“We move much quicker and better when we bring the academic and private sector together”

Marcel Tanner about 20 years of Swiss collaborations to develop anti-malarials

Photo: Danielle Powell

Today, there are many drugs against malaria on the market, which didn’t exist 20 years ago. Swiss collaborations have contributed extensively to the development of these drugs. How did it come that Switzerland plays a key role in the fight against malaria?

Marcel Tanner: A lot of innovations came out from the Northwestern part of Switzerland, which contributed to save the lives of thousands of people. The pharmaceutical industry in Basel has played an important role. In the past, basically each pharmaceutical company had a parasitology department and they were sensitive to malaria and other parasitic diseases recognising that these have a tremendous impact on the development of societies in the tropical areas.

Some of the very important early antimalarial drug developments came from Roche, partly together with the American Walter Reed Army Medical Research Institute, mefloquine (Lariam) for example. And then of course there was the Swiss Tropical Institute (now Swiss Tropical and Public Health Institute; Swiss TPH), the *“Tropeli”* maintaining collaborative links with these parasitological departments. Out of this nucleus in Basel, it has spread to collaborations in Neuchâtel, Lausanne, Geneva, Zürich and Bern as well as later Bellinzona.

With the leadership changes in Roche, research and development (R&D) on malaria and later broadly on infectious diseases was devolved. It is important to note that R&D on malaria was maintained for a long time at Roche at high profile as the chair of the Board also representing the main shareholders, the funder family, insisted that this R&D is to be maintained irrespective of shareholder considerations. With the change of leadership mentioned, Swiss TPH could take over key equipment for transmission studies and mainly brilliant minds who could find continuation of their work within Swiss TPH.

Then there was an important coincidence that Ciba did an exploration in China to find new anti-helminthic drugs. There, the Chinese also presented another interesting drug against malaria that was the lumefantrine and the artemether combination. This is how this Chinese invention that already underwent clinical trials among adults was further developed by Ciba (later to be merged into Novartis) towards what we know as Coartem®. Swiss TPH together with the Ifakara Health Institute undertook part of the clinical trials in children and Swiss TPH also assisted Novartis in preparing the files for the fast track registration at the national drug authority, Swissmedic.

It was hence shown how much quicker and better we move when we bring the academic and the private sector together: The transfer from Roche, the experience with Coartem®, as well as the mind-set of leaders in the private industry and academia, brought together the thinking that we should have something like a drugs for neglected diseases initiative. So, a strategic planning group with members from the World Health Organization (WHO), World Bank, International Federation of Pharmaceutical Manufacturers & Associations (IFPMA), Swiss Agency for Development and Cooperation (SDC), Wellcome Trust, Rockefeller Foundation, and Roche worked towards a virtual institution as public-private-partnership (PPP) for drug R&D on malaria and the neglected tropical diseases. The industry was very much behind this idea, but they wanted to see first that this PPP could develop drugs against one disease, malaria. This is how the Medicines for Malaria Venture (MMV) was created 20 years ago.

How did anti-malarial drug discovery start at Swiss TPH?

It started with the knowledge transfer from Roche. Jacques Chollet, who worked for Roche at that time, had started to develop artemisinin synthetically. For the chemistry, they collaborated with Professor Jonathan Vennerstrom of the University of Nebraska. This collaboration continued when Jacques Chollet and Huges Matile and their team moved to work at Swiss TPH. Besides, there was Reto Brun at Swiss TPH who had been very skilled in in-vitro cultivation for many years and had cultivated many parasite species successfully, and also developed assays allowing drug testing. The advantage was that Reto Brun's team could directly test potential anit-parasite molecules against live organisms. In addition, Swiss TPH had a broad collection of field isolates and hence could test besides classical laboratory strains. This was key in order to test new compounds also against resistant and low sensitive isolates.

What were the milestones of anti-malarial drug development at Swiss TPH?

Establishing the screening system with the live organisms was an important milestone. That's when we went to the leaders of pharmaceutical companies, and tested interesting substances. Later and with Reto Brun, Matthias Rottmann, Marcel Kaiser and Sergio Wittlin were involved in the discovery of new classes of compounds, one of them being KAE609, a new synthetic anti-malarial spiroindolone. It was developed together with Novartis, MMV and

the Wellcome Trust. The compound is now very promising in clinical trials and will surely be a building block of new effective antimalarials.

Today, progress achieved in the fight against malaria is overshadowed by an increasing number of new cases in some parts of the world. Challenges include funding shortfalls, emerging drug and insecticide resistance, etc. What are your main concerns?

I would not fully sign your statement. First of all, in the past 15 years, we had tremendous progress in the reduction of transmission. If you also take into account the population growth, you do not see an increase in malaria. The only problematic countries are ten in Africa and one in Asia. That's why the new global strategy of WHO and the RBM to End Malaria Partnership entails a focus on "high burden to high impact."

Where we really have a problem is resistance. The K13 mutations associated with reduced sensitivity and resistance to artemisinins have become known as a problem in the Greater Mekong Subregion with six countries involved: Thailand, Cambodia, Mynamar, Lao PDR, Vietnam, PR China. For a long time, we thought they are mainly transmitted but it shows now that these mutations pop-up independently in many different locations. You will also find these K13 mutations in Africa, but we do not yet see reduced sensitivity to artemisinins in Africa.

If we are only focusing our resistance surveillance on the Greater Mekong Subregion, we will fail. But if surveillance is done well and comprehensive with a swift public health response, I'm not too much afraid; particularly also knowing that we have drugs in the pipeline like KAF156 and the KAE609 that will come as new building blocks to prevent the emergence of resistance.

So you are more optimistic?

You have to be. You cannot work in this field if you are not optimistic but you should not be naive of course and not underestimate the dimension of a problem like resistance.

Do you see a real chance that malaria can be eliminated within our generation?

Yes, I think elimination is possible in many more areas and this will gradually lead to eradication. We have a lot of positive examples from different countries. For example, next year, we will even certify big China as malaria-free and many more countries will follow as outlined in the Global Technical Strategy (GTS) of WHO endorsed by all countries in 2015. If we keep this momentum and use the existing drugs integrated with the other tools and strategies that we have, together with good surveillance-public health response approaches, we will be able to eliminate malaria. We will also have continuous R&D that will bring new tools, not only drugs. But we don't just wait for the new tools. We use the ones we have in an integrated manner tailored to a given epidemiological setting and we add the new tools once we get them.

It is very important that we keep the spirit in a determinate way that malaria elimination is possible. But we need to bring all our strengths together. With the GTS that is well broken down to the country levels and pursuing it rigorously leads to elimination and we will achieve malaria eradication – certainly not in my life time. I see that we continue to eliminate and this gives me hope for the next generation to meet this goal of a malaria free world.

What should be the role of Switzerland and Swiss TPH in the future in the fight against malaria?

We should continue as we have been involved and even strengthen these efforts. The Swiss malaria group, where Swiss TPH is a member, brings people together, recognising that each organisation has their role and responsibility. For Swiss TPH, it is very important to keep the basic research as well as contributions to R&D, direct application and public health action. This means to maintain strong links with partner centres in disease endemic areas such as the Ifakaka Health Institute (IHI) with its clinical trial centre in Bagamoyo, Tanzania. With this partnership, we can develop a product from the very first discovery over all phases of clinical trials (phase 1-4) to public health application. The future of Swiss TPH lies - not only for malaria – in living the value chain from innovation over validation to application through excellent research, R&D contributions and public health action complemented by training and capacity building. Impact factors of journals are not the guidance here, what counts is that we are all sitting in the same boat and pursue in our roles and responsibility this value chain. What I miss sometimes in the global health community, is that many young and older people are not very enthusiastic, they just perform, although it is a pleasure and privilege to work in global public health. Of course, scientists and public health specialists are very intelligent but this is not always enough. Joy and curiosity, the joy to discover, the joy to share and the joy to translate into action - that's the spirit we must keep, then we can contribute to global health development even more effectively.

What has been driving you personally in the fight against malaria?

I have studied medical biology in Basel and I always thought I was going to be a laboratory scientist in the field of parasitology and infection biology, because I was fascinated by that. But the key moment was when I did field work for onchocerciasis (river blindness) antigen collection in Cameroon in 1979. We went to the villages in very remote and poor areas. Every day I saw the many health problems of these people. That was the switch in my life from the laboratory scientist to epidemiology and public health. Later, in Tanzania I saw that over 50% of the admissions at the hospital were due to malaria. I have not chosen malaria as just an interesting parasite; it has to do with your responsibility to address priorities. It should not be about your own scientific interest but about what the needs of the people are. It is tragic that people die, that's why you devote yourself with joy to do something against it.

About Marcel Tanner

Professor Marcel Tanner was the Director of the Swiss Tropical and Public Health Institute (Swiss TPH) from 1997 until 2015 where he emphasised the importance of combining research, education and training with their translation into public health action, thereby covering the value chain from innovation and validation to application. Until 2017, he was also Professor and chair of Epidemiology and Medical Parasitology in the faculties of science and medicine at the University of Basel and at the Federal Institute of Technology in Zurich (ETH). Since 2016, Professor Tanner has been the President of the Swiss Academy of Sciences. His research and global public health activities have ranged from basic research on the cell biology and immunology on malaria, schistosomiasis, trypanosomiasis and filariasis to epidemiological and public health research on risk assessment and health impact. For the past 40 years, his work has also highlighted urbanisation, health service utilisation

and decentralisation in health planning and resource allocation with extensive on-the-ground experience in Africa, Asia and Europe. He has been and still is an expert advisor and member of various national and international boards and agencies, including WHO/STAC-TDR, Wellcome Trust, DNDi, FIND, INCLEN-Trust and INDEPTH Network. Prof. Tanner obtained a PhD in medical biology from the University of Basel and an MPH from the University of London.

Interview: Layla Hasler

Press release

https://www.swisstph.ch/en/news/news-detail/news/two-decades-of-swiss-leadership-for-new-malaria-medicines/

Video

https://www.youtube.com/watch?v=FWCt5QCR2vM#action=share

Publication

https://malariajournal.biomedcentral.com/articles/10.1186/s12936-019-2728-8

Antimalarial drug development at Swiss TPH

https://www.swisstph.ch/en/topics/malaria/antimalarial-drug-development/