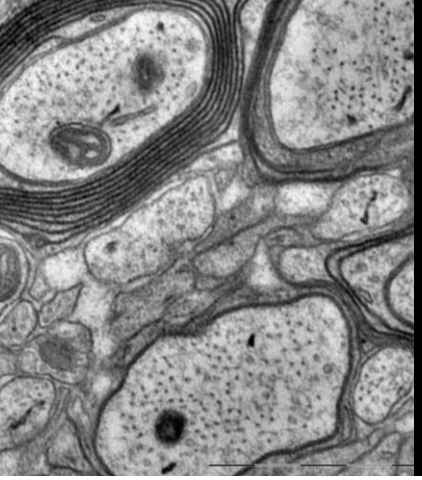
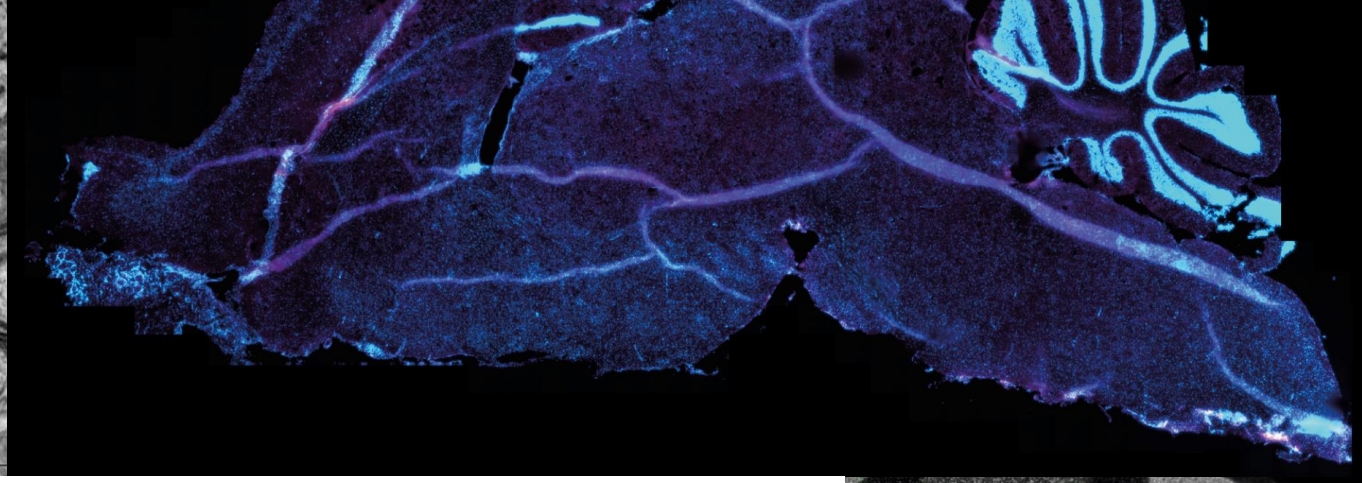
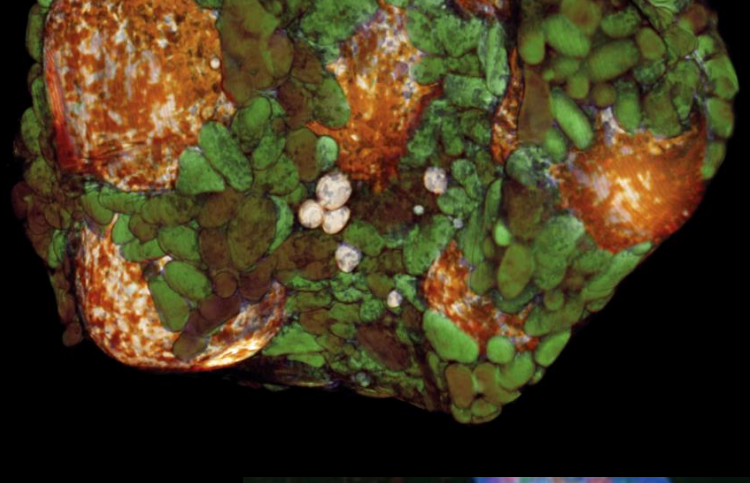
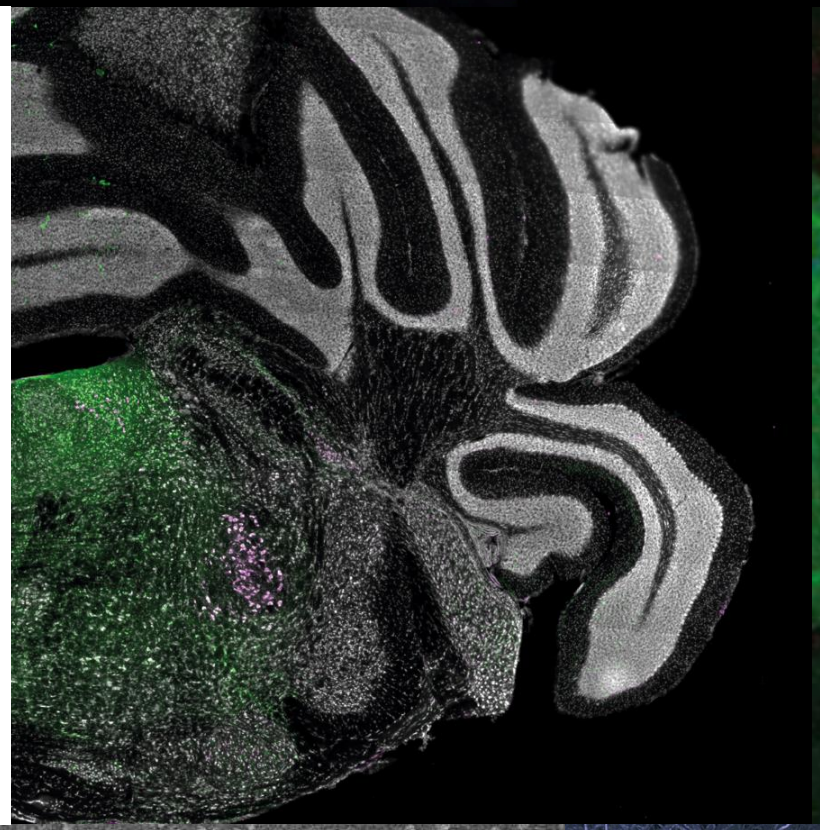
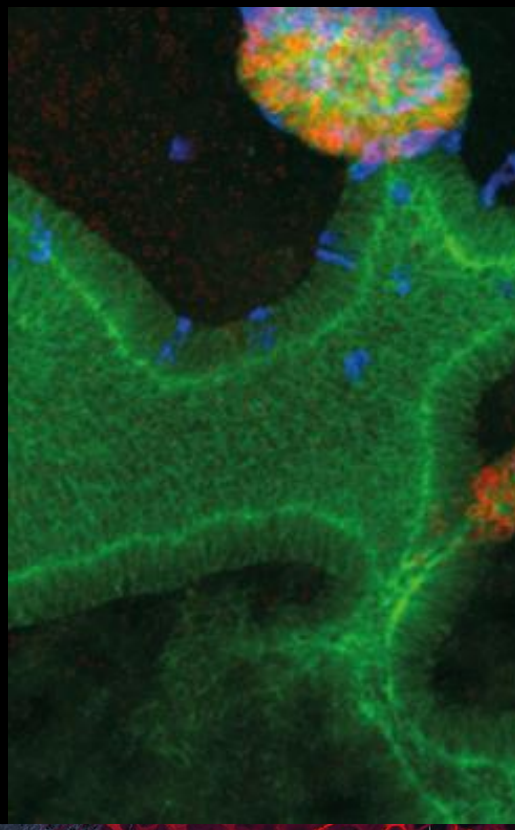
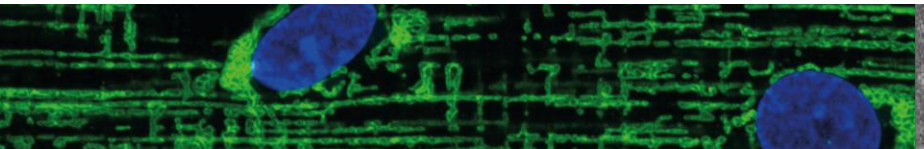
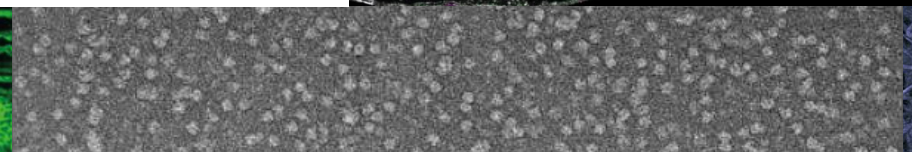
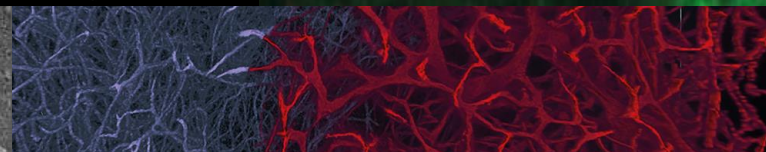




Core Facility for Integrated Microscopy

10th Anniversary Exhibition

UNIVERSITY OF COPENHAGEN

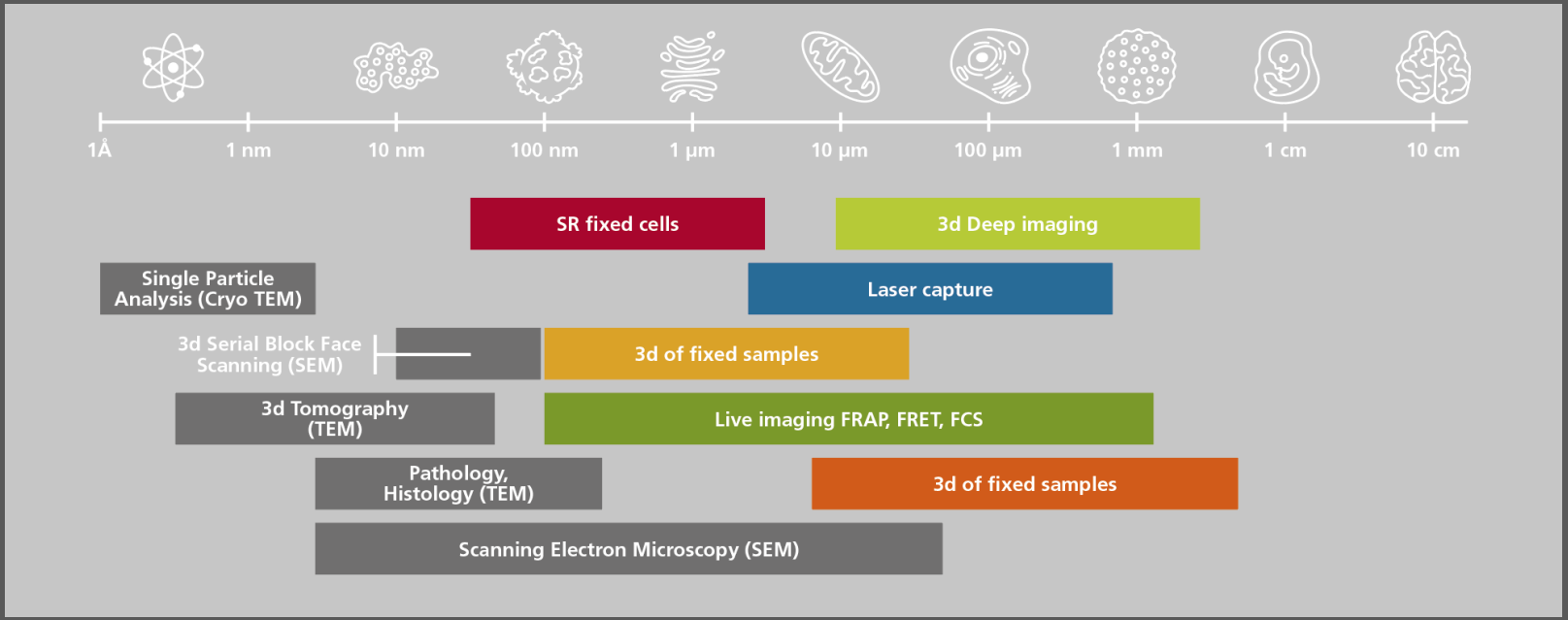






Core Facility for Integrated Microscopy
10th Anniversary Exhibition

Core Facility for Integrated Microscopy (CFIM) at The Faculty of Health and Medical Sciences, University of Copenhagen is celebrating its 10th anniversary of serving researchers world class microscopy.

This exhibition shows imaging from CFIM equipment used in recent high impact papers, cool images with broadly applicable microscopy technologies and then & now-examples of how microscopy has advanced over the last decade.

Applications available across scales



Visit us

At CFIM, you can use a wide range of state-of-the art light and electron microscopes. CFIM provides expertise, training, and support. CFIM welcomes all users of any level of microscopy experience from the University of Copenhagen as well as other universities and hospitals.

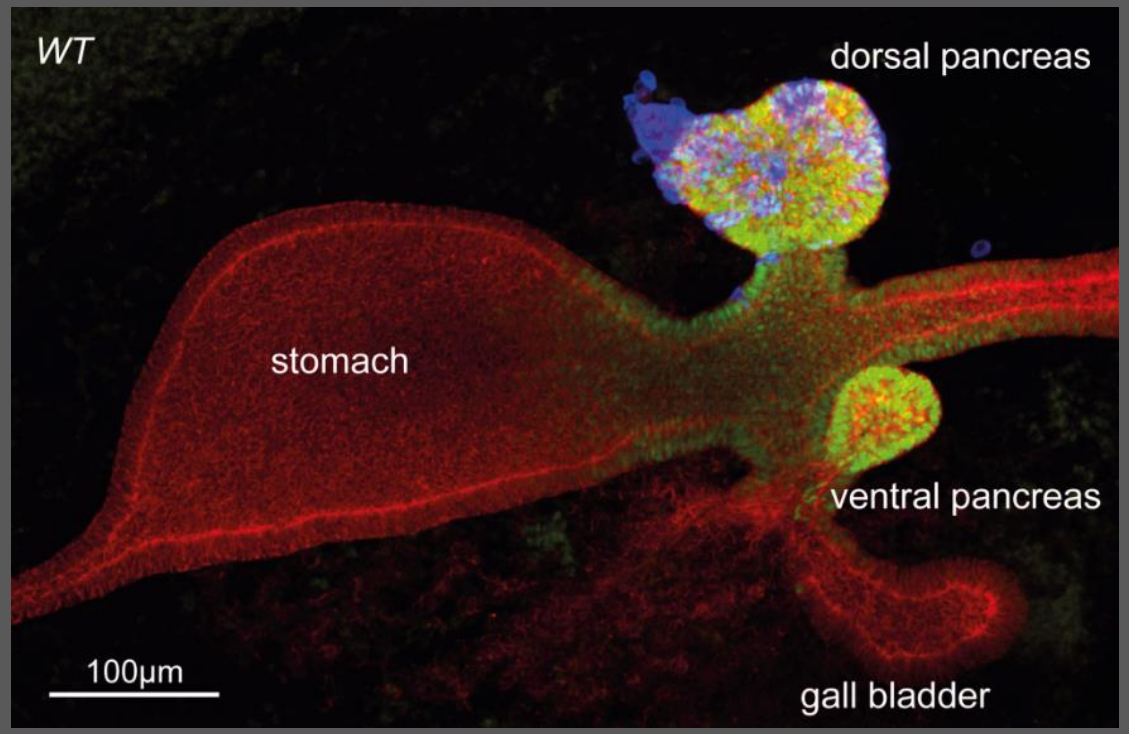
Find us at Panum, building 21.1 and at cfim.ku.dk

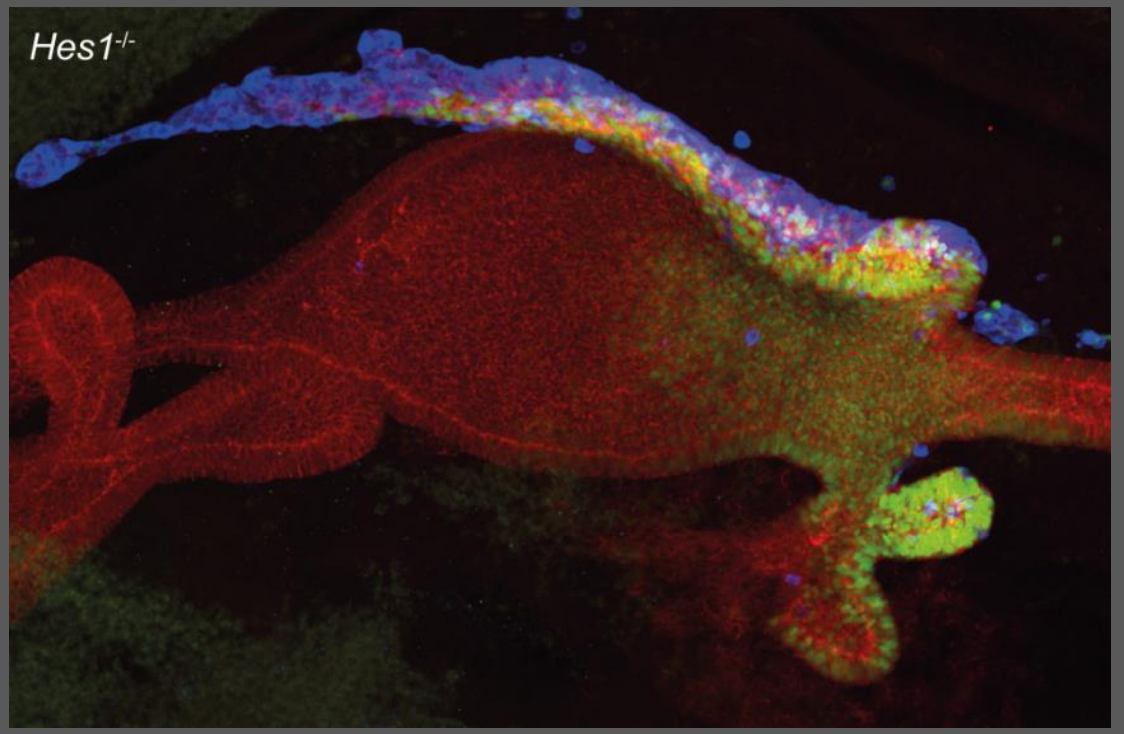
First row: Thomas Hartig Braunstein, Jacqueline van Hall, Klaus Qvortrup, Clara Prats, Cristiano Di Benedetto
Second row: Michael Johnson, Tillmann Pape, Pablo Hernandez-Varas, Zhila Nikrozi

EQUIPPED FOR HIGH IMPACT

Mutant mice embryos in confocal microscopy

Published in *Development*, 2018



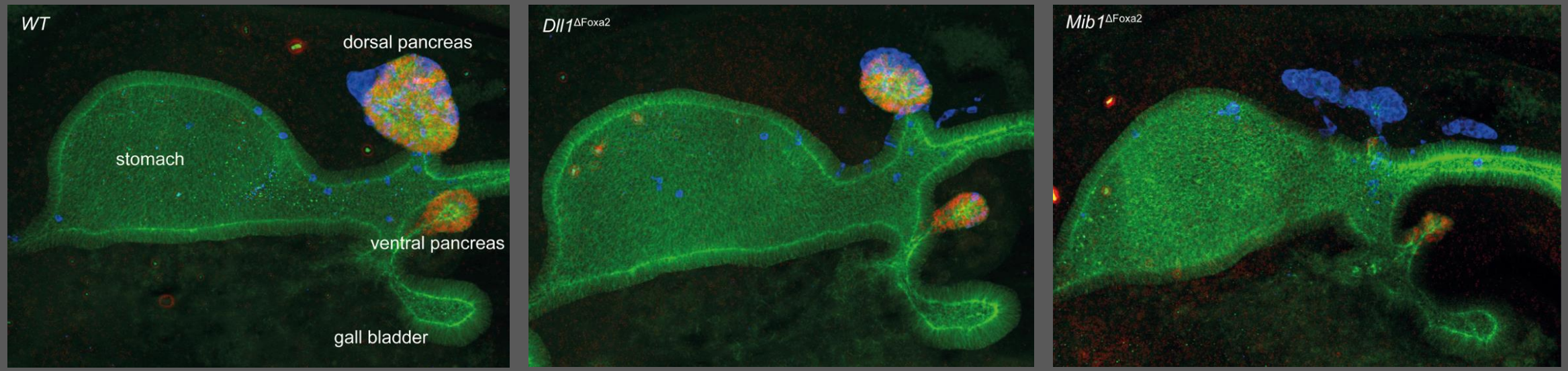


Hes1 is a main target gene of Notch signaling during pancreas development.
The images show how the dorsal pancreas (and the gall bladder) is malformed in *Hes1* mutant mouse embryos at gestational day 10 (E10.5). Microscope: Zeiss LSM700

EQUIPPED FOR HIGH IMPACT

Mutant mice embryos in confocal microscopy

Published in *Development*, 2018



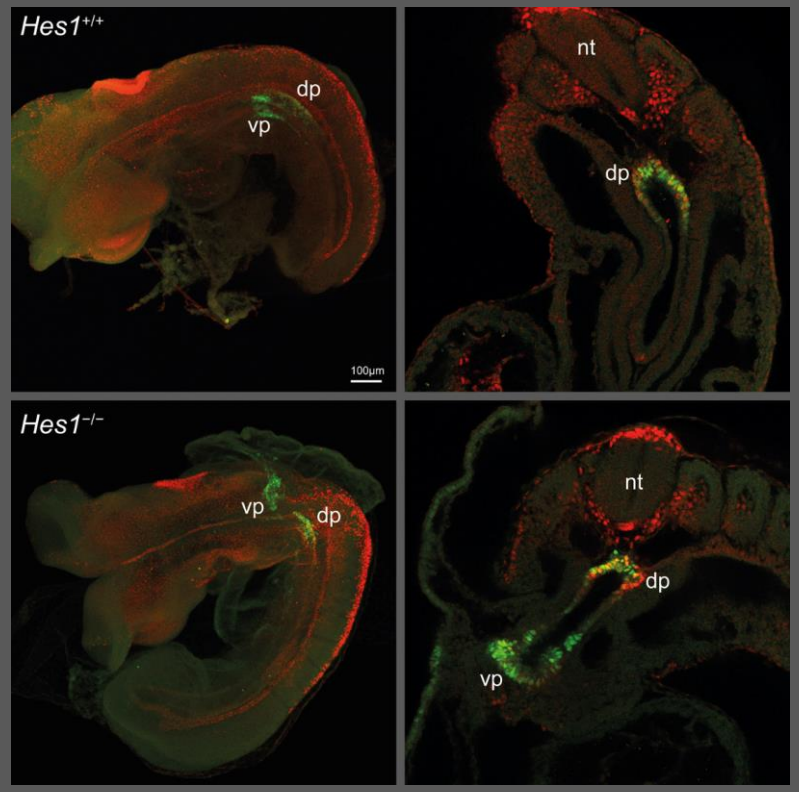
The development of the pancreas is affected differently in the other Notch signaling mutants, *Dll1*^{DFoxa2} and *Mib1*^{DFoxa2}. Microscope: Zeiss LSM710.

> Good image data means everything in my research!
> It's about 80-90 percent of my data. At CFIM I have a good selection of microscopes and can discuss my results with experts.
>
> - Mette C. Jørgensen, Staff Researcher, Novo Nordisk Foundation Center for Stem Cell Biology, University of Copenhagen

EQUIPPED FOR HIGH IMPACT

Mutant mice embryos in confocal microscopy

Published in *Development*, 2018



The expression of the important transcription factor *Sox9* is maintained in the earliest pancreatic cells in *Hes1* mutant mouse embryos at gestational day 8 (E8.5).
Microscope: Zeiss LSM710

"We gained knowledge on a signaling pathway which is key to understanding pancreas development. When you mutate different components of the pathway, you get a variation of morphological phenotypes. It was very surprising!"

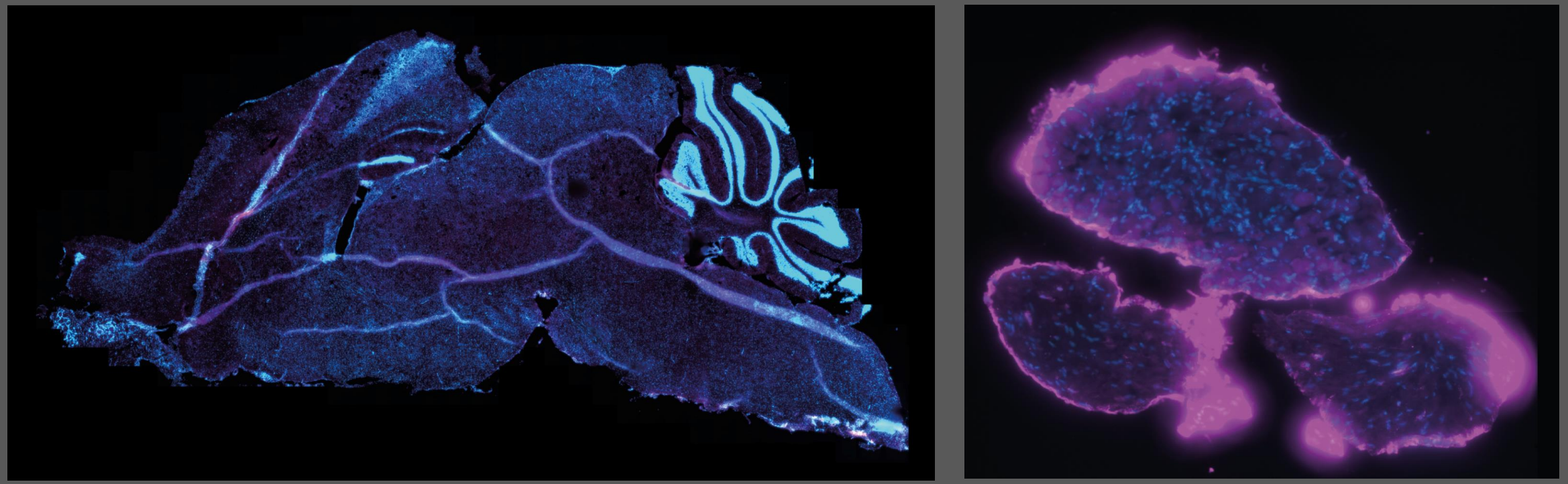
- Mette C. Jørgensen, Staff Researcher, Novo Nordisk Foundation Center for Stem Cell Biology, University of Copenhagen

Paper: "Neurog3-dependent pancreas dysgenesis causes ectopic pancreas in Hes1 mutant mice". Mette Christine Jørgensen, Kristian Honnens de Lichtenberg, C. A. Collin, R. Klinck, J. H. Ekberg, M. S. Engelstoft, H. Lickert, Palle Serup.
Development, September 2018

EQUIPPED FOR HIGH IMPACT

Brain samples in axio scan light microscope

Published in *EMBO Molecular Medicine*, 2020



TPD5 distributes efficiently to dorsal root ganglions (right), which contain the cell bodies of peripheral neurons, but not much to the brain (left). Microscope: Zeiss Axio Scan.Z1.

EQUIPPED FOR HIGH IMPACT

Brain samples in axio scan light microscope

Published in *EMBO Molecular Medicine*, 2020

"We identified a novel promising drug lead for treatment of neuropathic pain. At CFIM, we were able to image whole brain slices and assess the presence of the drug.

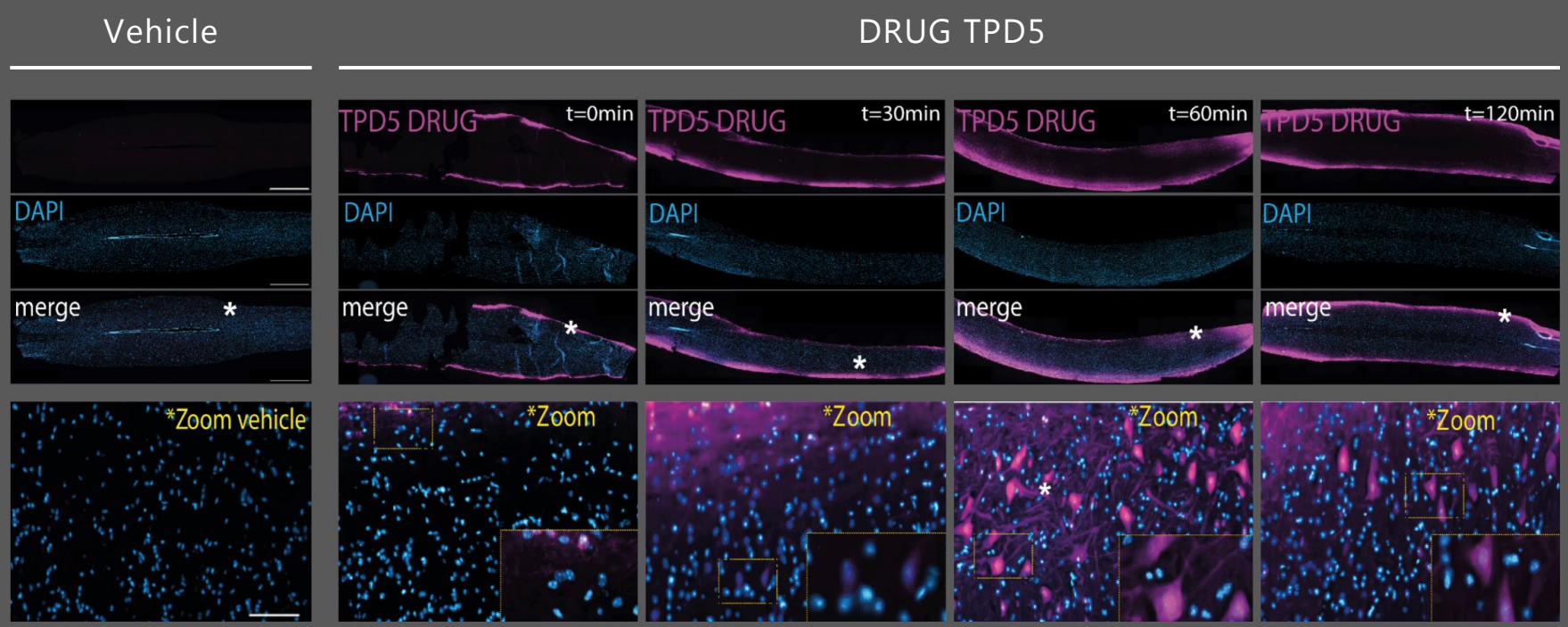
The imaging of whole spinal cord slices at high resolution enabled us to see whether drug was taken up into individual neurons.

– Kenneth L. Madsen
Associate Professor, Department of Neuroscience, University of Copenhagen

EQUIPPED FOR HIGH IMPACT

Brain samples in axio scan light microscope

Published in *EMBO Molecular Medicine*, 2020

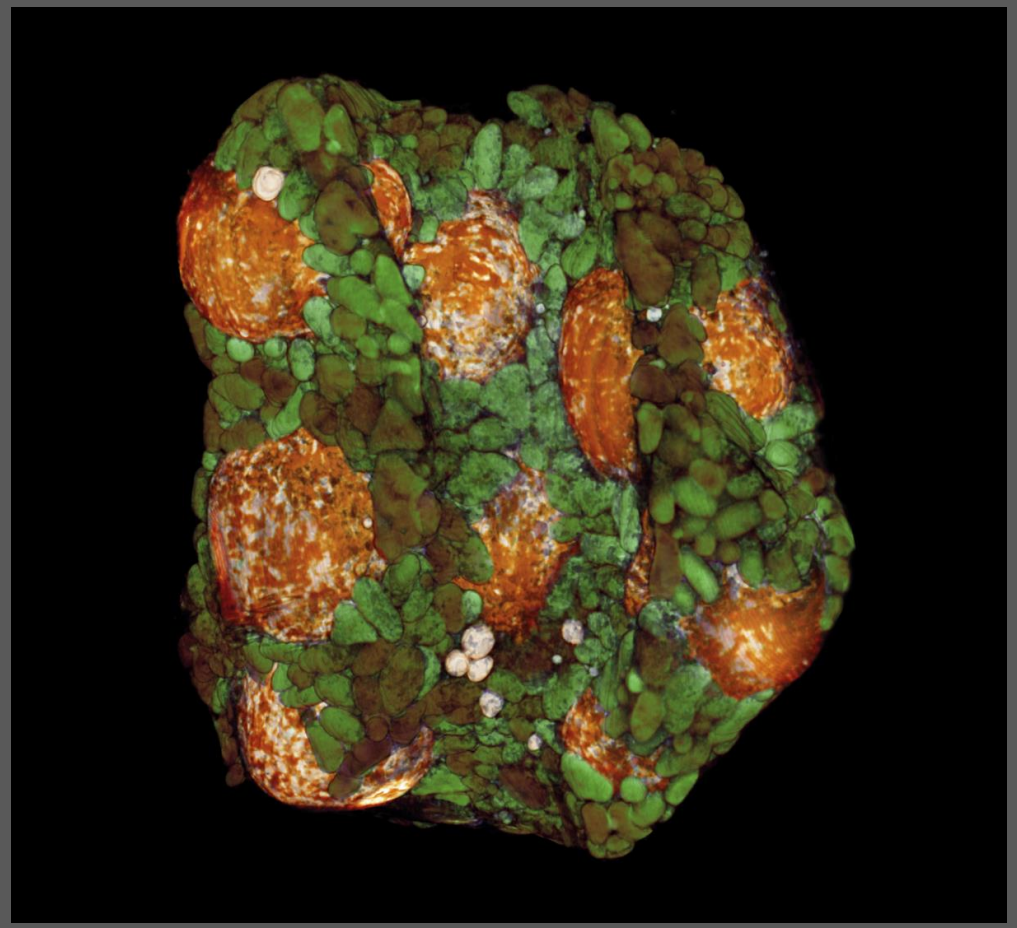


Paper: "A high-affinity, bivalent PDZ domain inhibitor complexes PICK1 to alleviate neuropathic pain"
Nikolaj R. Christensen, Marta De Luca, Michael Lever, Mette Richner, Astrid Hansen, Gith Noes-Holt, Kathrine Jensen, Mette Rathje, Dennis Bo Jensen, Simon Erlendsson, Christian Bartling, Ina Ammendrup-Johnsen, Sofie Pedersen, Michèle Schönauer, Klaus Nissen, Søren Midtgaard, Kaare Teilum, Lise Arleth, Andreas Sørensen, Anders Bach, Kristian Strømgaard, Claire Meehan, Christian Vægter, Ulrik Gether, Kenneth Madsen.
EMBO Molecular Medicine, June 2020

EQUIPPED FOR HIGH IMPACT

Building a brown fat cell with electron microscopy

Published in *Cell Metabolism*, 2018



"No matter how much data is presented in a paper, nothing makes a more lasting impression than a spectacular image."

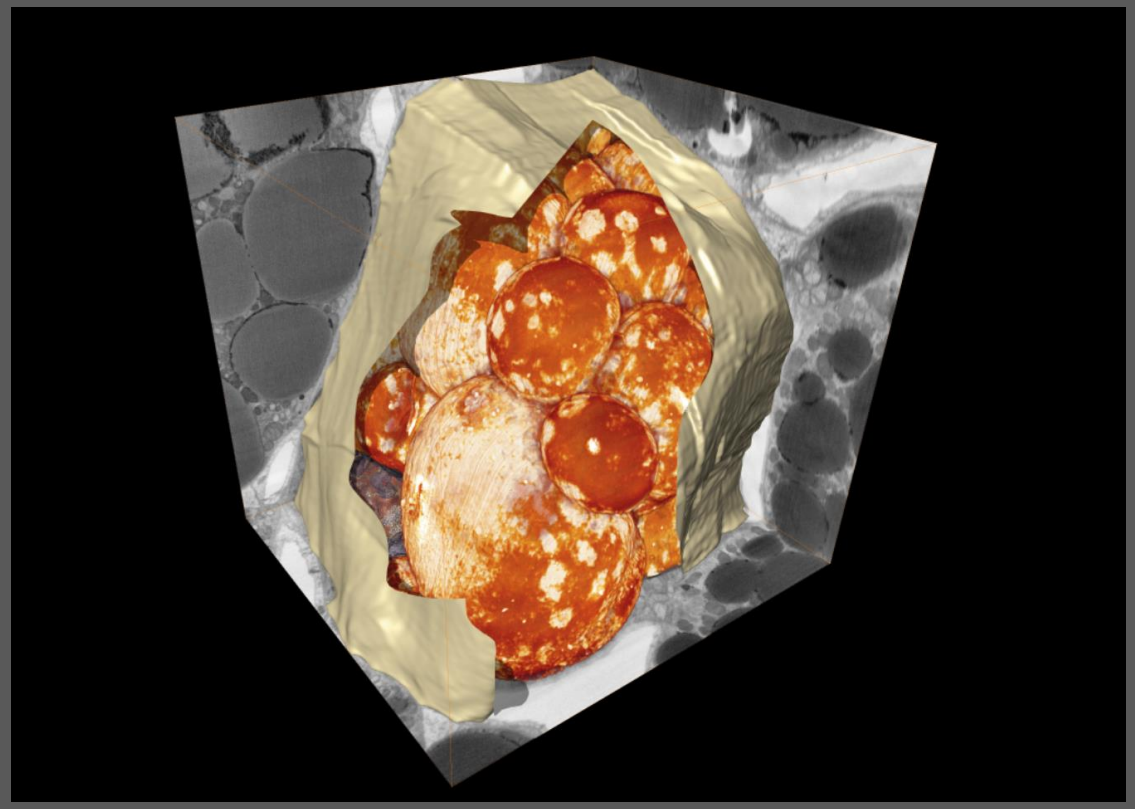
- Elahu Gosney Sustarsic
Assistant Professor, Novo Nordisk Foundation Center for Basic Metabolic Research, University of Copenhagen

Green mitochondria on fat: The inside of a brown fat cell with multilocular lipid droplets (white and brown) surrounded by mitochondria and other smaller organelles (green).
Microscope: Quanta FEG 3D.

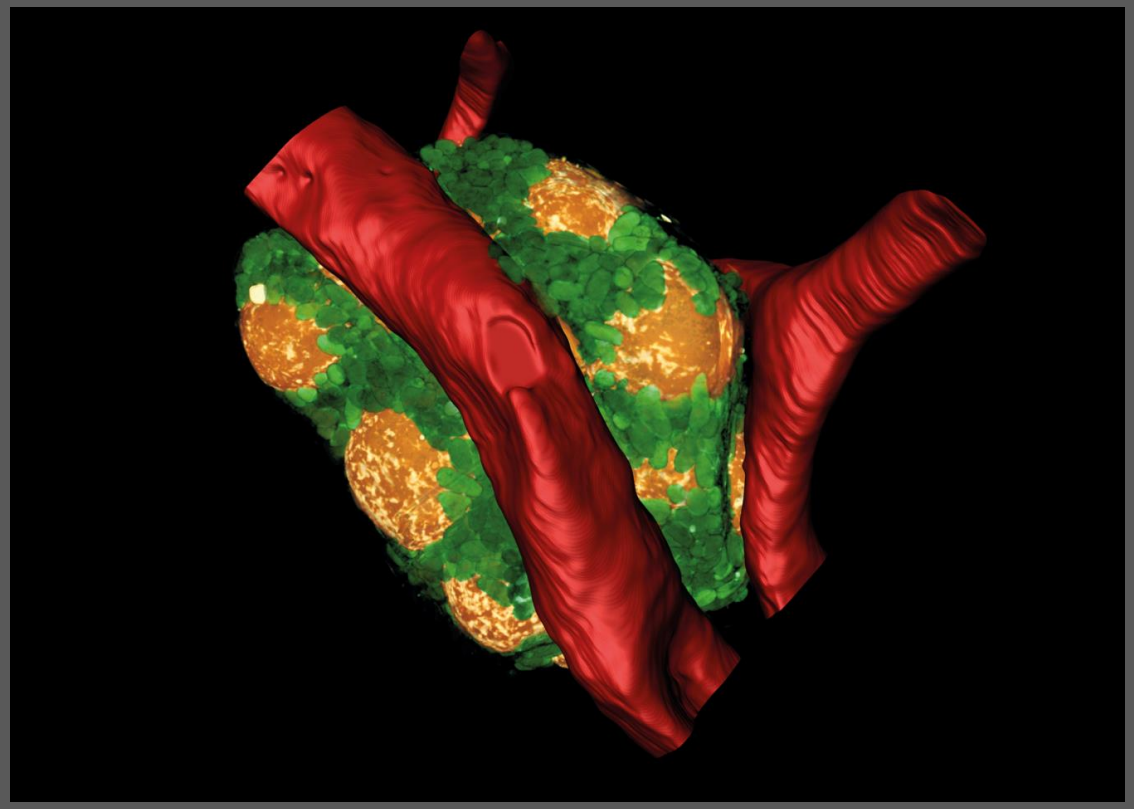
EQUIPPED FOR HIGH IMPACT

Building a brown fat cell with electron microscopy

Published in *Cell Metabolism*, 2018



3D cutaway of the cell membrane of a brown fat cell, with all contents of the cell removed except for the multilocular lipid droplet.



3D reconstruction of the interior of a single brown fat cell surrounded by blood vessels. The cell is primarily made up of multiple lipid droplets and abundant mitochondria.

Images generated by Michael Larsen, PhD Student, DanStem, University of Copenhagen.

EQUIPPED FOR HIGH IMPACT

Building a brown fat cell with electron microscopy

Published in *Cell Metabolism*, 2018

> We were able to reconstruct and visualize a single brown fat cell from whole tissue and gain unprecedented insights into cellular morphology.

- Zach Gerhart-Hines,
Associate Professor, Novo Nordisk Foundation Center for Basic Metabolic Research, University of Copenhagen

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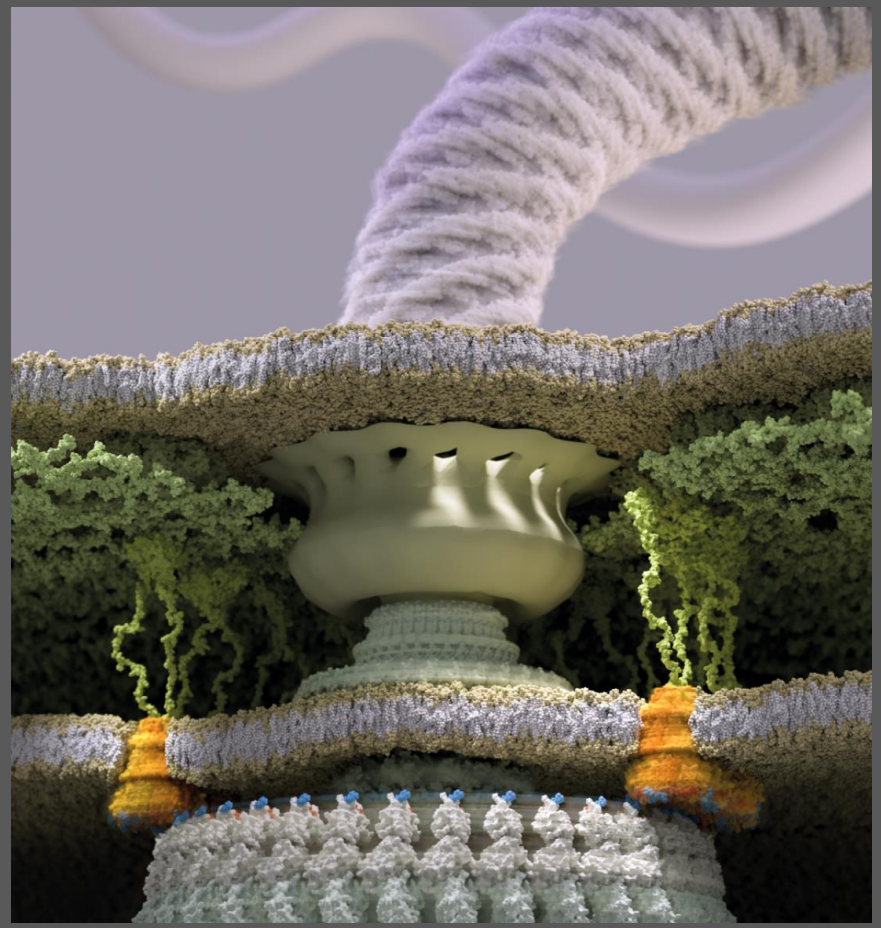
Paper: "Cardiolipin Synthesis in Brown and Beige Fat Mitochondria Is Essential for Systemic Energy Homeostasis"
Elahu G Sustarsic, Tao Ma, Matthew Lynes, Michael Larsen, Iuliia Karavaeva, Jesper Havelund, Carsten Nielsen, Mark Jedrychowski, Marta Moreno-Torres, Morten Lundh, Kaja Plucinska, Naja Jespersen, Trisha Grevengoed, Barbara Kramar, Julia Peics, Jakob B Hansen, Farnaz Shamsi, Isabel Forss, Ditte Neess, Susanne Keipert, Jianing Wang, Katharina Stohlmann, Ivan Brandslund, Cramer Christensen, Marit E Jørgensen, Allan Linneberg, Oluf Pedersen, Michael A Kiebish, Klaus Qvortrup, Xianlin Han, Bente Klarlund Pedersen, Martin Jastroch, Susanne Mandrup, Andreas Kjær, Steven Gygi, Torben Hansen, Matthew Gillum, Niels Grarup, Brice Emanuelli, Søren Nielsen, Camilla Scheele, Yu-Hua Tseng, Nils Færgeman, Zachary Gerhart-Hines.
Cell Metabolism, July 2018

EQUIPPED FOR HIGH IMPACT

Finding a tiny protein motor with cryo-electron microscopy

Published in *Cell*, 2020



"We are structural biologists – we solve mysteries. People used to think this protein was static, that's why they called it stator. With cryo-EM we saw the entire structure's exact molecular mechanism. It rotates!

Knowing how this system works, we might one day be able to use it to target bacteria".

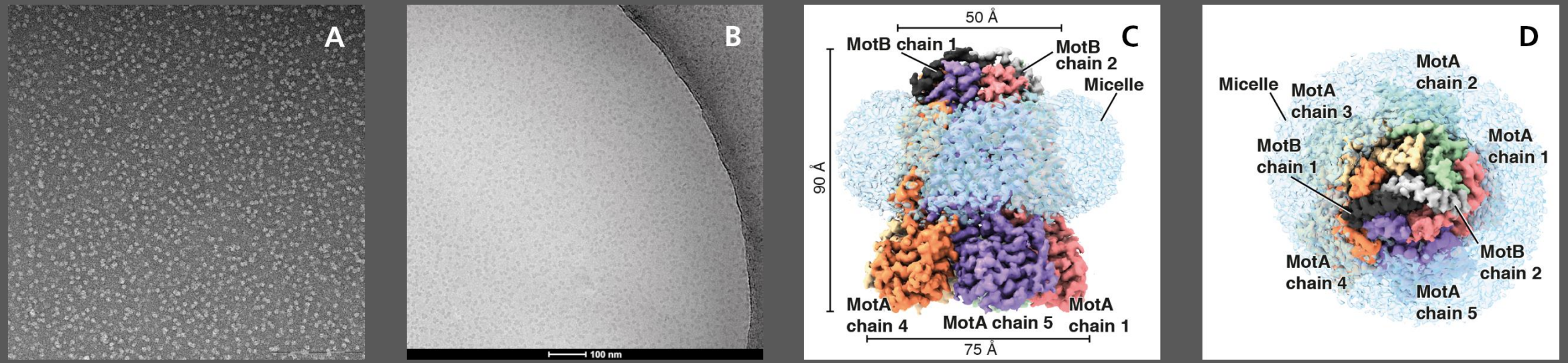
– Mònica Santiveri Saez,
Research Assistant, Novo Nordisk Foundation Center for Protein Research, University of Copenhagen

3D model based on data from the Titan Krios electron microscope. The MotB protein (green) is anchored to the cell wall, and is surrounded by MotA proteins (orange), which, upon dispersion of the ion motive force, rotates around MotB. The rotation of MotA in turn powers rotation of the large bacteria motor. Model image by Dan W. Nowakowski.

EQUIPPED FOR HIGH IMPACT

Finding a tiny protein motor with cryo-electron microscopy

Published in *Cell*, 2020



Imaging from CM100 **(A)** and Tecnai **(B)** does not look like much to the naked eye, but it shows that the protein sample is intact, homogeneous and nicely spread in both negative staining and cryo-EM grids, respectively. The model shows side **(C)** and top **(D)** views of the cryo-EM map of the MotAB stator unit from Campylobacter Jejuni in a detergent micelle

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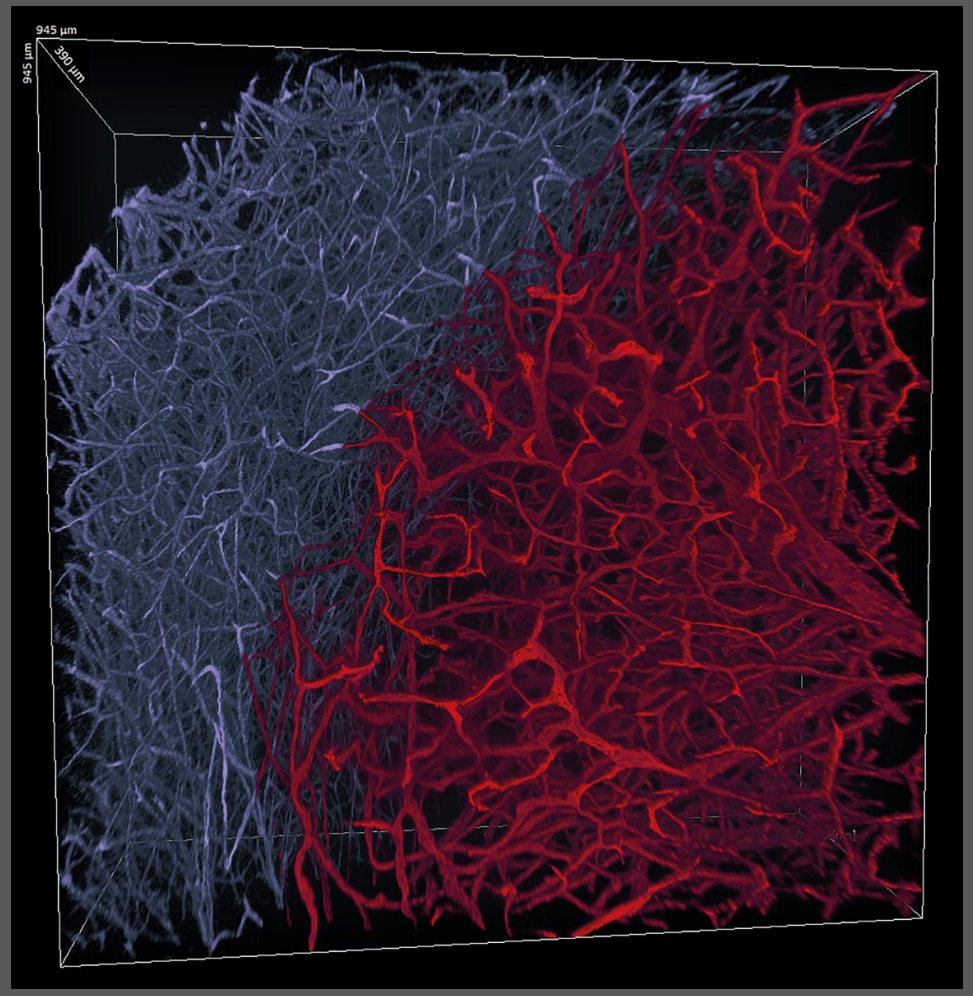
Paper: "Structure and Function of Stator Units of the Bacterial Flagellar Motor"
Mònica Santiveri, Aritz Roa-Eguiara, Caroline Kühne, Navish Wadhwa, Haidai Hu, Howard Berg, Marc Erhardt & Nicholas Taylor.
Cell, September 2020

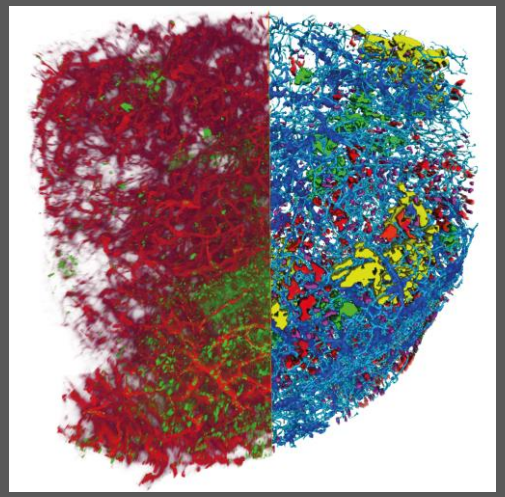
WHAT YOU CAN DO

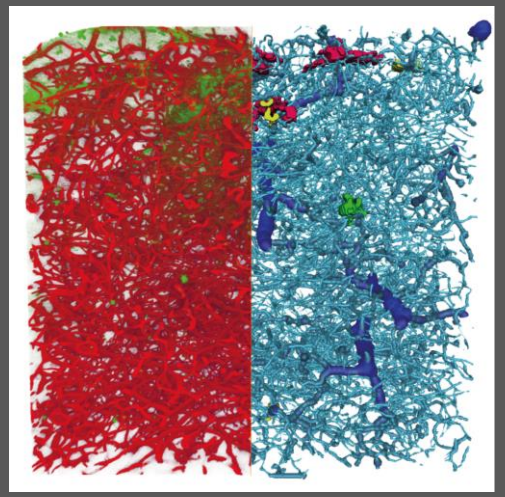
Deep imaging and 3D reconstruction of large samples



Live image of the vasculature of a glioblastoma (aggressive brain cancer) as an orthotopic xenograft in a mouse brain. Pseudocolor red = tumor vessels and grey = normal vasculature.

Microscope: Zeiss. The LSM780 is an inverted laser scanning confocal microscope for live imaging. This technology has become the golden standard in imaging biological samples, allowing for good resolution and flexibility in stainings.



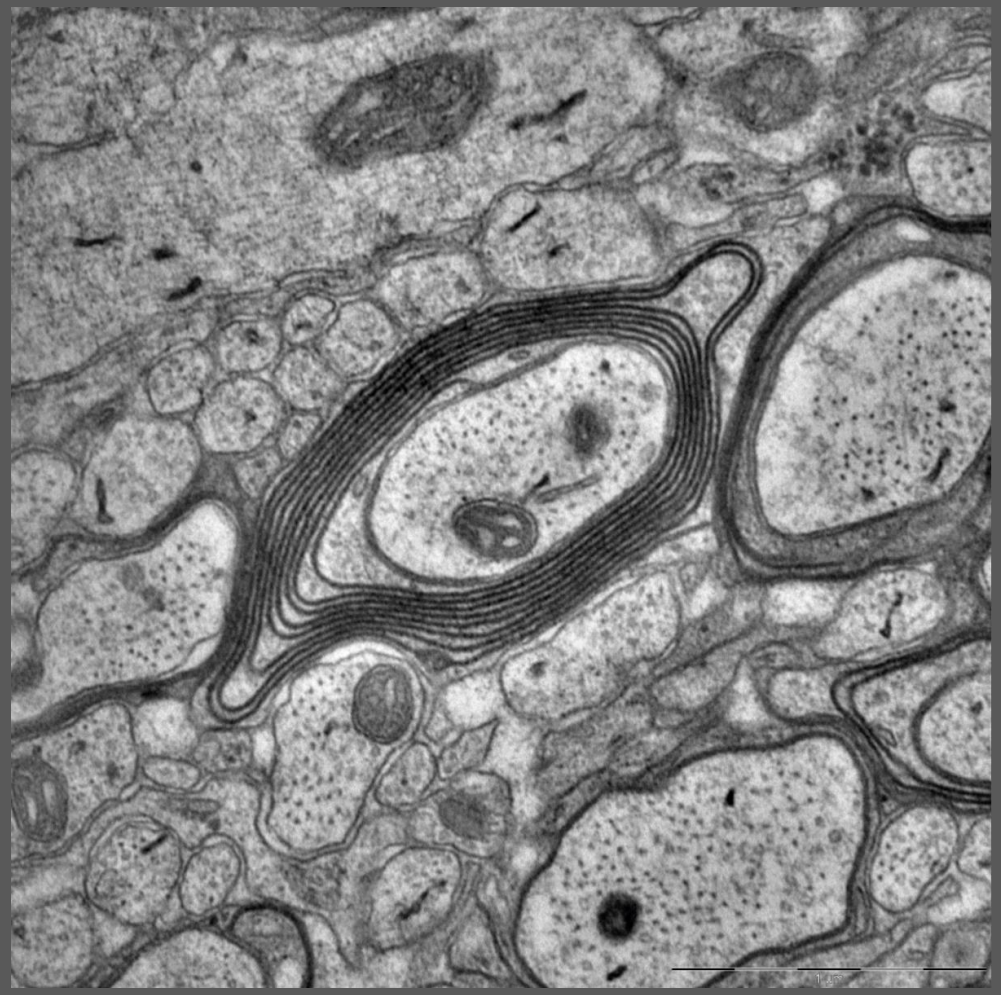


The vasculature of the same glioblastoma model with Zeiss LSM710. It has a dipping lens making it the system of choice for imaging cleared tissues. Reconstruction done with Amira software.

Images by: Serhii Kostrikov, Postdoc, DTU Health Tech.

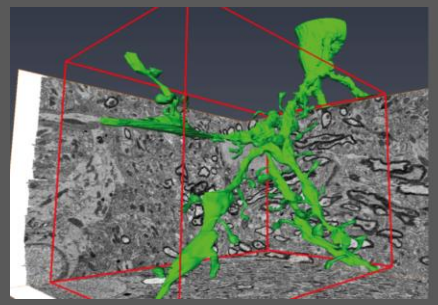
WHAT YOU CAN DO

3D analysis of ultrastructures using electron microscopy

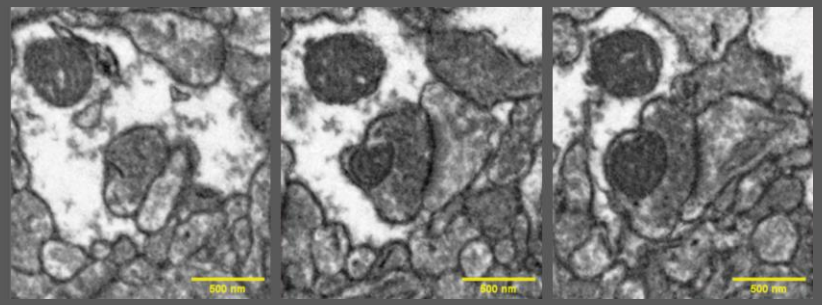


Serial block-face 3D reconstruction of a brain slice cut perpendicular to the corpus callosum to record the layers and quality of myelination as a consequence of genetic knockout of structural anchors.

Microscope: CM100(b) TEM, which is for standard ultrastructural investigations. It provides excellent contrast, even in inherently low-contrast and beam-sensitive biological specimens.



3D rendition of a neuronal environment based on Volume Scope electron microscopy. Segmentation done with Amira software.

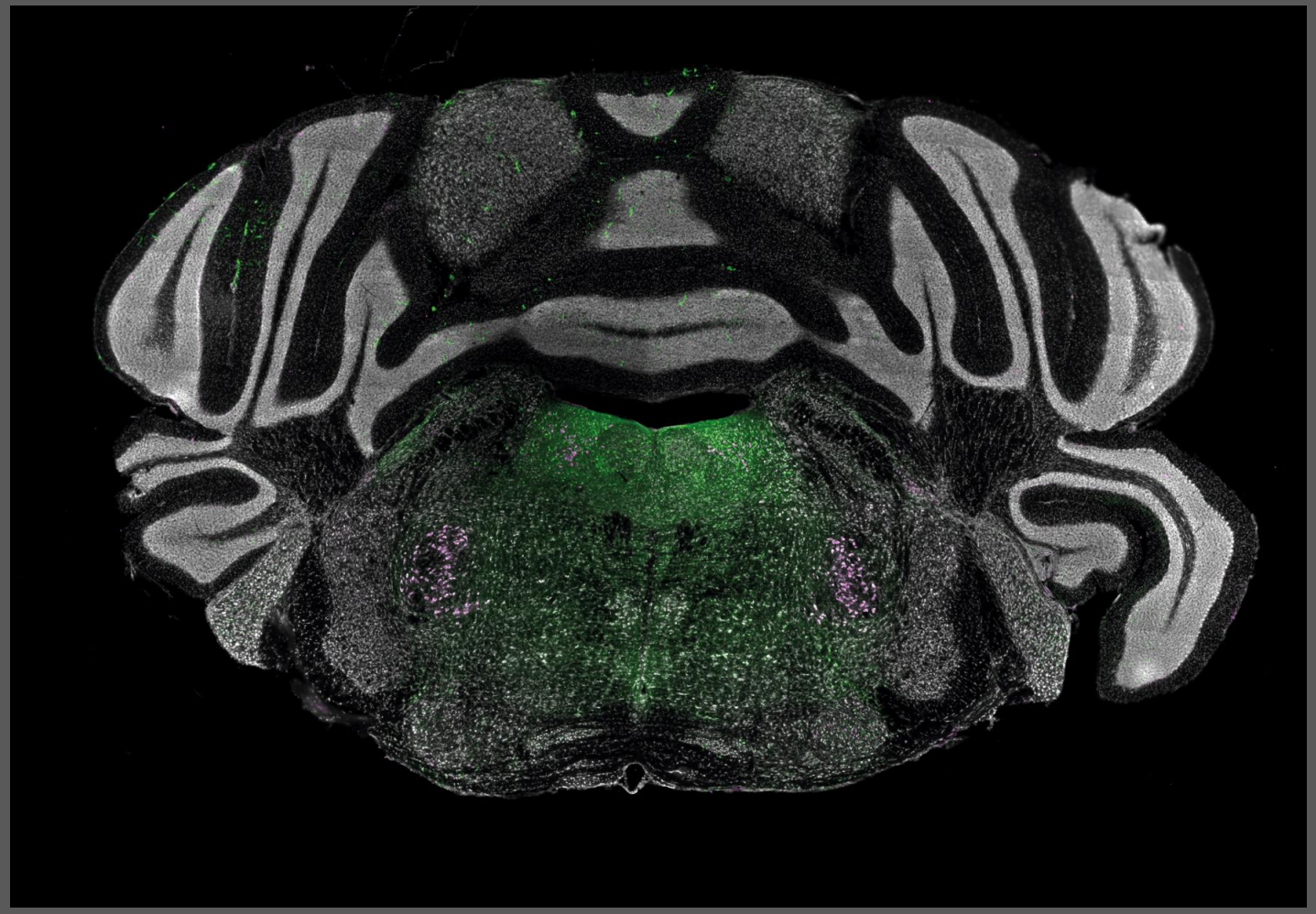


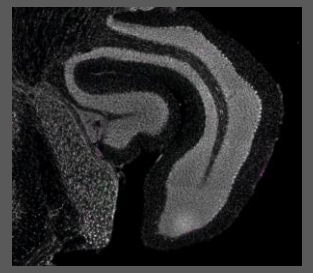
Serial sections that show a synapse surrounded by an astrocytic proces. The axon terminal is dark in the middle, the astrocyte is the surrounding white environment.

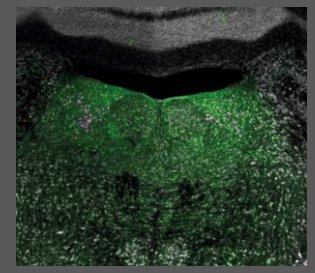
Images by: Carlos Benitez Villanueva, PhD Student, Center for Translational Neuromedicine, University of Copenhagen

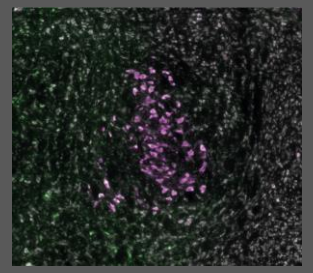
WHAT YOU CAN DO

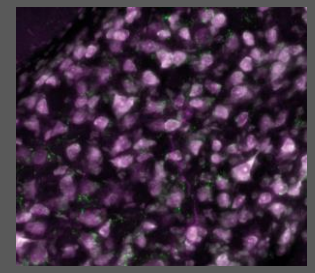
High resolution imaging of large tissue sections











Coronal sections of adult mouse brain. With various staining techniques, all neurons were labelled white, then a subset of glutamatergic neurons were labelled green, and cholinergic neurons were labelled magenta.

Microscope: Zeiss Axio Scan.Z1 Slide Scanner, a digital scanner that can digitalise tissue sections and cell cultures with high numerical aperture dry objectives, both with bright field and fluorescence.

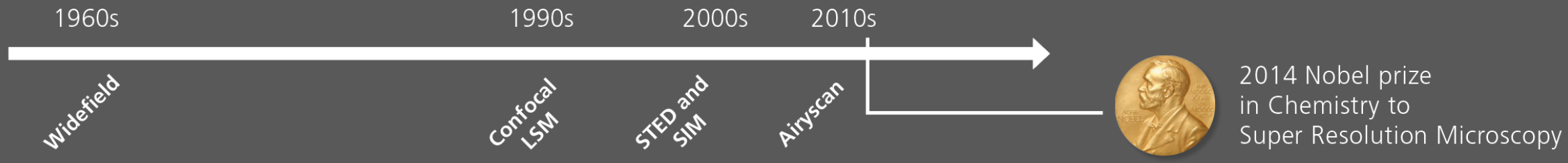
Images by: Haizea Goñi-Erro, PhD Student, Department of Neuroscience, University of Copenhagen

THEN & NOW

Light microscopy – from sub-cellular to molecular levels

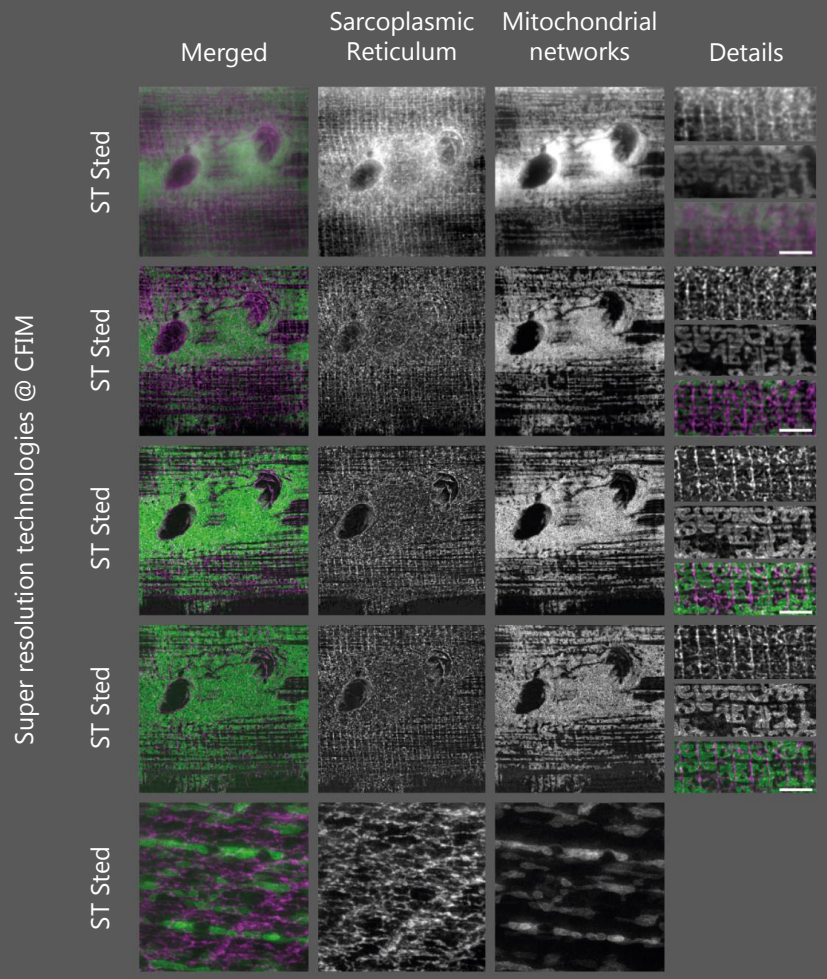
> With the new super resolution light microscopy technologies we have been able to overcome the limits of light microscopy resolution, going from the sub-cellular level to the sub-organelle, and even molecular levels!

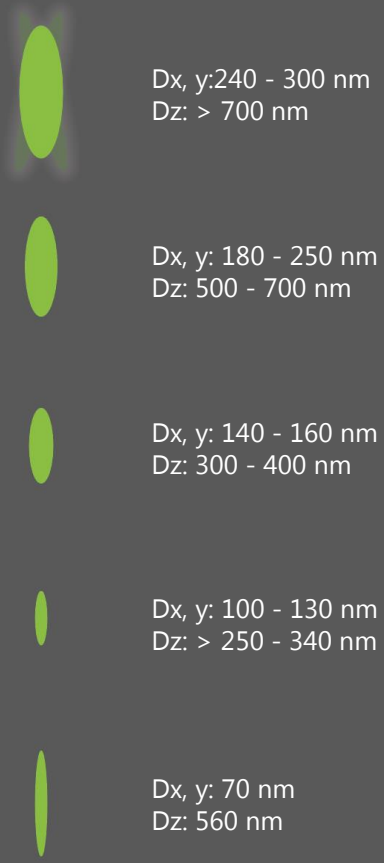
- Clara Prats Gavalda
Head of Light Microscopy, CFIM



THEN & NOW

Light microscopy – from sub-cellular to molecular levels





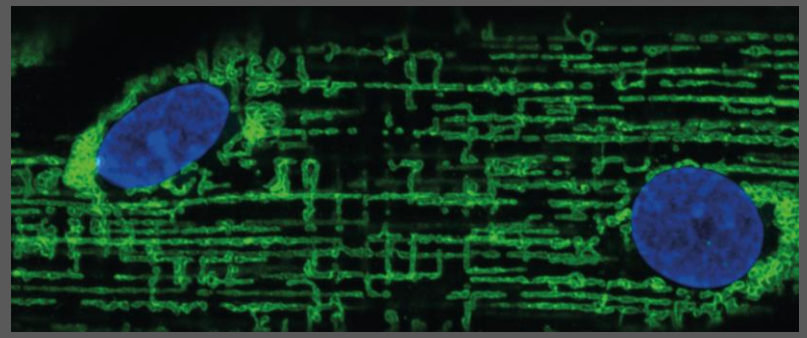
Dx, y:240 - 300 nm
Dz: > 700 nm

Dx, y: 180 - 250 nm
Dz: 500 - 700 nm

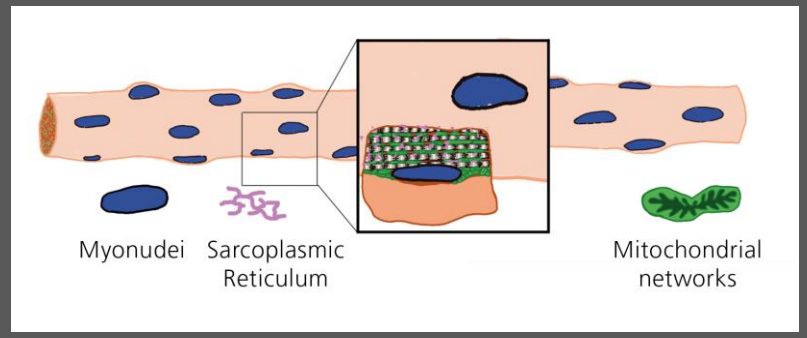
Dx, y: 140 - 160 nm
Dz: 300 - 400 nm

Dx, y: 100 - 130 nm
Dz: > 250 - 340 nm

Dx, y: 70 nm
Dz: 560 nm

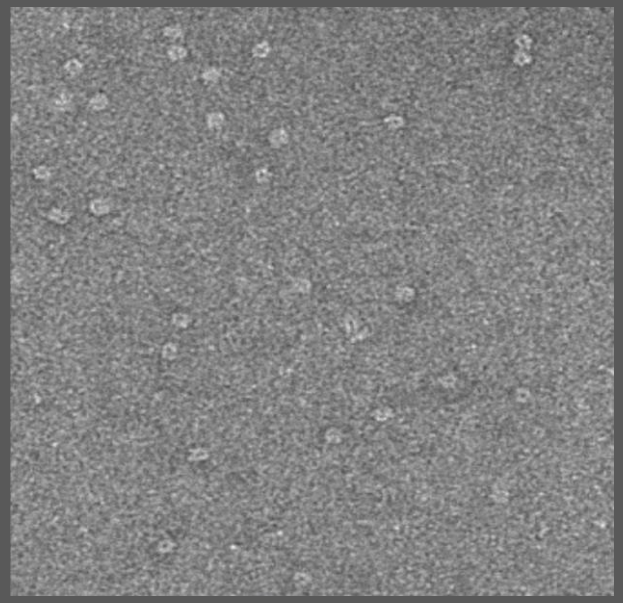


Super resolution light microscopy image (above) and corresponding illustration (below) of single muscle fiber from human vastus lateralis muscle. Mitochondrial networks (green) and myonuclei (blue).



THEN & NOW

From blobology to atomic resolution



The resolution of electron microscope has gradually improved over the last 30 years. In 2013, the introduction of a new type of electron detector provided a huge breakthrough. Now, the electron microscopy from before 2013 is nicknamed ‘blobology’.

=

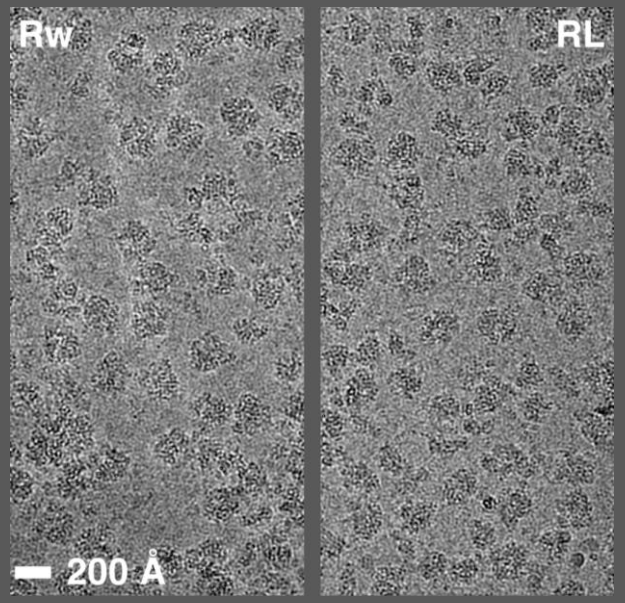
An example of ‘blobology’ of a complex solved in 2012 by Montoya et. al. This model was produced by negative stain using a 120 Kv TEM.

“To the human eye, the output looks pretty much the same now as 10 years ago, but there’s a remarkable difference. With today’s electron microscopes we can produce 3D images that show every atom in life’s molecular machineries.

- Professor Klaus Qvortrup, Director of CFIM

THEN & NOW

From blobology to atomic resolution



The resolution of electron microscope has gradually improved over the last 30 years. In 2013, the introduction of a new type of electron detector provided a huge breakthrough. Now, the electron microscopy from before 2013 is nicknamed ‘blobology’.

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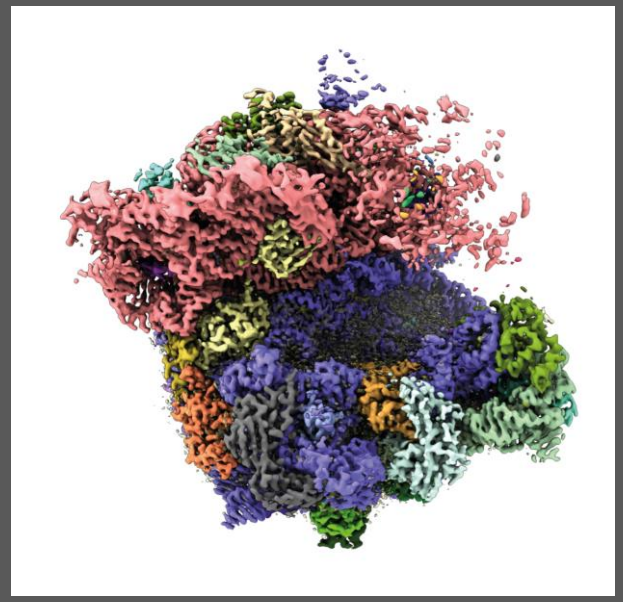

A recent 2.6 Å resolution map of a ribosome (cellular particle made of RNA and protein) by Montoya et. al. The model fits a whole atomic structure and lets researchers know all the positions of the atoms the particle is composed of.

> With these results, we can really understand how the proteins work. Knowing that, you can design applications or drugs that target them.

- **Guillermo Montoya**
  Research director and professor,
  Novo Nordisk Foundation Center for
  Protein Research, University of Copenhagen