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Cutting-edge imaging tech brings disease mechanisms into focus

Bioimaging insights are helping researchers at the Rudolf Virchow Center to improve the understanding and treatment of disease.

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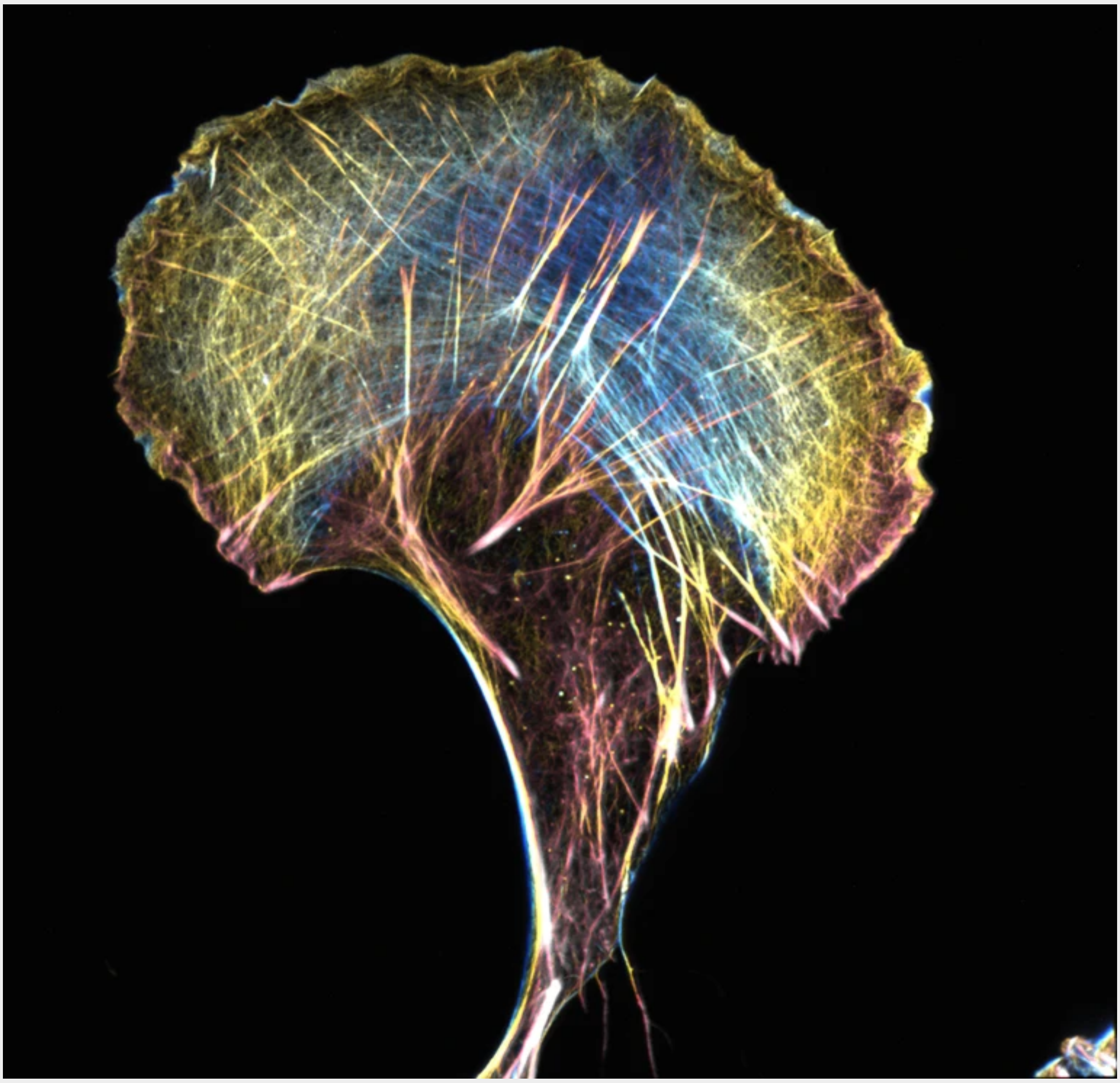


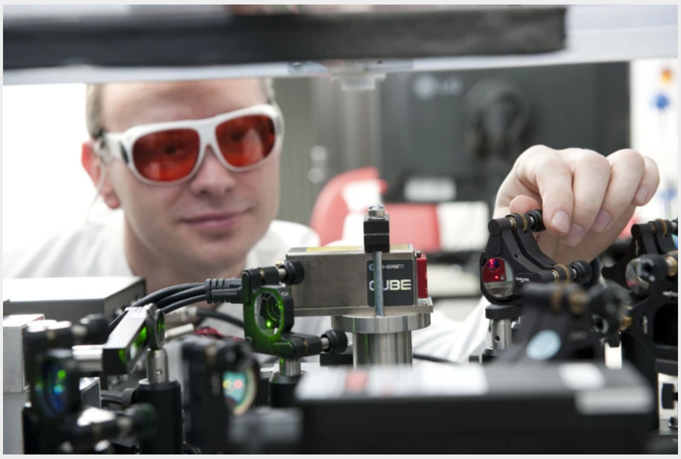
The actin cytoskeleton of a COS-7 cell, stained with phalloidin-ATTO643, imaged using rescan confocal microscopy. Credit: Beliu, Kurz & Sauer, RVZ

In the mid-nineteenth century, Rudolf Virchow postulated that cells are the smallest functional units of living organisms, and that cellular malfunction triggers disease. “Today, we’re using fluorescence imaging techniques to search for culprits on a far smaller scale, among the tens of thousands of proteins and RNAs encoded by the human genome,” says Markus Sauer, chair of biotechnology and spokesperson of the Rudolf Virchow Center for Integrative and Translational Bioimaging (RVZ) at the University of Würzburg, Germany. “The old saying ‘seeing is believing’ underpins our work — we’re visualizing and examining the molecular factors that cause disease.”

The centre has seen a whirlwind of developments in the last two years, with exciting work in the pipeline to shed new light on the mechanisms underpinning disease.

Pin-sharp vision

Following an explosion of activity in the field, the RVZ shifted its central research focus to bioimaging. Twelve interdisciplinary research groups liaise with clinical researchers to investigate health and disease — using pioneering techniques in super-resolution fluorescence microscopy and structural biology such as cryo-EM and X-ray crystallography.



Preparation for bioimaging in the Rudolf Virchow Center. Credit: RVZ

Sauer offers an example of the potential for bioimaging innovation to transform the understanding of human health. “Wouldn’t it be amazing,” he says, “if we could resolve the 3D molecular architecture of synapses to visualize changes during Alzheimer’s and Parkinson’s?”

One group at the RVZ is looking into platelet function using super-resolution microscopy and expansion microscopy to quantify and visualize platelet membrane proteins. Expansion microscopy uses standard confocal microscopes, but samples are treated and soaked overnight to enlarge them, so proteins of interest are easier to examine in detail.

Another team is optimizing personalized immunotherapies for cancers. Visualizing precisely how CAR T-cell therapies work is complex, but super-resolution fluorescence microscopy is helping RVZ scientists to understand and thereby improve such therapies. Similar fluorescence techniques are also being used to understand a novel mode of controlled cell death — this could yield new concepts in cancer therapy.

“We integrate various types of imaging to visualize elementary life processes from the sub-nano to the macro scale,” says Sauer. Cryo-EM and X-ray crystallography can be used to decipher the function of molecules involved in ubiquitylation — where proteins are tagged for degradation — or visualize components of the DNA repair machinery; both of which are relevant for developing new cancer therapies.

Overcoming visualization challenges

Smaller targets create problems of scale for existing fluorescent probes used to label samples. A 10-nanometre probe isn't suitable for a target molecule in the range of one to five nanometres. The centre is applying click-chemistry — an approach awarded the Chemistry Nobel Prize in 2022, whereby molecular building blocks snap together quickly and efficiently — to optimize visualization of targets in the single nanometre range.

Imaging intricate biological processes in living animal models poses another challenge. Working with synthetic chemist Martin Schnermann of the National Cancer Institute in Maryland, RVZ scientists are trialling fluorescent probes in the infrared range. These are used for deep tissue imaging and could support *in vivo* experiments.

"We're linking advances in optical hardware and chemistry with progress in computational biology and genomics," says Schnermann. "This is an exciting time to work in imaging."

Sauer believes the RVZ is poised to become a bioimaging centre that can match any in the world. "We warmly welcome new talent and innovative partnerships to achieve this goal."

For more information on the innovative research underway at the Rudolf Virchow Center for Integrative and Translational Bioimaging, visit: https://www.uni-wuerzburg.de/en/rvz/
