

BUILDING A CULTURE OF TRANSLATION

Researchers at the **COMPREHENSIVE CANCER CENTER TÜBINGEN-STUTTGART** strive to accelerate the delivery of innovative, personalized treatments to the clinic.

In 2019, German researchers published a paper demonstrating the potential of a vaccine adjuvant called XS15¹. When the new water-soluble formation was mixed with a multi-peptide vaccine and injected into a healthy volunteer, it prompted a strong immune response, raising hopes that the approach could be used to help shrink cancers.

Discoveries are made every day in the life sciences, but all too often they languish in the literature because the culture and commitment needed to translate them into clinical trials is lacking. Fortunately, the adjuvant was developed on fertile ground.

The research, led by immunologist Hans-Georg Rammensee, fell under the umbrella of the Comprehensive Cancer Center Tübingen-Stuttgart (CCC), a collaborative network of clinicians and researchers based at the University of Tübingen and University Hospital Tübingen. The goal of the centre is to propel its innovative research out of the lab and into the clinic, to improve the lives of cancer patients.

THE FAST TRACK TO CLINICAL TRIALS

Rammensee discussed his findings with clinical trials experts in the dedicated Immunotherapy Translational Unit, and less than 18 months later, two phase I clinical trials were underway.

"The way things are organised here, you immediately get to know if there's something

coming in the pipeline that is super interesting, so your mind is prepared to take that and move it forwards," says neuro-oncology specialist Ghazaleh Tabatabai, deputy spokesperson for the CCC and principal investigator for one of the trials.

Both trials focus on therapeutic cancer vaccines, which seek to prime the immune system to recognize specific tumour antigens and destroy cancer cells. The strategy holds great promise, but its limited success is partly due to a lack of effective adjuvants.

In one of the trials, for glioblastoma, the adjuvant is being paired with a multi-peptide vaccine designed by researchers at the university and produced in its GMP manufacturing facility. "The last patient was vaccinated just a few days ago," says Tabatabai.



▲ **CCC Tübingen-Stuttgart is built on a culture of collaboration, with an aim to accelerate the translation of innovative cancer research to the clinic.**

The other trial, for chronic lymphocytic leukaemia, is led by Juliane Walz, and has an individualized approach where each patient receives the adjuvant with a personalized vaccine tailored to their own immunological profile. The components for these bespoke vaccines are being chosen from an established 'warehouse' of peptides², produced at the own GMP facility at the University Hospital Tübingen and each vaccine takes three to four months to produce.

The vaccines in both trials are being given alongside standard treatment, and the studies are due to conclude in 2024. Alongside safety and tolerability, the researchers will look for signs of an immune response and assess the feasibility of using personalized cancer vaccines in a clinical setting.

PERSONALIZED TREATMENT

Researchers at the CCC also specialise in functional genomics and target discovery, as well as molecular imaging. Each area has its own translational unit, facilitating the flow of new diagnostics and therapeutics from bench to bedside. A few years ago, researchers developed a tracer for senescent cells. They talked with clinician-scientists in the CCC Imaging Translational Unit, and less than two years later, the tracer was being tested in a phase I clinical trial to visualize senescent cancer cells.

"The beauty is that we have everything in one place, on one campus, and a culture that facilitates translation," says Sara Brucker, a women's health clinician and CCC spokesperson. Since 2019, as a development of CCC's three research areas driven by Rammensee, Lars Zender and Bernd Pichler, the iFIT consortium has been funded by the German Research Foundation (DFG) as the only Cluster of Excellence for oncology in Germany. In 2022, CCC Tübingen-Stuttgart joined forces with CCC Ulm and established the National Center for Tumor Diseases (NCT) South West. NCT South West will be funded as one of only six NCTs in Germany. With the additional funding this brings to bridge the translational gap, Brucker estimates that within 10 years, the CCC could be launching up to 50 new investigator-initiated clinical trials each year.

With such an eclectic mix of research, CCC scientists and clinicians are privy to a diverse range of opportunities and training programmes that reflect the network's key strengths. There's also a dedicated mentoring programme, not to mention close links with industry and the prospect of collaborative projects. Tabatabai, for example, is working on a phase I trial with Tübingen-based company CureVac to test an RNA version of the glioblastoma multi-peptide vaccine.

At present, the CCC treats around 10,000 cancer patients every year, and although around a fifth become enrolled in clinical trials, some patients with rare or advanced cancers can find themselves without treatment or trial options. To meet this unmet need, in 2016 the Tübingen team founded the Center for Personalized

Medicine, which now operates at state level, offering personalized treatments at four university hospitals in Baden-Württemberg. Patients receive a thorough molecular profile, which is then studied by a panel of experts on the Molecular Tumour Board, who then determine any actionable molecular targets. The result is that 70% of these patients receive a molecularly guided treatment recommendation. The scheme, driven by Nisar Malek, has been so successful that it is being rolled out nationally as the German Network for Personalized Medicine³.

A DIVERSE SCIENTIFIC COMMUNITY

Recently, the CCC added another string to its bow with the M3 Research Center, led by founding director Mathias Heikenwälder. Researchers will study the role of the

metabolome and microbiome in cancer. Drawn by its close links to hospitals and the facility's rich biobank, cancer researcher Lisa Sevenich, who currently works at the Georg-Speyer-Haus in Frankfurt, hopes to relocate her team there.

"So many people leave academia to go into industry," she says. "But academia gives me the freedom to work on what I am interested in, and where I feel there is need."

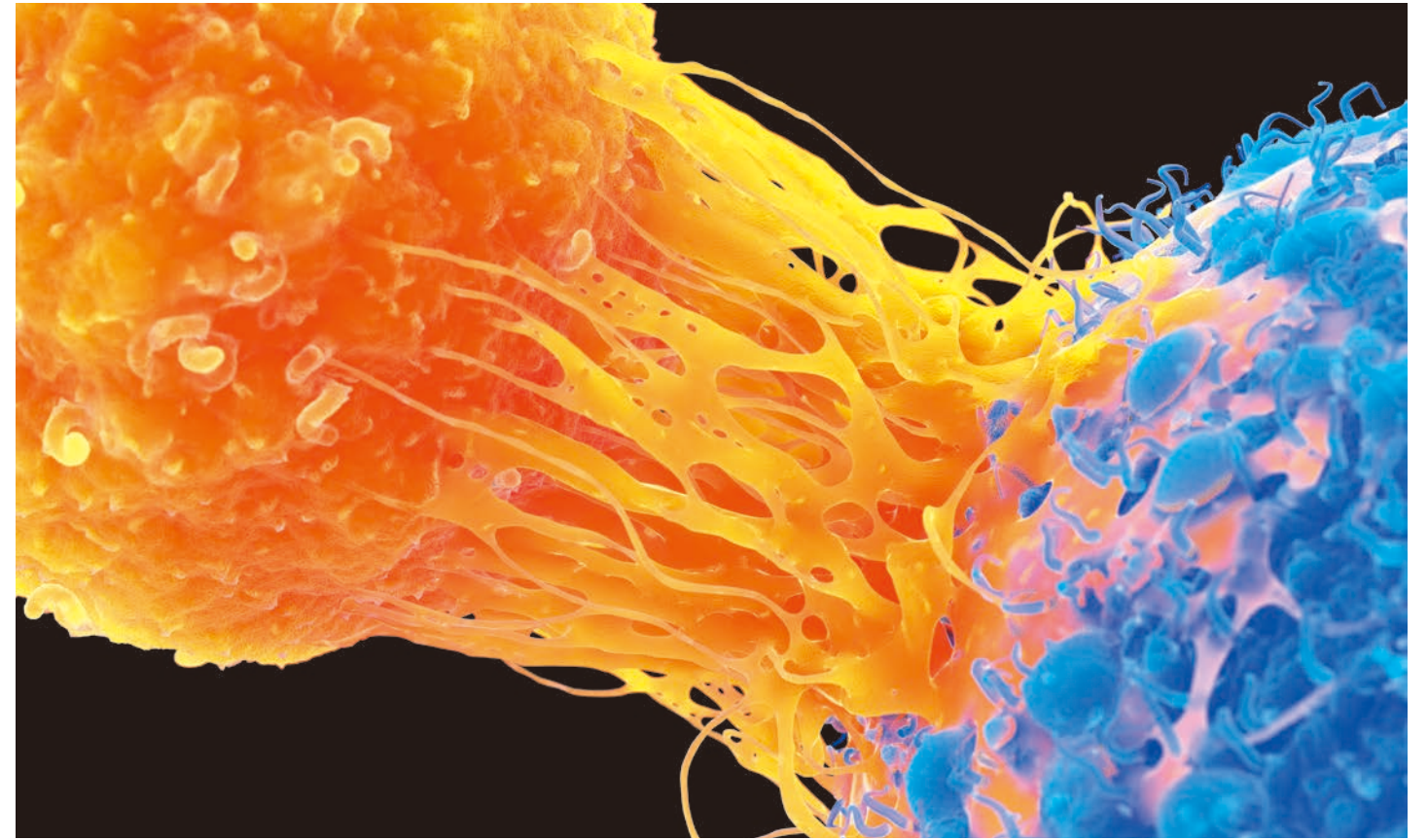
Sevenich plans to explore how the microbiome affects brain metastasis. When cancers metastasize to the brain, outcomes can be poor. Pharmaceutical companies have only recently started to fund research in this area and there are few clinical trials for metastatic brain cancer compared to primary brain cancer, she says. Sevenich hopes to change this, translating her lab-based findings into patient

studies, and then using this information to drive further research.

For her, the CCC is the perfect match for her interests. "Its scientific landscape is super rich. There are a lot of leading experts. For anyone who wants to do fast translational research, I think it's one of the few places in Germany to be," she says. "And if you like hiking and biking, it's even better." ■

REFERENCES

1. Rammensee, H.G. *et al. J. Immunother. Cancer* **7**, 307 (2019).
2. Nelde, A. *et al. Front. Immunol.* **12** <https://doi.org/10.3389/fimmu.2021.705974> (2021).
3. Illert, A.L. *et al. Nat. Med.* **29**, 1298-1301 (2023).



▲ **Therapeutic cancer vaccines seek to prime the immune system to recognize specific tumour antigens and destroy cancer cells.**