

Prof. Dr. Stephan Urban: The University Researcher

In the early 2000s, Prof. Dr. Stephan Urban achieved a major breakthrough. He identified the "key" on the surface of the hepatitis B virus that allows the pathogen to enter liver cells. This brought a drug with a new mechanism of action against hepatitis B within reach.

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However, much initiative was still required before reaching a promising clinical application. Preclinical studies needed refinement, a lead substance had to be developed and tested for toxicity, and utilization rights had to be secured since commercial development is futile without a patent. At that time, neither Heidelberg University nor the University Hospital had their own technology transfer office.

This posed challenges for Stephan Urban: "While we had our basic patent, the open question was: Who would protect the technology if we further developed it at the University Hospital Heidelberg?" Stephan Urban and his team could draw on the expertise of EMBL and EMBLEM Technology Transfer GmbH, which temporarily represented the interests of the hospital. The experts there – all experienced industry professionals – recognized the potential of the project and assisted with patent protection and licensing issues. This enabled the development of various patents, their registration for the University Hospital, and the conduct of contract negotiations with a licensee. Later, this task was taken over by Heidelberg University's technology transfer office.

The second challenge was acquiring financial resources for the development, testing, and manufacturing of the drug. "At that time, there was hardly any advisory infrastructure like there is today with BioRegio," recalls Stephan Urban. "There were many ups and downs in obtaining funding." Urban successfully applied for federal funding from the BMBF (Innovative Therapies), but less success was met with applications to local NCT (National Center for Tumor Diseases Heidelberg) calls. Occasionally, the Urban team faced stiff competition from spin-offs that had already established companies and thus had a better starting position: "There were situations where we, as purely academic researchers, did not receive funding, but spin-offs did." Crucial to their success was the establishment of the German Center for Infection Research (DZIF), where Urban received the first professorship for translational virology.

Additionally, the team benefited from the excellent scientific infrastructure on-site, as Stephan Urban reports: "Heidelberg boasts brilliant university facilities. An example is clinical pharmacology with its 'FIH (First in Human) Trial Unit,' which, thanks to its excellent equipment and analytical lab, can conduct a Phase I study. Such structures are incredibly important for clinical development." The team also closely cooperated with nuclear medicine at the Head Clinic: "This support was particularly important for us because we could conduct peptide syntheses and pharmacokinetic studies there," says Stephan Urban. "Without this cooperation, the project would not have advanced so far. We would not have been able to develop the methodology for detecting our drug Hepcludex in serum and the liver. That would have

exceeded our financial means." Another advantage was the proximity, allowing the team to control their project as needed.

Thus, Heidelberg's infrastructure provided Stephan Urban's research with an ideal environment for both preclinical and early clinical development of the hepatitis drug. Despite all the advantages, pragmatism was required here: "For many scientific tasks, Heidelberg was a good location; for other things, you have to cooperate nationally and internationally with partners who can implement them best," Urban explains.

Four Questions on Technology Transfer

Mr. Urban, what is required for a well-functioning technology transfer?

Stephan Urban: Initially, a precise analysis should be prioritized to determine which inventions are worth protecting. This is not an easy task, as even experts may not immediately see the potential of an invention. The questions are: What implementation possibilities are actually available for an invention? Does the new development fill a gap? A critical assessment by an experienced, independent expert panel is crucial. Ideally, this panel should be part of the technology transfer office. Second, good patent attorneys are very important for patent filing. They are expensive and usually not employed by the institution itself. However, the investment in renowned law firms is worthwhile. Third, researchers need to exercise some degree of restraint in publishing – at least initially. Although difficult and not in line with the "publish or perish" maxim, it is necessary to successfully protect their invention.

Why are spin-offs so important?

Stephan Urban: I think it makes sense to separate actual product development from the scientific part of research through a spin-off at a certain point. At the same time, both pillars should be close enough to coordinate their work well. Then, the employees in the spin-off can focus on VC financing, for example. Meanwhile, the core lab on-site can pursue the accompanying research work, often driven by regulatory authorities' demands. For such cooperation to benefit everyone, the associated administration should be kept as flat as possible.

Moreover, spin-offs should be licensed in a low-threshold manner, meaning that license fees and milestone payments should not be due immediately upon founding. This way, the university can earn money while the start-up remains economically viable. Heidelberg has already realized this potential in many areas. A good example is "silent partnerships," where the university waives early license fees to receive a high profit share later.

What role does the financial aspect play in technology transfer?

Stephan Urban: The financial aspect cannot be overstated. This includes simple things like patent attorneys, who are highly paid experts and usually do not work based on a collective agreement. A university must also build a good network and invest money in external expertise in many other areas. The open question is where the necessary funds should come from.

One option would be to use the returns from certain inventions for investments in infrastructure and urgently needed services. This could also speed up processes in later phases. Internationally, we are often too slow: If a large company has inquiries about licensing – for example, as part of due diligence – it should not take weeks or months to provide a binding response.

Finally, there is a glaring lack of venture capital (VC) in Germany to support the early phases of a start-up. More models similar to the High-Tech Gründerfonds (HTGF) could be considered. Many start-ups fail, but if a large fund supports about 20 young companies, a successful exit can finance the others. Sponsors and patrons could act as investors. I believe Heidelberg and its surroundings offer ideal conditions for such models, given the concentration of knowledge and patronage here.

How is cooperation between university institutions and companies?

Stephan Urban: There is much room for improvement in Germany. Renowned US universities have special departments that connect students with companies early in their education. This happens before students have a product to offer companies. In Germany, companies often do not know about new developments at universities, and vice versa. The network needs to be much closer. However, Heidelberg is already on the right track.

by Dr. Stefan Burkhardt