to open up to the world,” she said. “Women in African countries, especially Muslim countries, do not take their chances as they are too often afraid to go anywhere. And I will pass my message to them: go and see the world, open your mind and eyes to the world,” she expressed enthusiastically.

After she came back to Egypt, Olfat concentrated on transferring her new knowledge and skills to her colleagues at the Theodor Bilharz Research Institute. She hopes that one day her lab will be equipped in some high-tech machines, such as tissue microarrayer, like the ones she used at Stanford. However, she stated, “the financial situation in Egypt is not very good at the moment so they do not have money for this.”

Olfat sees the sabbatical at Stanford as a great boost in her research, “This one year may be equal to ten years working in Egypt. At Stanford, you have great facilities, nice people you work with, speak about your ideas every day, and think how to transfer this from words to real work. So every day there is practical work,” she highlighted.

Olfat believes that WIPO Re:Search is going in a good direction by supporting research in developing countries like Egypt. “It boosts local capacity because when researchers come back home, they transfer the new skills and knowledge to their colleagues,” she noted.

She particularly appreciates what she referred to as "the human aspect" of WIPO Re:Search. "The consortium is concerned about the diseases that no one cares about," she explained. Many people suffer immensely due to NTDs, Olfat highlighted, and the projects facilitated by WIPO Re:Search are not only concerned with science but also human beings.

Meanwhile, Olfat is continuing her research on schistosomiasis, and planning another visit to the USA.

DR. CHRISTIAN AGYARE, KWAME NKRUMAH UNIVERSITY OF SCIENCE AND TECHNOLOGY (KNUST), GHANA

Dr. Christian Agyare is a professor at the Department of Pharmaceutics, Kwame Nkrumah University of Science and Technology (KNUST), Kumasi, Ghana, specializing in investigating medicinal plants for their potential to treat infectious, including neglected diseases.

In developing countries, including Ghana, patients often rely on traditional medicine for their health needs, such as treatment of infectious diseases. Indeed, African folk medicine has a vast repository of plants and herbal preparations with documented usefulness against infections.[44] In his research, Christian studies bioactive agents based on such natural products against parasitic agents responsible for some NTDs. "Ghana is part of the tropical region and we suffer from most NTDs," Christian noted, "and rural areas are especially affected." Even before his sabbatical, conducting collaborative research was not new to Christian, "Getting compounds, whether from natural products or synthetic, is not done in Ghana. Most of the time, we do it in collaboration with scientists in the developed world, obviously, because of the lack of facilities" (for more information on natural products, see Box 11).

Dr. Christian Agyare

In October 2013, Christian came to the Center for Discovery and Innovation in Parasitic Diseases

Box 11:

NATURAL PRODUCTS

A natural product is a chemical compound or substance produced by a living organism found in nature that usually has a pharmacological or biological activity for use in pharmaceutical drug discovery and drug design.[45]

Chinese traditional medicine is one of the most important examples of how natural products can be efficient in the treatment of diseases.[46] In the recent years, the development of new bioassay techniques, biotechnology methods, bio-guided phytochemical studies, automated high throughput screening, and high performance analytical methods, presented new possibilities in the area of drug design and drug discovery.[47] Natural products continue to provide unique structural diversity in comparison to standard combinatorial chemistry, which presents opportunities for discovering mainly novel low molecular weight lead compounds.[48] Since only less than 10% of the world's biodiversity has been evaluated for potential biological activity, many more useful natural lead compounds await discovery.[49]

(CDIPD), University of California, San Francisco (UCSF), to start a ten-month sabbatical. “My collaboration with Dr. Conor Caffrey from CDIPD started with a project on parasites responsible for NTDs and, thanks to WIPO Re:Search, it could be continued,” Christian explained his initial interaction with WIPO Re:Search. As with all the WIPO Re:Search fellowships, BVGH identified interested host institutions and recruited qualified candidates from among WIPO Re:Search’s membership in developing countries.

The key goal of Christian’s training was to enhance his experience in cultivating, maintaining, and screening compounds against various parasites, including the causative agents of Chagas disease, lymphatic filariasis, human African trypanosomiasis, and schistosomiasis.[50] During his placement at CDIPD, natural products sourced in Ghana were screened against various parasitic organisms.[51] As a result, Christian found that at least three hit compounds, fractions, and extracts were identified for each of the parasites and worms. His initial idea was to perform the extraction and purification of compounds from the anti-parasitic products back in Ghana and then return to California to further examine their activity. However, new demands of his time arose in Ghana, and instead of returning to California himself, one of his students, Ms. Gertrude Kyere-Davies, was invited to the University of California – this time in San Diego – to continue Christian’s research. (Dr. Caffrey’s group moved in 2015 from UC San Francisco to UC San Diego). “Gerty got interested as a result of my sabbatical,” Christian explained. The research looks promising: “Gerty is getting more isolates, we believe something will come out of it,” he noted. Christian is in the process of writing a manuscript on the research findings. “We are working on it, but first we want to isolate pure compounds and find out the activity of the bioactive fractions,” he clarified.

Christian was also pleased that during his stay at CDIPD, he could establish a network of collaborations with other researchers. Among others, he visited Dr. Philip Rosenthal’s lab for malaria and, Dr. Michael Hsieh’s group, both at Stanford, for *S. haematobia*, and Dr. Roger Linington’s lab for natural product research at University of California, Santa Cruz (UCSC). “I am in contact with Mike and we are just waiting to have pure active compounds so that we can move on,” he remarked. Christian added that he was also in touch with Dr. Linington, “we have stressed the need for us to collaborate on the natural products.”

When asked about other noteworthy experiences related to his sabbatical, he replied, “back in my university, it seems like everybody is working on his own, but here, there is collaboration. For instance, if I screen a compound and it is active against schistosomes, another group may be working on leishmania, but they would encourage me to come and see if what I discovered can also have effects on these parasites. Everyone is prepared to help, and this is what I appreciate.”

What could Conor and other researchers at CDIPD learn from Christian? “They realized the potential of medicinal plants in the search for bioactive agents against neglected tropical diseases,” answered Christian. Conor highlighted that, thanks to the WIPO Re:Search sabbaticals, his lab was able to access unique Ghanaian plants, “Christian and Gerty themselves are very aware of these plants from their own family backgrounds.” Conor saw a unique opportunity in elevating this knowledge and consciousness from their ethno-medical context.

Thanks to the state-of-the-art equipment at CDIPD, she had an opportunity to do advanced research and leverage her and Christian’s work done in Ghana.

In the meantime, the exchange between Kwame Nkrumah University of Science and Technology (KNUST) and CDIPD continues. Christian explained how the two institutions collaborate, “we have natural products, for example a medicinal plant, that traditional herbalists use and we do some preliminary studies in Ghana, get the active compounds, and then go to San Francisco or San Diego to do more research.” Additionally, Christian and Conor are considering new ways to expand the collaborative activities between KNUST and UCSF. Conor believes that a more regular student exchange would contribute to promoting a sustainable partnership between the two institutions.

Although his sabbatical ended, Christian is very satisfied with the gains from the program, “I think with the sort of experience and skills that I have gained, it is going to help us set up new projects in Ghana, and train some of my colleagues and graduate students, and transfer the new skills to them,” he illustrated. After staying at CDIPD, he only regrets that he does not yet have an HPLC machine in his lab, “I have not been able to procure one, but if WIPO Re:Search can help, that would enable us to get isolation work done here in Ghana,” he hopes. “It would be used to train the grad students too,” Christian added.

Christian was grateful for the opportunity that WIPO Re:Search provided him for and appreciates how many spillovers this experience has brought. He thinks that WIPO Re:Search “should be maintained and, if possible, the numbers of the fellows should be increased.[52]

GERTRUDE KYERE-DAVIES, KWAME NKRUMAH UNIVERSITY OF SCIENCE AND TECHNOLOGY, GHANA

Gertrude (Gerty) Kyere-Davies is a Master's student at Kwame Nkrumah University of Science and Technology (KNUST), currently pursuing a degree in pharmaceutical microbiology.

In October 2015, she arrived in California for her six-month fellowship in Conor Caffrey's group at the Center for Discovery and Innovation in Parasitic Diseases (CDIPD), University of California, San Diego. There, her main task was to screen various plant extracts and compounds against schistosomes. In addition, Gerty, Conor, and Christian decided to expand the screening activities to include most of repertoire of parasites maintained at the CDIPD, including *Trypanosoma cruzi, Leishmania, Trypanosoma brucei*, *Giardia lamblia* and *Entamoeba histolytica*. "A substantial training element was also involved to allow Gerty to translate her new skills back to Kumasi," stated Conor. The research was partly based on Christian's earlier work and, in particular, the three-hit molecules he found during his sabbatical at CDIPD. "When he came back home, we tried to work on the extracts and bring them down to different components," she said, "so, I brought samples to screen to see which of these components are responsible for the activity against the bacteria and parasites that we know cause disease," she elaborated. "It is a continuation of what he did plus some new things," Gerty highlighted.

While in the CDIPD labs, Gerty learned various methods for growing the organisms and how to safely store them. "After the training, I cultivated the parasites on my own for about two weeks to ensure I got everything right," she said. In addition, Gerty developed skills on how to operate new, cutting-edge equipment. She explained that thanks to the state-of-the-art equipment at CDIPD, she had an opportunity to do advanced research and leverage her and Christian's work done in Ghana, "The results are validated using the right equipment, and the right techniques."

Gerty was aware, though, that in her lab in Ghana she would not be able to apply many of the new skills relating to the use of such high-tech equipment. However, she and Conor designed certain protocols that will make it easy to run assays (i.e. investigative procedures aimed at the assessment of the composition of a substance) on certain nematodes (like *C. elegans*) and protozoa (*Giardia lamblia* and *Entamoeba histolytica*). "These particular organisms are relatively easy to cultivate and no special equipment is needed for their maintenance," she explained. Gerty believes that all these relevant abilities will make it easy for her to fit in new labs in the future.

Building collaborations and friendships was another benefit of Gerty's time in San Diego. In the lab, she was supervised by, and worked with different CDIPD members who shared their expertise with her. "I have made friends with people from different parts of the world," she stressed.

After she returned to Ghana, she felt determined to teach her fellow students at KNUST the valuable skills and knowledge that she acquired. "I expect to pass on this knowledge to my colleague students who will be going into the field of parasitic research, through seminars and helping them with the practical work," Gerty highlighted. She was particularly inclined to transfer her knowledge and skills relating to growing and handling parasites. "Christian sent some parasites to his lab after his fellowship but his other students did not know how to handle the parasites, so they all died and no research could be done," Gerty explained. "The other skills I want to transfer are the procedures that will be used, especially the molecular aspects, to do the screenings," she continued.

> All of the skills and knowledge gained during this internship is applied directly to guide and benchmark our program.

Just as Gerty hoped, the work done in the CDIPD labs brought promising initial results, "I have screened my plant extracts against all the selected parasites and in each case I have obtained hits that can be further worked on," she explained. Gerty also presented her findings to the faculty of the Skaggs School of Pharmacy and Pharmaceutical Sciences in March 2016. When asked about her next steps, she replied, "I intend to continue the work I have started on parasitic research and the plant extracts. I will further work to isolate the active compounds that are responsible for the activity that was seen in the screens I ran, and also determine the mechanism of action of these compounds," she added, "I also want to run in-vivo assays to confirm these activities."

Gerty enjoyed her time in San Diego and valued the WIPO Re:Search fellowship program for supporting such collaborations. "Christian was at CDIPD two years before and I was glad to have the opportunity to continue his work with the same team. After I leave, perhaps the work can be continued." Above all, Gerty believes that programs like WIPO Re:Search are a sustainable approach in terms of facilitating the development of drugs for NTDs. She highlighted the importance of the continuity aspect of this initiative because of "the complexity of the research, and the need for time to obtain tangible results."

Speaking about the more distant future, she said, "my biggest hope is to be able to come out with a compound that can be developed as a drug for the treatment of some parasitic infections in Ghana and the rest of the world. It would not be bad if I win a Nobel Prize for discovering a drug for parasitic infections," she laughed.

DR. KRUPA NARAN, INSTITUTE OF INFECTIOUS DISEASES AND MOLECULAR MEDICINE, UNIVERSITY OF CAPE TOWN, SOUTH AFRICA

Dr. Krupa Naran is a postdoctoral fellow at the Institute of Infectious Diseases and Molecular Medicine, University of Cape Town, South Africa.

Krupa's adventure with WIPO Re:Search started when she was still writing her Ph.D. thesis. One day, the Medical Research Council (MRC) in South Africa contacted her supervisor at the time asking if he had any students interested in going to AstraZeneca's research lab in Bangalore, India. Krupa was quick to take up the opportunity, as she knew exactly what she wanted to achieve.

When asked about the goals she intended to pursue at AstraZeneca, Krupa responded, "At the time when I went to AstraZeneca, our lab just started doing some initial drug discovery in tuberculosis. On the biology side, it meant setting up different assays [investigative procedures aimed at the assessment of the composition of a substance] to try to figure out which would be the best drug to treat TB," she added, "so for me the objective was learning these different assays and how to best perform these research questions." Further details on the repercussions of TB are found in Box 12.

Dr. Krupa Naran

During the sabbatical, the experts at AstraZeneca supported her in developing new skills and knowledge relating to assay development and beyond. "Although I had the basic skills that were required for the various techniques that I performed, every experiment I was introduced to was novel to me," Krupa highlighted. "I have gained incredible knowledge and experimental skills in areas such as the culturing of non-replicating bacteria, kill kinetics, and intracellular assays, all of which forms the basis of our drug discovery program," she elaborated.

At AstraZeneca, Krupa was commonly the first person in the lab, "This is just the nature of how I work, I like

Box 12:

TUBERCULOSIS

Tuberculosis, or TB, is an infectious bacterial disease caused by Mycobacterium tuberculosis, which most commonly affects the lungs. It is transmitted from person to person via droplets from the throat and lungs of people with the active respiratory disease.

In 2014, 9.6 million people fell ill with TB and 1.5 million died from the disease. Over 95% of TB deaths occur in low- and middle-income countries. In 2014, the largest number of new TB cases occurred in the South-East Asia and Western Pacific Regions, accounting for 58% of new cases globally. However, Africa carried the most severe burden, with 281 cases per 100.000 people in 2014 (compared with a global average of 133).

TB is a treatable and curable disease. Active, drug-susceptible TB disease is treated with a standard 6-month course of 4 antimicrobial drugs. However, anti-tuberculosis drug resistance is a growing public health issue.

Source[53]

to start early," she said. Another advantage of beginning her experiments early was the time constraints on many of her procedures. "I would be at my computer until nine or ten in the morning, reading papers, filling out reports." Later, Krupa and her supervisor planned the day together and went into one of the laboratories. Unfortunately, for safety reasons, Krupa had to be accompanied by her supervisor at all times, something she feels limited her ability to conduct independent work.

Krupa also believes that the visit at AstraZeneca helped her gain new skills on how to redefine and manage her research. "In academia we tend to waste too much time and ask ourselves a lot of irrelevant questions, whereas in the pharma industry it is very objective-driven," she remarked, "They know exactly what their object is, what their final goal is and they march until they get there. It was extremely valuable to come here with end-goal orientated assay development."

Additionally, Krupa feels like the opportunity of going to Bangalore boosted her personal skills, "It forced me to go to another country and socialize - I had to make friends, talk about work, and about my interests in the field," she said smiling. "I opened up and it gave me hope that besides academia there is the whole industry that is available. It was a great opportunity to go and do something very different than what I am used to," Krupa continued. She believes that the discussions she had with the colleagues at AstraZeneca were mutually beneficial. Krupa enjoyed speaking about her lab in Cape Town and the research she performed there. "I think that the individuals benefited from having me there," she said.

After she returned, her enhanced expertise was useful in setting up the drug discovery program at her institute in Cape Town. "All of the skills and knowledge gained during this internship is applied directly to guide and benchmark our program," she emphasised, "and assays that I have learned at AstraZeneca are implemented into our drug discovery programme." She transferred her skills to her colleagues. Moreover, her stay at AstraZeneca contributed to her PhD thesis, as she was able to incorporate some of the assays in her study.

As for her plans, Krupa is open to joining the pharma industry. "Maybe next year I will start looking at different career options, and one of them is going to the pharma industry," she said. Currently, she is considering opportunities in Germany - she is looking forward to working abroad. "They have an amazing industry-based environment there. I would like to try options over there," she highlighted. "But so far, I am writing papers and I am very busy," she laughed.

When asked about WIPO Re:Search's potential she is very positive. Krupa believe that it is not only useful on a personal and career enhancing level, but also as a means to fight NTDs.

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18 "Over many generations, some bacterial lineages evolved ways of attacking other bacteria. In response, the defenders with stronger protections were favoured, and the assailants, in turn, evolved even better weapons, and so on. This arms race has been playing out over four billion years of bacterial evolutionary history, so the combatants have had plenty of time for natural selection to fine-tune their weaponry. Antibiotics like vancomycin and teixobactin are the munitions that certain bacteria species have evolved over the course of this ongoing fight. We humans have simply co-opted these highly evolved compounds and put them to work against the bacteria that attack us." See: 'Want a New Drug? Look to Evolution', accessed 30 November 2015, http://evolution.berkeley.edu/evolibrary/news/150202_antibiotics.

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Section 3:
Insights from the Hosts

DR. CONOR CAFFREY, CENTER FOR DISCOVERY AND INNOVATION IN PARASITIC DISEASES, SKAGGS SCHOOL OF PHARMACY AND PHARMACEUTICAL SCIENCES, UNIVERSITY OF CALIFORNIA, SAN DIEGO, USA

Dr. Conor Caffrey is an Associate Adjunct Professor at the Skaggs School of Pharmacy and Pharmaceutical Sciences, University of California at San Diego and a senior scientist at the Center for Discovery and Innovation in Parasitic Diseases (CDIPD), University of California, San Francisco. In this capacity, Conor was Christian and Gerty's mentor and collaborator.

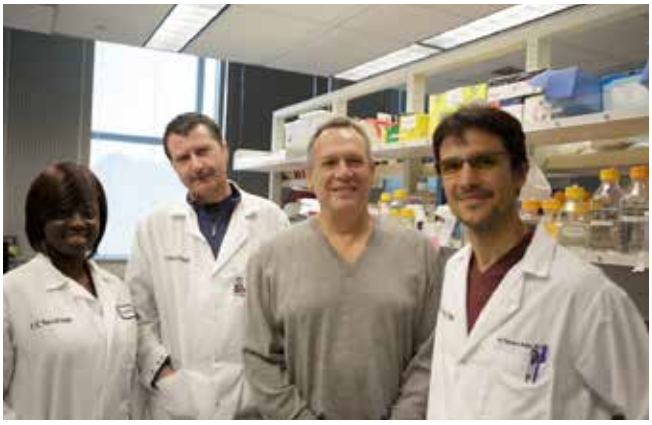
"The benefits are clear: we host motivated scientists with skills in natural products and the home institution (and country) gains a cadre of scientists with research skills to foster further learning and development,"

When asked why an institution such as his own decided to invite researchers from low- to middle-income countries to work in their labs, he replied that "first and foremost, it is the basic principle of collaboration that is very important. Great things happen when you work with others, when you talk and share ideas." Conor went on to say that collaborating with people who are motivated and strive to attain similar goals is both more productive and more fun. "Gerty was really excellent. She is talented, enthusiastic, hard-working, and made a strong contribution to our team's culture while she was here. We'd love to have her back!"

Moreover, Christian and Gerty work in Ghana, where medically useful plants and herbs are widely used and this knowledge was extremely valuable for the researchers at CDIPD. "Natural products have been fundamental to improving the human condition by providing the drugs to treat cancer, and many metabolic and infectious diseases. Conor elaborated, "in Ghana, there is a rich oral tradition in ethno-medicine and curing through plant-related remedies – something that 'developed nations' have lost." The possibility of benefiting from this knowledge and its ethno-medical context has been both fascinating and useful for Conor. Likewise, he is interested in many parasitic organisms in Ghana. It is an endemic country, in particular in the West and Northern part, "where there is schistosomiasis which is one of the diseases that we were particularly interested in," he elaborated.

At Kwame Nkrumah University of Science and Technology (KNUST), in Ghana, researchers have the ability to use those plants to generate fractions that may contain active components of medicines. This is where the two institutions complement each other. Researchers at CDIPD readily assisted Christian and Gerty with screening these fractions, in search for their antiparasitic activity. This opportunity of sourcing Ghanaian plants and performing various screens allowed Conor, Christian, Gerty and other researchers to achieve interesting results. Conor appreciated that this knowledge and skills exchange would not have been possible without the WIPO Re:Search sabbatical. "They have particular plants and terrestrial plants that are pretty unique to this area of the world and that should be rigorously explored to understand their medical potential," the researcher stated.

Conor is well aware that scientists in low- and middle-income countries frequently do not have access to state-of-the-art lab equipment. "Sometimes there is a focus on learning a new technology or technique, but when you go back home, you do not have access to those technologies, so the benefits are limited," he emphasised, "in essence, you have knowledge translation but without the follow-on implementation." At the CDIPD, the fellowship programs "are specifically designed to allow for translation such that the equipment, the methods, and the design of experiments are robust yet simple to perform anywhere," Conor specified. "We expose our research visitors to the technologies that we have, but at the same time, there are other ways of doing the work that are just as relevant," he continued. To illustrate how this is done in practice, he



Conor and his team in the lab with Tom Bombelles of WIPO.

described Gerty's training, "She developed the skills in culturing a variety of relevant organisms using simple media and in relatively unconstrained environments." Conor affirmed that, "it is quite possible to do excellent science in the absence of high tech." Striking a middle ground was the imperative and this is also why among the different parasitic organisms that Gerty worked with, many (such as C. elegans and Giardia) are

relevant in the Ghanaian context and have low maintenance costs.

Conor hopes that the research sabbaticals with Christian and Gerty will lead to establishing a more permanent collaboration. “The hard work is to maintain the interaction in the absence of specific funding,” he remarked. Because the degree courses at KNUST are well established, they are therefore “attractive in terms of providing long term and fruitful interactions with CDIPD, especially if the talent is as good as we experienced with Gerty.” Conor added that reciprocal student exchanges between the two universities would be a positive development. “It just requires a return flight and some allowances for living – a few thousand dollars a year,” he stated. “The benefits are clear: we host motivated scientists with skills in natural products, and the home institution (and country) gains a cadre of scientists with research skills to foster further learning and development,” Conor explained

Meanwhile, Conor hopes to visit KNUST in Ghana and explore the possibility of furthering collaboration. “WIPO Re:Search provided for the initial funding – now what we need to establish requires face-to-face contact with the senior faculty there,” he said. Moreover, he believes that going to Ghana could also benefit him in terms of getting a sense of epidemiology, the diseases, and geographical relevance. Similarly, he would like to observe the ongoing work and progress in regards to clinical trials.

DR. DOMINIC EHRISMANN, NOVARTIS, SWITZERLAND

Dr. Dominic Ehrismann, Executive Assistant Scientific Coordination, Novartis Institutes for BioMedical Research, Basel, Switzerland was Fidelis and Wellington’s supervisor during their sabbaticals.

Dominic firmly believes that a shared passion for making medicines for patients was an important factor for the successful collaborations with Fidelis and Wellington. Indeed, Novartis’ interest and expertise in NTDs is not new – the company has a dedicated research institute in Singapore which does drug discovery to combat these diseases. While Fidelis and Wellington were able to learn about Novartis’ strategy to work with science-based innovation to treat patients with unmet medical needs, their colleagues in Basel gained first-hand experiences from the two fellows. “We are getting people that are experts in NTDs here and we get them from the frontline where the patients are. This is very helpful as our labs are not embedded in areas where NTDs are,” Dominic explained. “It was very interesting for us to learn what methodologies would work best to fight NTDs in least developed countries,” Dominic elaborated. “We are very curious,

Fidelis, Wellington and Dominic with Petra Kyle of Novartis.

we tend to learn almost more than they do while they are here. It is really rewarding from that perspective,” Dominic said with a smile.

Dominic observed that the lessons from these sabbaticals also helped the researchers at Novartis answer how the company can “accelerate drug discovery and development programmes that are aimed at tropical diseases, and what is actually needed to bring them to the patients in sometimes very remote regions of the world.”

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For Novartis, the benefits of working with skilled researchers from Africa and other regions go even further. Through such sabbaticals, the company is able to build relationships with professors and key opinion leaders from Africa’s top universities. This approach is in line with Novartis’ diversity and inclusion strategy. Moreover, Dominic added, “We have the Novartis Next Generation Scientist Program where we invite researchers from these countries to come and spend three months with us.” Looking forward, Novartis puts efforts to make sure that these initial exchanges lead to receiving other students from the institutions that are already engaged.

When asked how Novartis ensured that Fidelis and Wellington could make the most out of their experiences back home, Dominic stressed, “we combine simple techniques with our state-of-the-art facilities,” he elaborated, “their knowledge was quite complementary to what we have here, also the technology – you do not always need high-tech to fight a disease or to do good research.” He went on to explain that it was not only a matter of costly acquisition of such equipment,

but “even more importantly, the maintenance is difficult - you can ship equipment but it will be completely non-functional if it is not maintained properly.” Dominic continued by saying, “what we need to do is to combine the strengths of both institutions.”

For example, in the case of Wellington, “what we have done is a follow-up collaboration. What we saw in South-East Asia is that you have growing resistance to malaria drugs and this is a big issue. So what we wanted to know was what resistance looks like in Nigeria,” he observed. This is when Novartis, jointly with Wellington, engaged in the dried blood spot analysis project. “We bring all our capabilities into the game and we can sequence for the resistance gene in malaria,” Dominic explained.

WIPO Re:Search can contribute to the understanding of how intellectual property (IP) facilitates technology transfer.

Beyond this initiative, the collaboration initiated by WIPO Re:Search has generated other follow-up activities. One of them, mentioned by Dominic, was Wellington’s engagement with Novartis in the SMS for Life initiative in Nigeria. Wellington played a crucial role there in making the connections with the key actors in government. In addition, Dominic said that he was also “helpful in supporting our clinical studies for our antimalarial programs that are in Phase II clinical development.”

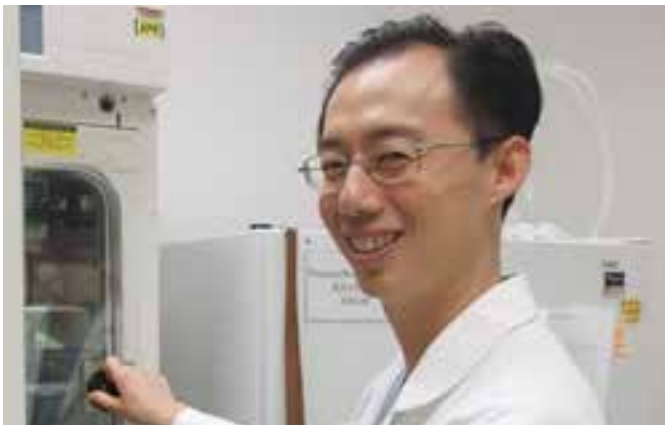
As for Fidelis, there was an effort to isolate some natural products and assess the activity against river blindness. Unfortunately, “the initial screens were negative so there was no follow-up. But we have to see. Maybe when he has a new library we can do some screenings again,” Dominic remained positive. “He has a lot of collaborations with other pharma companies which helped him to set up a new lab,” Dominic said, “he must be a very busy man!” He then reflected that “maybe we were helpful in giving him some visibility in the river blindness community and also with other pharma companies. He is doing very well.”

Dominic trusts that programmes such as WIPO Re:Search can contribute to the understanding of how intellectual property (IP) facilitates technology transfer. “That is the purpose of WIPO Re:Search, this is why we are participating, and the sabbaticals are a testimony to these efforts,” he said. At the same time, he thinks that even more can be done to show that IP can be used to combat diseases.

DR. MICHAEL HSIEH, BIOMEDICAL RESEARCH INSTITUTE, USA (FORMERLY: STANFORD UNIVERSITY)

Dr. Michel Hsieh, currently Stirewalt Endowed Director at the Biomedical Research Institute (BRI), was Olfat’s host at the Stanford University School of Medicine in 2013.

What Michael and Olfat have in common is their expertise and dedication to researching schistosomiasis. He emphasized the urgency of addressing this problem, “It affects at least two hundred million people worldwide, of which the majority have urogenital schistosomiasis, and there is a more recent estimate that the actual prevalence may be several times that,” he continued to explain, “at least a billion people live in areas endemic for schistosomiasis.” Michael recognized that the current methods of diagnosing and treating this important infection are “unfortunately quite primitive.” Thus, he stressed that there is a pressing need for more research to try and help develop better diagnostics, therapeutics, and vaccines that can address schistosomiasis.



Dr. Michael Hsieh

Michael was working with Olfat on a daily basis and valued her work, “Olfat’s skills as a urogenital pathologist focused on the effects of schistosomiasis were a unique skill set that only a well-trained physician-scientist from an endemic area would possess.” He went on to explain, “Although my lab has expertise in mouse models of schistosomiasis, we lacked a certain amount of perspective on the human impact of the disease, and Olfat’s contributions in terms of providing that perspective were invaluable.”

One of the key lessons that Michael learned during Olfat’s sabbatical is that, “even sophisticated visitors to the United States (or any country, for that matter) need help to get settled in.” He personally took Olfat to the bank to set up accounts, drove her around to look at apartments, and had her come to his house for

Thanksgiving. “One of most humorous experiences was seeing my environmentally conscious Chinese mother show Olfat a pair of reusable, portable metal chopsticks at Thanksgiving dinner!” he said with a smile.

Michael is enthusiastic about the long-term impact of collaborations fostered through WIPO Re:Search. As an example of the ability of this program to help diffuse knowledge, he observed that “in her one year in my laboratory, Olfat co-authored four peer-reviewed articles with me in prestigious journals,” he highlighted, “all of these articles have important implications for combating urogenital schistosomiasis, one of the major neglected tropical diseases.” Such knowledge sharing is beneficial for the research community in this field and beyond.

Michael was glad to announce that he is still collaborating with Olfat. “We are putting together an NIH R01 grant submission based, in large part, on the work started during her sabbatical and made possible by WIPO Re:Search,” he affirmed.

Section 4:
Concluding Observations

The stories presented in this report highlight the important role WIPO Re:Search has in facilitating collaborations across various sectors aimed at developing products to prevent, diagnose, and treat NTDs, malaria, and tuberculosis. Through the WIPO Re:Search fellowship programme, talented researchers from low- and middle-income countries have the ability to gain new skills and knowledge at the state-of-the-art facilities of some of the world's biggest pharmaceutical companies and leading academic institutions. This process is, however, not a one-way street. As the six stories from this report show, knowledge and skills exchange are at the heart of each interaction, making these collaborations mutually beneficial. Apart from the fellows and their hosts, there is a third group that will hopefully be able to exploit the products developed in connection with the WIPO Re:Search fellowship program, namely, the patients suffering from NTDs around the world.

The spillover effects associated with the sabbaticals presented in this report are numerous:

- **Capacity building:** The opportunity to work in the state-of-the-art laboratories of developed country research centres and of companies helps scientists from low- and middle-income countries to enhance and develop skills, techniques, and knowledge. The new skills can be a strategic contribution to building quality platforms for research and for clinical trials. Moreover, the sabbaticals can support the participants in the procurement of new equipment for their labs. The IP sharing aspect of the programme permits access to proprietary assets samples for diagnostic testing, which are mainly owned by pharmaceutical companies. Additionally, many of the researchers reported that the sabbatical provided them with a facilitated access to funding opportunities. All this contributes to empowering researchers from low- and middle-income countries.

- **Knowledge & technology exchange**: The hosting institutions mainly taught skills and knowledge that were easily transferable and useful in less or under-equipped labs. During and after the sabbaticals, the visiting researchers can transfer their skills and knowledge on various levels:

    - To their students & colleagues back home;

    - To the researchers at the hosting institutions;

    - To the research community at large, for instance, through publications;

    - To the new collaborators that they established a connection with as a result of the initial sabbatical.

- **Network-building:** Both their daily work as well as the participation in various seminars, courses, conferences, and building connections helped the fellows create their professional network and establish additional collaborations. Moreover, some of the sabbaticals inspire other long-term engagements between institutions from the developed and developing world, for example, building exchange programmes for students and researchers.

- **Career & personal growth:** WIPO Re:Search helps the researchers from low- and middle-income countries gain recognition in their research community. Additionally, many of the fellows mentioned personal growth and other advantages such as the possibilities of exploring career options, opening up to new opportunities, confidence, acquiring new perspectives and ways of work.

- **Women in Science, Technology, Engineering and Mathematics (STEM) fields:** In many low- and middle-income countries, female scientists face social, cultural, and economic barriers in participation in STEM fields. By providing equal opportunities for women to partake in its fellowship programme, WIPO Re:Search supports women from such countries in realizing their potential and gaining recognition for their work.

As highlighted throughout the report, the benefits from the collaborations facilitated through WIPO Re:Search are mutual. The case studies indicate that the hosting institutions were able to:

- Gain the opportunity to work with highly qualified and talented researchers from endemic areas who possess robust expertise on prevention and treatment of NTDs;

- Increase their awareness and knowledge related to patients infected with neglected tropical diseases and areas affected by such diseases – information that can be best acquired by presence on the ground or by learning from researchers from such areas;

- Access rare natural products and organisms and learn how to utilize them in drug or diagnostic development;

- Establish links between research institutions and engage in long-term collaborations;

- Identify up-and-coming talents who may not have access to global R&D networks.

This is in no way an exhaustive list of how WIPO Re:Search contributes to the global fight against NTDs. Both the visiting researchers as well as their respective hosts perceive their experiences as tremendously valuable and as having strong, and unexpected spillover effects. As this report shows, the collaborations established through this program have proven to have long-term impacts and result in facilitating technology and knowledge transfer. Subsequently, they contribute to a broader goal of capacity building in low- and middle-income countries. Hence, the effects of WIPO Re:Search reach far beyond the originally stated goals of accelerating drug, vaccine, and diagnostics discovery for neglected tropical diseases, malaria, and tuberculosis.

WIPO Re:Search is a valuable addition to the global endeavour to reduce the impact of NTDs. In many ways, the initiative demonstrated that intellectual property is not a barrier to research for products to diagnose and treat NTDs, malaria and TB. Indeed, WIPO Re:Search Members have been embracing a collaborative framework and proven that effectively managed IP and know-how can support the goal of catalzying more R&D for NTDs, malaria, and TB.

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