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## Hot from the press!

## Life sciences at FHNW Muttenz An Innovative Network of Strong Partners

*Abstract:* The School of Life Sciences at the University of Applied Sciences and Arts Northwestern Switzerland FHNW in Muttenz excels in molecular technology, bioanalytics and *in vitro* diagnostics – three very active areas of current biotech research. Cooperation with industry partners enables knowledge to be transferred to the education process and gives companies access to qualified individuals and markets.

**Keywords:** Calprotectin test · Cyclosporine and tacrolimus in blood · GHB in blood · Therapeutic monitoring device · Triterpenoids

### The Test for GHB in a Drink

GHB (gamma-hydroxybutyrate) has made a name for itself in the rave scene under the name of liquid ecstasy, but it has also gained notoriety for its use as knock-out drops. Criminals exploit the anaesthetic effect to sexually assault and rob their victims. A combination of GHB and alcohol can potentiate the psychoactive effects and lead to respiratory standstill. Unfortunately, GHB can only be identified in blood or urine for about 12 hours after it has been taken.

The research group working with Prof. ***Daniel Gygax*** therefore developed an enzymatic assay for rapid detection of GHB in blood and urine in a project managed by BÜHLMANN Laboratories Ltd in Schönenbuch. The research consortium protected its *in vitro* diagnostic test system with a patent, and industrial partner BÜHLMANN Laboratories Ltd brought it onto the market. Yet it would be even more efficient to have a test – based on the same enzyme reaction – to identify GHB and GBL in drinks. "GBL – gamma-butyrolactone – is a conventional industrial product, a precursor of GHB and currently a popular party drug. At the moment it can still be obtained legally on the internet in 5-litre canisters," explains Dr. ***Michel-Angelo Sciotti***. The task facing the team was therefore to convert the clinical liquid-phase GHB assay into a user-friendly solid-phase GBL and GHB assay. The test uses the activity and specificity of a bacterial enzyme known as GHB-dehydrogenase.

Several modifications were necessary to convert the test into a new format. "We had to couple the determination reaction with a colour-generating enzymatic reaction involving diaphorase," says Sciotti, R&D Innovation Senior Scientist and Project Manager. "It was also necessary to design a suitable paper substrate and buffers and reagents in order to limit matrix interference. This interference is due to the ethanol and vitamin C that occur in samples. It had to be reduced to make the system suitable for use in tests for GHB and GBL in drinks." A functional, flexible and low-cost prototype is now available and needs to be refined to keep the manufacturing costs below 10 cents per unit. Michel-Angelo Sciotti is looking for a commercial partner to assist with this step, because he is convinced that "there is enormous potential in tests that enable people to check foodstuffs themselves, for example to identify methanol in alcohol during trips abroad."

### Rapid Tests on the Rise

BÜHLMANN Laboratories Ltd in Schönenbuch, whose innovative test methods regularly set new standards, is also involved in point-of-care (PoC) tests. One example is the Quantum Blue® Calprotectin rapid quantitative calprotectin test, the only one of its kind in the world, for the management of IBD patients. Large quantities of the protein calprotectin occur in the neutrophils (inflammatory cells) of people with inflammatory disorders. The neutrophils travel to the site of the inflammation, where they secrete calprotectin into the surrounding tissue. This fact helps doctors to differentiate between irritable bowel syndrome (IBS, negative for calprotectin) and inflammatory disorders (IBD, irritable bowel disease, positive for calprotectin) such as Crohn's disease and ulcerative colitis when examining the patient's stools. Millions of people worldwide suffer from these symptoms, and there is certainly a need for a rapid and efficient test that avoids the need for unnecessary diagnostic endoscopic procedures and colonoscopies. Moreover, the treatment of patients who test positive for IBD can be monitored by regularly measuring the level of calprotectin in their stools. The Quantum Blue® Calprotectin Assay is based on a simple, established lateral flow technology which, with the aid of a user-friendly reading device, produces quantitative results for calprotectin within 12–15 minutes, a speed comparable to the ELISA reference test.

Today BÜHLMANN Laboratories is the leading 'calprotectin company', supplying the widest range of calprotectin assays for fully automated laboratory applications and a unique rapid quantitative test called 'Quantum Blue®'. Photo BÜHLMANN Laboratories

### High-tech for New Applications

But the researchers at BÜHLMANN Laboratories Ltd wanted to take the process one step further, even closer to the patient. "What prompted this move was the decision by the Technology and Innovation Commission (KTI) in September 2011 to make CHF 100 million available to industry to promote innovations as a one-off measure in response to the strength of the Swiss franc," recalls Dr. ***Thomas Jermann***, Vice President Science & Technology. The company collaborated with the FHNW in

Muttenz and forteq Ltd. in Nidau, a specialist in highly complex precision polymer components, to develop the CALEX® device. "It's an extremely sophisticated 'plastic tube' filled with a buffer solution," explains Dr. ***Jakob Weber***, Corporate Scientific Officer. "It helps prospective patients take a small amount of stool rapidly and hygienically. The same tube is then used to homogenize the sample and apply an accurately metered drop of the resulting mixture to a calprotectin test cassette. The treated test cassette is managed using an app and measured using a smartphone camera. In just a few seconds, the result appears on the screen in the form of a traffic light (normal, moderate, high). It is then sent by internet to the requesting doctor, who saves it in a web-based patient dossier. This IB*Doc*™ system generated a lot of interest among healthcare professionals at the ECCO (European Crohn's and Colitis Organisation) fair in Copenhagen in February 2014 and is scheduled for what is expected to be a very successful commercial launch in the middle of this year.

IB*Doc*™ is a user-friendly tool that allows patients to perform a calprotectin stool test in the comfort of their own homes. It is scheduled for market launch by the end of 2014. Photo BÜHLMANN Laboratories

## The Future is in Point-of-Care

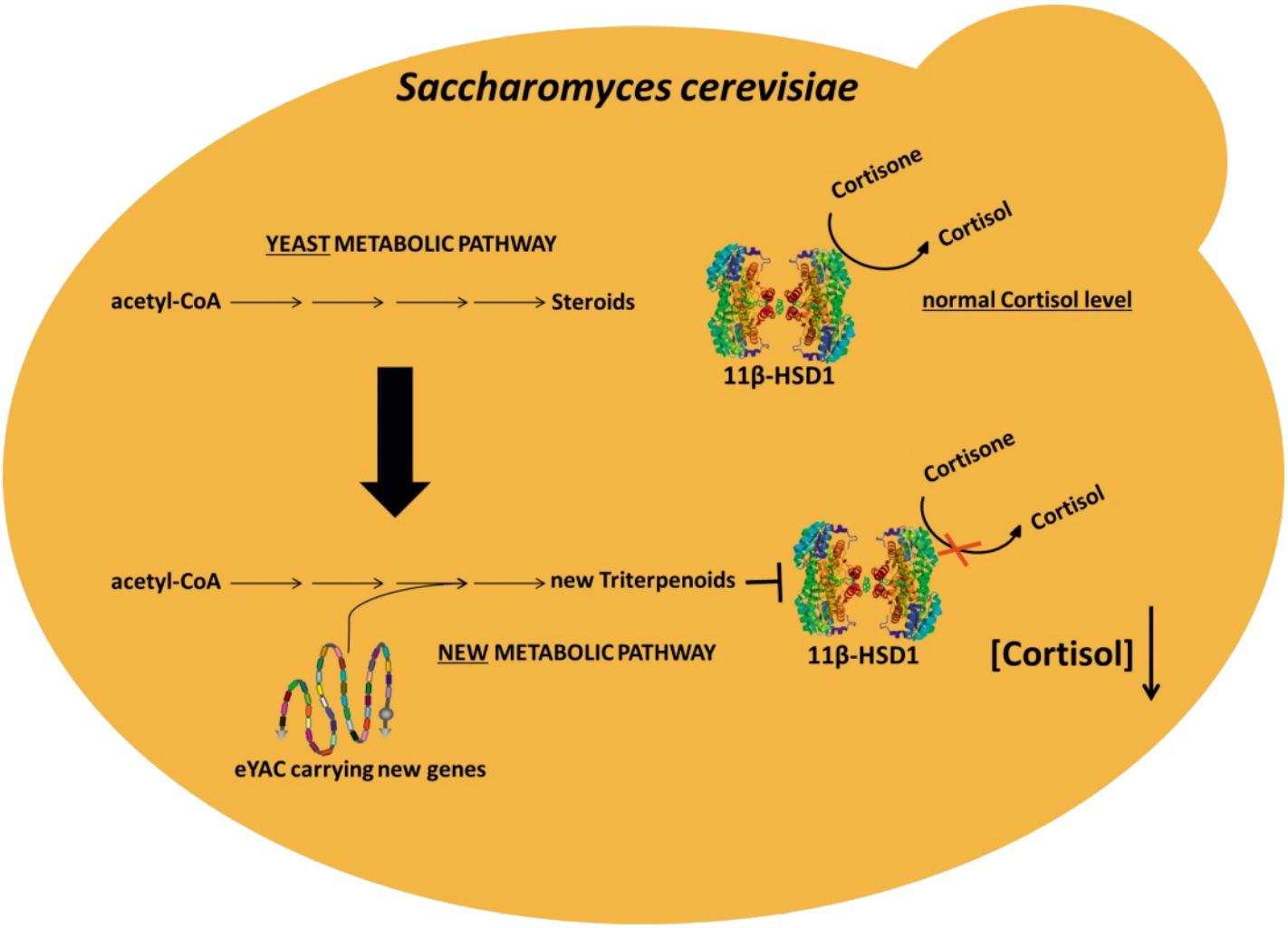
Point-of-care is also the focus of a project initiated by Prof. ***Daniel Gygax*** with funding from the FHNW as a 'strategic project of the University Board of the FHNW'. He assembled a team of skilled partners, comprising bioanalysts, pharmacologists and laboratory clinicians, engineers, medical informatics specialists, psychologists and industrial designers from universities of applied sciences and Basel University Hospital, to help him implement a smart, integrated PoC system. These specialists together create an innovative, interdisciplinary basis for developing biochemical sensor technology, data processing, design and clinical trials. The platform is being put to the test with the development of a prototype of an integrated *therapeutic drug monitoring device (TDMD)* intended to measure concentrations of the immunosuppressant drugs cyclosporine and tacrolimus in blood. These drugs are used after an organ transplant to prevent the recipient's body from rejecting the new organ. They have a narrow therapeutic window, which means that slight deviations in the level of these drugs in the patient's body can either promote rejection of the transplanted organ or suppress the immune system too powerfully and at the same time damage the kidneys. Blood levels of these drugs need to be measured regularly in order to avoid these effects because not everyone absorbs the drugs to the same extent.

"The projected TDMD will make life easier for transplant patients. They will no longer have to spend an entire day at hospital just to have their drug levels checked; they will be able to do it from the comfort of their own home," explains ***Cédric Wernli***, a doctoral candidate in the biochemistry group headed by Prof. Daniel Gygax, who is also overseeing his thesis. Wernli received his Master of Sciences in Pharmacy from the University of Basel, qualified as a federally certified pharmacist in October 2013, and is now working on his thesis under the academic supervision of Prof. ***Stephan Krähenbühl***, Head of the Department of Clinical Pharmacology and Toxicology at Basel University Hospital.

## Clever Yeast

PhD student ***Rosario Vanella*** is also making use of the opportunity at the FHNW in Muttenz to follow his Master's at the FHNW with a doctorate under supervisor ***Michael Hall***, a professor at the University of Basel's *Biozentrum*. The subject of his thesis is a KTI project headed by Prof. ***Eric Kübler***, a lecturer in molecular biology, with industry partner Evolva Ltd in Reinach. Evolva is using artificial chromosomes developed in-house – what are known as expressible Yeast Artificial Chromosomes (eYAC) – to express a large number of foreign genes simultaneously in yeast cells. This makes it possible to


Development of a *therapeutic drug monitoring device (TDMD)* to measure the concentration of the immunosuppressant drugs cyclosporine and tacrolimus in blood. The picture shows a lateral flow test strip. The red solution contains gold nanoparticles that produce the stripes to visualize antibody binding. Photo Cédric Wernli




Production system inside a yeast cell to synthesize novel triterpenoids capable of inhibiting the activity of the enzyme 11beta-HSD1. Photo FHNW Rosario Vanella

introduce entire metabolic pathways into the cell and produce new bioactive substances that do not exist naturally. These substances can be used as lead structures for new medicines. "The aim of our project is to use the eYACs to make the yeast produce new specific inhibitors of 11beta-HSD1 which can be developed into innovative products," Rosario Vanella explains. Studies in animals and humans have demonstrated a connection between overexpression of 11beta-HSD1 and obesity and impaired glucose and lipid metabolism. "We are therefore assuming that selective inhibition of 11beta-HSD1 will be of interest in the treatment of diabetes and metabolic syndrome, the key risk factor in coronary heart disease." The researchers' attention is focused on the triterpenoids, a group of secondary plant metabolites thought to have anti-inflammatory, antiviral, anti-HIV, liver-protective and cardioprotective properties.

## Combining Expertise

Nowadays, innovation for dynamic biotech companies can only be realized if the research community works as one across disciplines. This is what the NTN Swiss Biotech offers. It comprises the *biotechnet Switzerland*, an affiliation of biotech scientists at Swiss universities of applied sciences and research organizations, and the Swiss Biotech Association, the body representing high-calibre industrial companies that are setting new standards in the field – in keeping with the motto "Have a look at what we offer – because we help you biotech!"

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**Further information:**
*http://www.fhnw.ch/lifesciences/icb/*
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