Microscopy Imaging Center (MIC)

Prof. Britta Engelhardt
Chair, MIC-Board
Representative of the Medical Faculty

Prof. Sabine Kässmeyer
MIC-Board
Representative of the Vetsuisse Faculty

Prof. Michael Raissig
MIC-Board
Representative of the Faculty of Science.

Prof. Ruth Lyck
MIC-Board
MIC coordinator

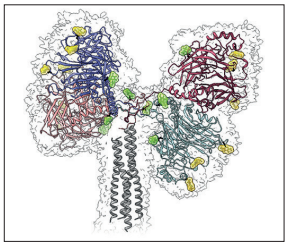
Dr. Yury Belyaev
Scientific Advisor
Light Microscopy

The Microscopy Imaging Center MIC disseminates expert knowledge and provides technical support in high-end microscopy. It implements new technologies, administers the MIC instrument portfolio, and ensures central access to equipment. It teaches at Master's and PhD levels and offers training for scientific staff at all levels.

Highlight Medical Faculty

Using cryo-electron microscopy (cryo-EM) and single-particle 3D reconstruction, Dimitrios Fotiadis and colleagues revealed the structure and organization of the tetrameric H-protein ectodomain of the canine distemper virus (CDV), which is a key component of the morbilliviral cell entry system. This cryo-EM structure lays the ground for developing novel antiviral drugs by structure-based drug design.

Kalbermatter et al., Proc Natl Acad Sci U S A, 2023.

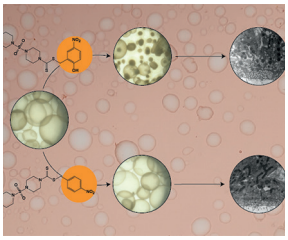


Cryo-EM unveils the structure and supramolecular organization of the CDV attachment glycoprotein

Highlight Vetsuisse Faculty

At the Institute of Parasitology, Marc Kaethner, Andrew Hemphill, Britta Lundström-Stadelmann and colleagues have analyzed structure-activity relationships (SAR) of dithiocarbamate derivatives against *Echinococcus multilocularis* metacestode vesicles. Light microscopy, transmission electron microscopy and *in vitro* assays showed a S-2-hydroxy-5-nitro benzyl residue to be crucial for anti-parasitic activity and structurally altered mitochondria.

Kaethner et al., Trop Med Infect Dis., 2023.

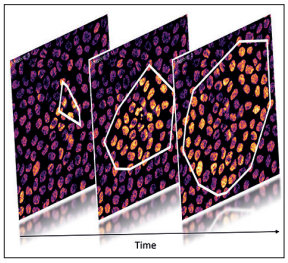


SAR of dithiocarbamate derivatives on *E. multilocularis* metacestodes vesicles

Highlight Science Faculty

Paolo Gagliardi, Maciej Dobrzynski, Olivier Pertz and colleagues from the Institute of Cell Biology developed a computational method called ARCOS to describe mitogenic signaling patterns that propagate differently between cells with different oncogenic mutations, from isolated „fireworks" to large, migratory waves of activity. Using ARCOS, they have determined how cells communicate in epithelial tissue and how signaling propagates in 3D organoids. R and Python packages as well as a Napari plugin for graphical interaction with ARCOS round off this research in the field of bioimage analysis.

Gagliardi et al. J Cell Biol., 2023.

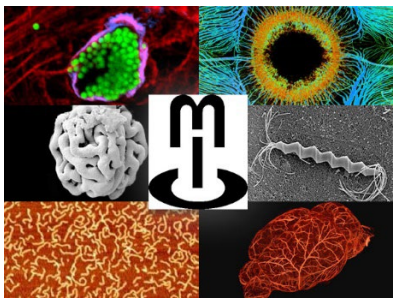


Collective Signalling in epithelial cells.

MIC Symposium 2023

On November 17, 2023, the traditional MIC Symposium took place under the motto „New Trends in Microscopy". The excellent selection of speakers attracted over 200 participants. The topics „Mesoscale Imaging", „Spatial Omics" and „Super Resolution and Expansion Microscopy" were discussed in three sessions. The lecture by Nobel Prize winner Stefan Hell and all the other inspiring speeches made the MIC Symposium 2023 a particularly impressive event.

Microscopy Imaging Center



The Microscopy Imaging Center MIC disseminates expert knowledge and provides technical support in high-end microscopy. It implements new technologies, administers the MIC instrument portfolio, and ensures central access to equipment. It teaches at Master's and PhD levels and offers training for scientific staff at all levels.

To the MIC website

Profile

- Instruments, users and usage hours: 84 instruments are registered at the MIC. In 2023, this equipment was used by 468 researchers in a total of 97,200 usage hours.
- Instrument types: 34 standard wide-field microscopes, 3 stereo microscopes, 3 slide scanners, 14 laser scanning microscopes, 5 two-photon microscopes, 6 spinning disc microscopes, 4 stereo microscopes, 5 transmission electron microscopes, 5 scanning electron microscopes, 2 light sheet microscopes, 2 atomic force microscopy systems, 1 mass cytometer, 1 imaging mass cytometer and 3 micro-computed tomography (micro-CT) instruments.
- Services: web-based booking system for microscopes (openiris.io); imaging and image and data analysis; handling of large data sets; sample preparation; training; publication of news, courses, events, and other activities on the MIC webpage (www.mic.unibe.ch)
- Teaching and events: Lecture series on advanced microscopy. MIC workshops, MIC trainings, instrument demonstrations, MIC Research Day, MIC Symposium.
- PhD program Cutting Edge Microscopy (CEM). The main aim of the CEM program is to provide an interdisciplinary training program for PhD students to become first-class experts in biological imaging. The unique and interdisciplinary framework established by the MIC provides the necessary infrastructure and expert knowledge. The program is scientifically directed by MIC members Benoît Zuber and Steven Proulx and administered by the MIC coordinator Ruth Lyck. An annual average of 20 students are enrolled in this PhD specialization program. In 2023, 6 students received their degree certificate, and 7 were newly enrolled.
- Close collaboration with the Data Science Laboratory (DSL) of the University of Bern. In 2023, Guillaume Witz, the former bioimage analyst of the MIC, moved to DSL. DSL

now offers free services to MIC users based on a service-level agreement with the MIC.
- Excellent cooperation with the Graduate School for Cellular and Biomedical Sciences (GCB) and individual master's programs to optimize the MIC teaching portfolio.

External Partners

Swiss Society for Optics and Microscopy (SSOM); Life Sciences Switzerland (LS2), Intersection Microscopy; Scientific Volume Imaging b.v. (SVI); Swiss Microscopy and Imaging Core Facility Network

Highlight Medical Faculty

Structure and supramolecular organization of the canine distemper virus attachment glycoprotein

David Kalbermatter[1], Jean-Marc Jeckelmann[1], Marianne Wyss[2], Neeta Shrestha[2], Dimanthi Pliatsika[3], Rainer Riedl[3], Thomas Lemmin[1], Philippe Plattet[2], Dimitrios Fotiadis[1]

Affiliations expand
PMID: 36716368 PMCID: PMC9963377 DOI: 10.1073/pnas.2208866120

Abstract

Canine distemper virus (CDV) is an enveloped RNA morbillivirus that triggers respiratory, enteric, and high incidence of severe neurological disorders. CDV induces devastating outbreaks in wild and endangered animals as well as in domestic dogs in countries associated with suboptimal vaccination programs. The receptor-binding tetrameric attachment (H)-protein is part of the morbilliviral cell entry machinery. Here, we present the cryo-electron microscopy (cryo-EM) structure and supramolecular organization of the tetrameric CDV H-protein ectodomain. The structure reveals that the morbilliviral H-protein is composed of three main domains: stalk, neck, and heads. The most unexpected feature was the inherent asymmetric architecture of the CDV H-tetramer being shaped by the neck, which folds into an almost 90° bent conformation with respect to the stalk. Consequently, two non-contacting receptor-binding H-head dimers, which are also tilted toward each other, are located on one side of an intertwined four helical bundle stalk domain. Positioning of the four protomer polypeptide chains within the neck domain is guided by a glycine residue (G158), which forms a hinge point exclusively in two protomer polypeptide chains. Molecular dynamics simulations validated the stability of the asymmetric structure under near physiological conditions and molecular docking showed that two receptor-binding sites are fully accessible. Thus, this spatial organization of the CDV H-tetramer would allow for concomitant protein interactions with the stalk and head domains without steric clashes. In summary, the structure of the CDV H-protein ectodomain provides new insights into the morbilliviral cell entry system and offers a blueprint for next-generation structure-based antiviral drug discovery.

Keywords: H-protein ectodomain; canine distemper virus; cryo-electron microscopy; morbillivirus cell entry; structure.

Conflict of interest statement

The authors declare no competing interest.

Figures

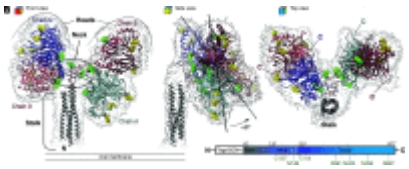


Fig. 1.

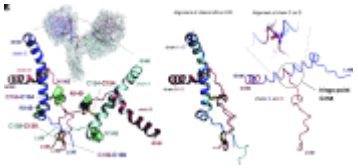


Fig. 2.

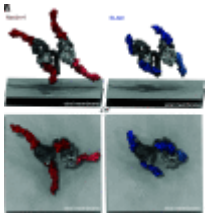


Fig. 3.

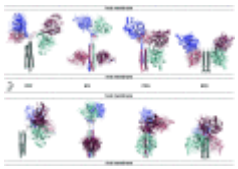


Fig. 4.

Highlight Vetsuisse Faculty

In Vitro Activities of Dithiocarbamate Derivatives against *Echinococcus multilocularis* Metacestode Vesicles

Marc Kaethner[1,2], Georg Rennar[3], Tom Gallinger[3], Tobias Kämpfer[1,2], Andrew Hemphill[1], Patrick Mäder[3], Ana Luque-Gómez[4], Martin Schlitzer[3], Britta Lundström-Stadelmann[1,5]

Affiliations expand
PMID: 38133449 PMCID: PMC10747736 DOI: 10.3390/tropicalmed8120517

Abstract

The metacestode stage of the fox tapeworm *Echinococcus multilocularis* causes the severe zoonotic disease alveolar echinococcosis. New treatment options are urgently needed. Disulfiram and dithiocarbamates were previously shown to exhibit activity against the trematode *Schistosoma mansoni.* As both parasites belong to the platyhelminths, here we investigated whether these compounds were also active against *E. multilocularis* metacestode vesicles in vitro. We used an in vitro drug-screening cascade for the identification of novel compounds against *E. multilocularis* metacestode vesicles with disulfiram and 51 dithiocarbamates. Five compounds showed activity against *E. multilocularis* metacestode vesicles after five days of drug incubation in a damage marker release assay. Structure-activity relationship analyses revealed that a *S*-2-hydroxy-5-nitro benzyl moiety was necessary for anti-echinococcal activity, as derivatives without this group had no effect on *E. multilocularis* metacestode vesicles. The five active compounds were further tested for potential cytotoxicity in mammalian cells. For two compounds with low toxicity (Schl-32.315 and Schl-33.652), IC_{50} values in metacestode vesicles and IC_{50} values in germinal layer cells were calculated. The compounds were not highly active on isolated GL cells with IC_{50} values of 27.0 ± 4.2 µM for Schl-32.315 and 24.7 ± 11.5 µM for Schl-33.652, respectively. Against metacestode vesicles, Schl-32.315 was not very active either with an IC_{50} value of 41.6 ± 3.2 µM, while Schl-33.652 showed a low IC_{50} of 4.3 ± 1 µM and should be further investigated in the future for its activity against alveolar echinococcosis.

Keywords: Echinococcus; disulfiram; drug treatment; in vitro drug screening; platyhelminth.

Conflict of interest statement

The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript; or in the decision to publish the results.

Figures

Figure 1

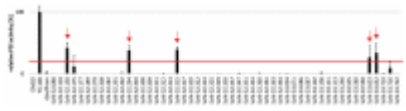


Figure 2

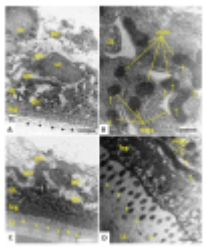


Figure 3

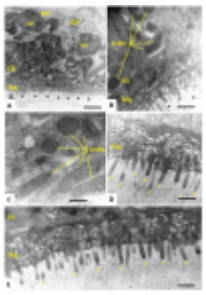


Figure 4

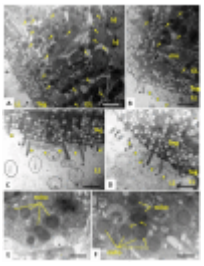


Figure 5

Highlight Science Faculty

Automatic detection of spatio-temporal signaling patterns in cell collectives

Paolo Armando Gagliardi[#1], Benjamin Grädel[#1,2], Marc-Antoine Jacques[1,2], Lucien Hinderling[1,2], Pascal Ender[1,2], Andrew R Cohen[3], Gerald Kastberger[4], Olivier Pertz[1], Maciej Dobrzyński[1]

Affiliations expand
PMID: 37516918 PMCID: PMC10374943 DOI: 10.1083/jcb.202207048

Abstract

Increasing experimental evidence points to the physiological importance of space-time correlations in signaling of cell collectives. From wound healing to epithelial homeostasis to morphogenesis, coordinated activation of biomolecules between cells allows the collectives to perform more complex tasks and to better tackle environmental challenges. To capture this information exchange and to advance new theories of emergent phenomena, we created ARCOS, a computational method to detect and quantify collective signaling. We demonstrate ARCOS on cell and organism collectives with space-time correlations on different scales in 2D and 3D. We made a new observation that oncogenic mutations in the MAPK/ERK and PIK3CA/Akt pathways of MCF10A epithelial cells hyperstimulate intercellular ERK activity waves that are largely dependent on matrix metalloproteinase intercellular signaling. ARCOS is open-source and available as R and Python packages. It also includes a plugin for the napari image viewer to interactively quantify collective phenomena without prior programming experience.

Conflict of interest statement

Disclosures: The authors declare no competing interests exist.

Figures

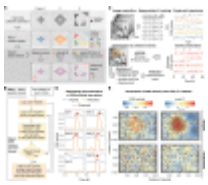


Figure 1.

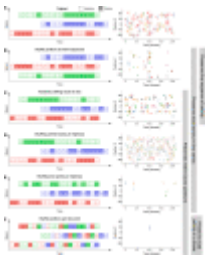


Figure S1.

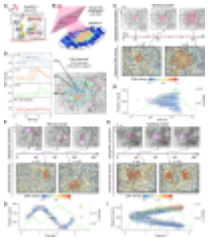


Figure 2.

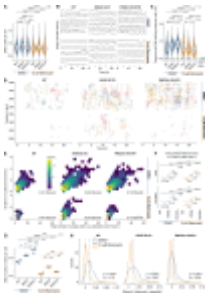


Figure 3.

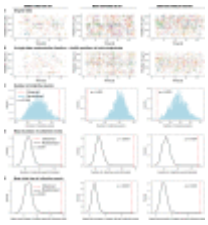


Figure S2.

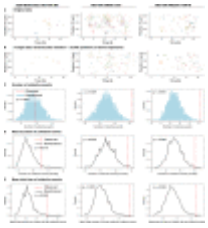


Figure S3.

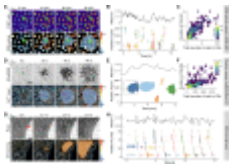


Figure 4.

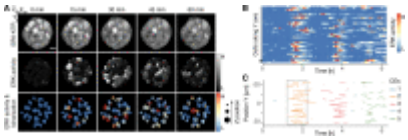


Figure 5.

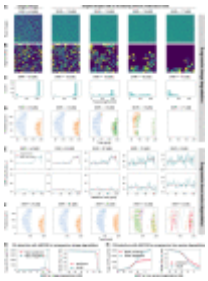


Figure S4.

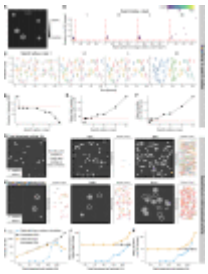


Figure S5.