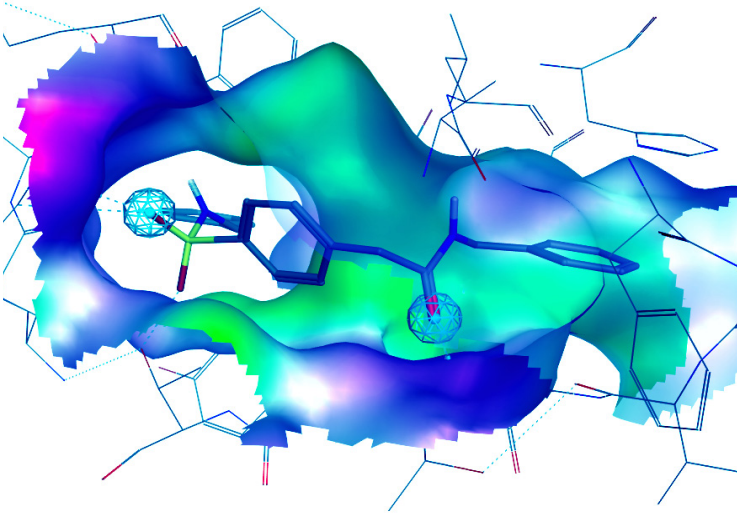
Zurich University
of Applied Sciences

Life Sciences and
Facility Management



Natural Products Drug Discovery

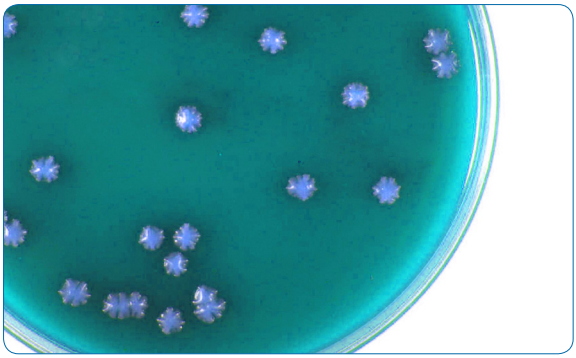
A Project from the Institute of Chemistry and Chemical Biology and the Institute of Biotechnology

Campus Grüental, Wädenswil, Switzerland
www.icbc.zhaw.ch / www.ibt.zhaw.ch

Zurich Universities of Applied Sciences and Arts

Objective

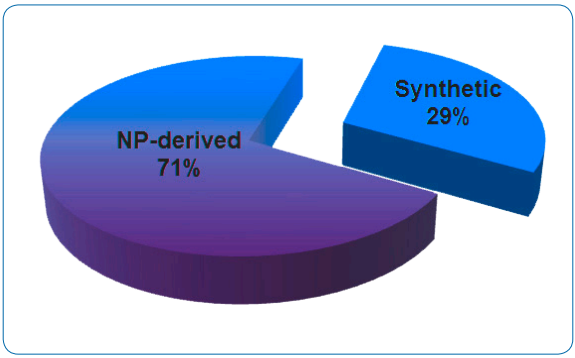
The aim of this project is drug discovery. A robust bioassay platform has been developed, which guides the isolation of small molecules from the Culture Collection of Switzerland (CCOS) library of *Actinobacteria*, aquatic cyanobacteria and environmental isolates.



Streptomyces sp. CCOS 631

Significance

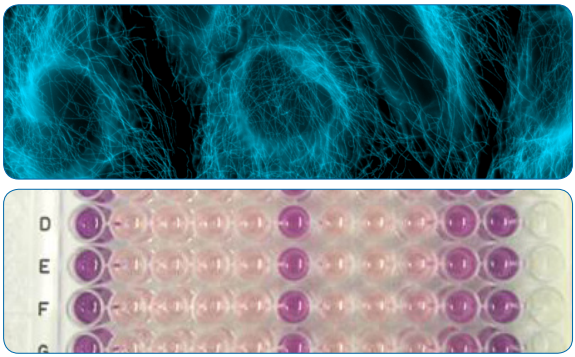
Small molecules derived from plants, bacteria and fungi are critically important to human health and agriculture. In fact, these 'privileged' natural products continue to provide the molecules, scaffolds and synthetic design inspiration for > 70 % of all drugs approved by the FDA over the past three decades (reference 1).



However, increasing occurrence of cancer and MDR-disease requires that we continue to search the biosphere for new and more effective drugs.

Screening Platform

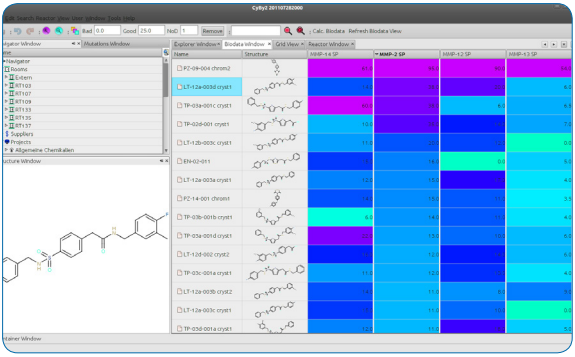
Our platform employs the MTT bioassay to determine efficacy against a variety of tumor cell lines. Our anticancer bioassay panel includes, breast (MCF-7), prostate (DU-145) and hepatocellular (HEP-G2) carcinomas, colon adenocarcinoma (HT-29). In addition we are developing assays against MRSA, Multi Drug Resistance (MDR)-*Pseudomonas* sp. and many others.



Breast cancer cell line MCF-7 and MTT assay

Medicinal Chemistry

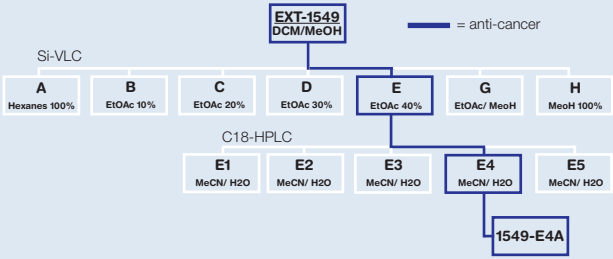
Semi-synthetic structural modifications of the natural products provide important structure activity relationship (SAR) data. These data enable subsequent computer aided ligand optimization and analog synthesis. Our CyBy^2 data management tool allows for data handling and visualization of chemical and biological data (reference 2).

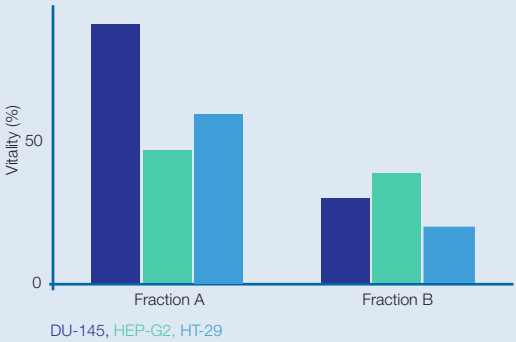


CyBy^2 data management

Bioassay-guided isolation

Organic fractions from CCOS strains are being evaluated for bio-activity in an iterative isolation / bioassay scheme. HPLC purification leads to active molecules with potent anticancer activity.

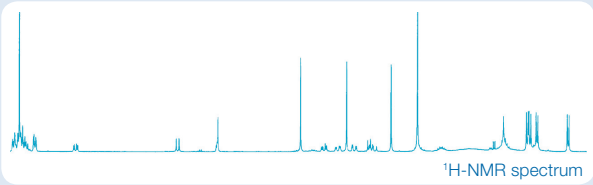




Cancer-cell growth inhibition concentrations are determined for active fractions and pure compounds.

Structure elucidation

The absolute chemical structures of new molecules are assigned by extensive spectroscopic and chemical analysis. A variety of techno-logies are employed, including multi-dimensional NMR, MS/MS, FT-IR, CD, and X-ray diffraction (reference 3).



CCOS

The Culture Collection of Switzerland (www.ccos.ch) currently maintains a library of > 1000 bacterial and yeast strains. This collection includes many novel, clinical MDR-isolates and environmental *Actinobacteria* (reference 4). The CCOS in addition has close working links with the depositors.

References:

1. D. J. Newman, G. M. Cragg *J. Nat. Prod.* **2012**, *75*, 311-35.

2. S. Höck, R. Riedl *Chimia* **2012**, *66*, 132-134.

3. T. L. Simmons, L. M. Nogle, J. Media, F. A. Valeriote, S. L. Mooberry, W. H. Gerwick *J. Nat. Prod.* **2009**, *72*, 1011-1016.

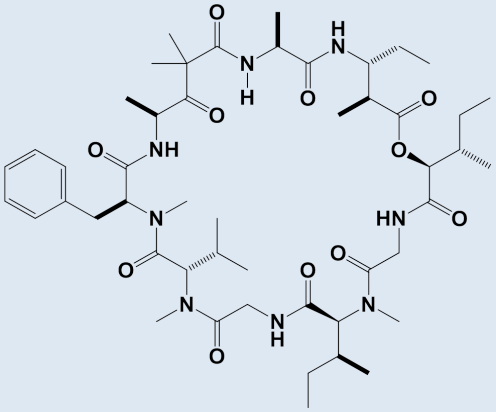
4. M. Sievers, G. Dasen, T. Wermelinger, S. Landert, D. Frasson *Chimia* **2010**, *64*, 782-783.

Partnerships

We offer a multitude of possible R & D collaborations. Long term CTI funded research projects are possible as well as mid-term contract research projects.

For additional information regarding exciting opportunities for collaboration please contact us.

We are looking forward working with you.



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Information

Institute of Biotechnology

Our aim is to apply biological systems to the analysis and manufacture of value-added products. The focus is on applications in the areas of pharma, food and ecology.

Contact

Zurich University of Applied Sciences
School of Life Sciences and Facility Management

Prof. Dr. Martin Sievers
Institute of Biotechnology
Head of Micro– and Molecular Biology
Chairman of Culture Collection of Switzerland AG
martin.sievers@zhaw.ch
+41 (0)58 934 57 16

www.ibt.zhaw.ch

Contact

Institute of Chemistry and Chemical Biology

The Center for Organic Chemistry and Medicinal Chemistry is focused on organic synthesis, medicinal chemistry, computer aided drug design and natural products drug discovery.

Contact

Zurich University of Applied Sciences
School of Life Sciences and Facility Management

Prof. Dr. Rainer Riedl
Institute of Chemistry and Biological Chemistry
Head of Organic and Medicinal Chemistry
Project Leader
rainer.riedl@zhaw.ch
+41 (0)58 934 56 18

www.icbc.zhaw.ch