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4HF Biotec Banking on Multiomic Data Analysis to Help Pharma Find New Oncology Compounds

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CHICAGO – With its first significant commercial partnership under its belt, German bioinformatics startup 4HF Biotec has begun making inroads for its multiomic approach to cancer drug discovery.

In October, 4HF Biotec announced a partnership with drug-discovery CRO Reaction Biology as they unveiled [a cell-based bioinformatics service](#) that combines Reaction's ProLiFiler cell assay service with 4HF Biotec's Biomarker Analysis and MoA Finder informatics tools to help inform drug discovery.

Biomarker Analysis searches for mutations, gene copy numbers, and gene expression data, while MoA Finder performs *in silico* analysis of modes of action in experimental drug compounds by running a Spearman correlation to compare data from novel compounds to drug sensitivity data. The combined service, aimed at the oncology market, will be run at Reaction Biology's lab in Freiburg, Germany. 4HF also has a lab in that city.

The Biomarker Analysis tool analyzes whole-exome sequencing, gene copy numbers, and gene expression data. MoA Finder helps researchers pinpoint the mode of action of a drug candidate by comparing the compound's sensitivity profile to profiles of nearly 800 existing drugs.

At the time the partnership was announced, Reaction Biology CSO Haiching Ma said that the combination of Reaction's cell profile studies and 4HF's bioinformatics "creates a roadmap for our customers' further development."

Reaction Biology is 4HF's largest deal to date in terms of scope and size, and marks its entrance into its commercial phase, according to CTO Vincent Vuaroqueaux. The

Freiburg, Germany-based firm has several undisclosed research collaborations in academia and at European hospitals, he added.

Reaction Biology, [formerly known as ProQinase](#), specializes in extraction biology, and offers a panel of 140 cell lines on which it tests novel anticancer compounds.

Reaction Biology, which also has a US office in Malvern, Pennsylvania, generates drug sensitivity data, which 4HF then connects to transcriptomic, mutation, and chromosome alteration profiles of each cell line. Algorithms developed by 4HF analyze these profiles for association with drug sensitivity in search of predictive biomarkers.

The primary target market for 4HF is early-stage biotech development, particularly smaller companies looking to sell their discoveries to bigger pharma firms when they reach clinical phases, Vuaroqueaux said.

4HF also is looking to develop predictive modeling for gene signatures using artificial intelligence to inform pharma and biotech researchers in the preclinical stage of drug development and improve the success rate of new compounds that do actually make it to clinical trials, according to Vuaroqueaux.

"With artificial intelligence, Google and others now are starting to develop really efficient tools to predict how aggressive is a cancer," he said. "It's a start, but I think we can do much more than that, and it should be with the information that we have today."

The company was founded by medical oncologist Heinz-Herbert Fiebig, who serves as CEO. Fiebig also founded preclinical CRO Oncotest in 1992 and sold it to Charles River Laboratories in 2015. That company, which is not related to Teva Pharmaceuticals subsidiary Oncotest-Teva, was among the pioneers in testing anticancer compounds on large tumor panels and in development of patient-derived xenografts.

After he sold Oncotest, Fiebig started 4HF Biotec to continue his work in cancer drug discovery. Vuaroqueaux led biomarker development and bioinformatics for Oncotest, and stayed on with Charles River until Fiebig brought him over to 4HF at the beginning of 2017.

4HF is a preclinical company that provides CRO services in drug development and drug discovery. In discovery, the company is looking mostly at antibody drug conjugates and small-molecule drug conjugates in hopes of reducing side effects from chemotherapy, according to Vuaroqueaux. He said that the company serves as a bridge between molecular data from tumors and knowledge about existing drugs.

"Our idea was to use big data and raw knowledge in cancer biology and precision therapies to try to identify new targets and new genomes to screen all the molecular [and] cancer information we have acquired ... to find new ways to treat cancer," Vuaroqueaux said. "Our work in this field is to identify novel targets."

The company's current projects include a study of binding properties of selected antibodies on small tumor molecules and an *in vitro-in vivo* pharmacology test, Vuaroqueaux said. 4HF plans to license new targets based on its findings.

4HF Biotec has just six full-time employees, who specialize in medical oncology, tumor biology, and bioinformatics. The company also relies on consultants across Germany and beyond for programming, chemistry, and legal issues including intellectual property rights. 4HF Biotec has built its own database pulled from publicly available datasets, as well as informatics algorithms to tease out detailed molecular characteristics of tumors and make the information easy to use for molecular biologists.

"We believe that this data and this database are really a unique source to identify novel targets and novel anticancer agents," Vuaroqueaux said.

Vuaroqueaux talked of the usual challenges facing bioinformaticians, including the large size of omics files and the decentralized nature of relevant data. "Our core business today is to collect data from external sources, to integrate them, to curate them, process, organize, and connect, to have everything ready for analysis," he said.

Sources include the Cancer Genome Atlas, the Genotype-Tissue Expression (GTEx) project, and various European Molecular Biology Laboratory (EMBL) databases, as well as sequencing done at the 4HF lab and by the company's partners.

The company has exomic, chromosomal aberration, and transcriptomics data on about 10,000 tumors and more than 22,000 normal tissues for comparison, plus cell-line and patient-derived xenograft on 1,800 tumor models. A drug sensitivity database of about 800 compounds includes tests on 200 drugs that are proprietary to 4HF.

"The general idea of that is that this data should be usable without the need of bioinformatics. It should be directly usable by the clinician or by the biologist," Vuaroqueaux said.

Vuaroqueaux said that 4HF is looking to add more analytics capabilities, including pathway analysis, in the future.

He added that the firm is interested in additional collaboration and partnerships, particularly in the area of drug development. "It's out of the question that we can do that on our own. You need experts in chemistry. You need experts in drug development," Vuaroqueaux said.

To date, Fiebig has funded the company out of his own pocket. Vuaroqueaux said that 4HF Biotec is now searching for grants to assist on academic or government R&D projects. He said that the firm is perhaps two or three years away from the seeking outside investors.