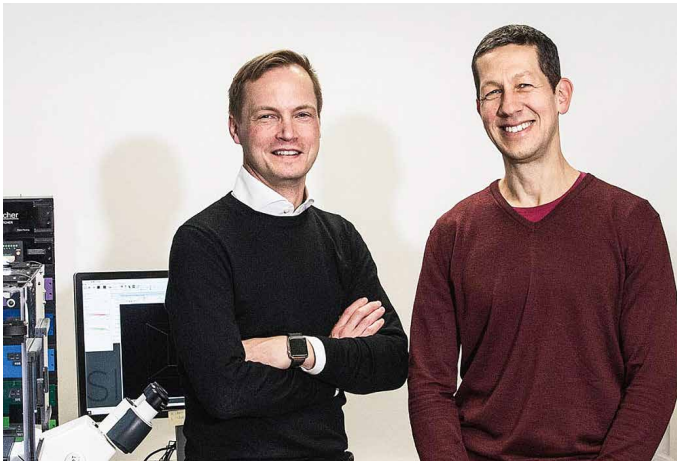
Understanding Blood Vessels

Cardiovascular diseases are still one of the most frequent causes of death worldwide. Scientists in the Focus Area »Translational Vascular Biomedicine« are investigating the role blood vessels play in these diseases.



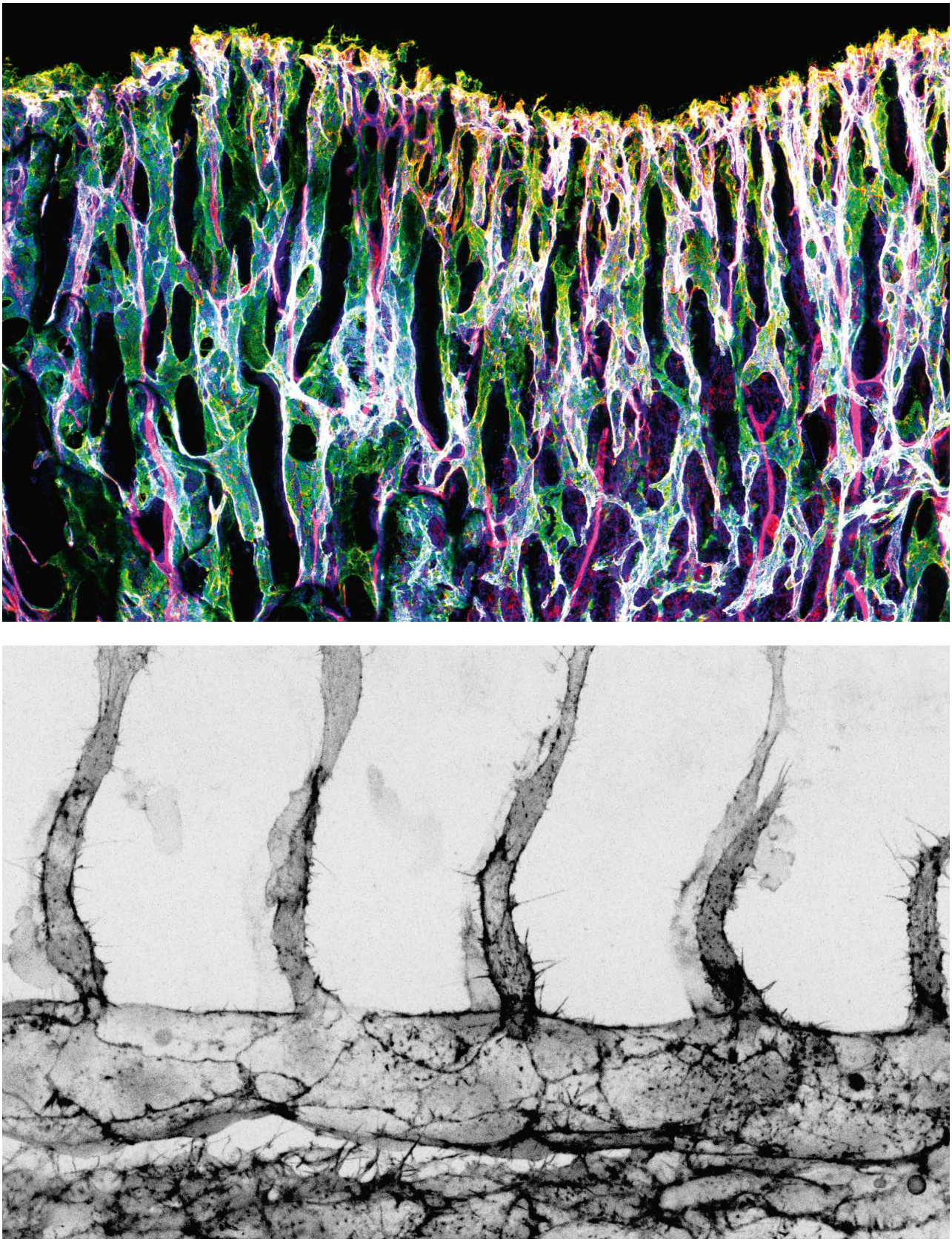
Michael Potente (left) and Holger Gerhardt are investigating the role blood vessels play in the onset of cardiovascular diseases.

»Since changes in vascular function underlie many diseases, the BIH decided some time ago to establish the Focus Area »Translational Vascular Biomedicine« to achieve significant progress and translational success in this field,« says BIH Professor Holger Gerhardt, who heads the Integrative Vascular Biology Lab at the MDC. Two years ago, the BIH initiated the ten-year BeLOVE study, in which a total of 10,000 patients with various cardiovascular diseases – from strokes to heart attacks to acute kidney injuries – will be observed over a long period of time. »We know that heart attack patients have a higher risk of suffering a stroke and vice versa,« Gerhardt says. »Vascular disease in one organ therefore increases the risk of disease in others. What they all have in common are problems in the small blood vessels. We want to find out not only the reasons for this, but also how we can prevent the second event from occurring.« BeLOVE has just enrolled its 2,000th patient.

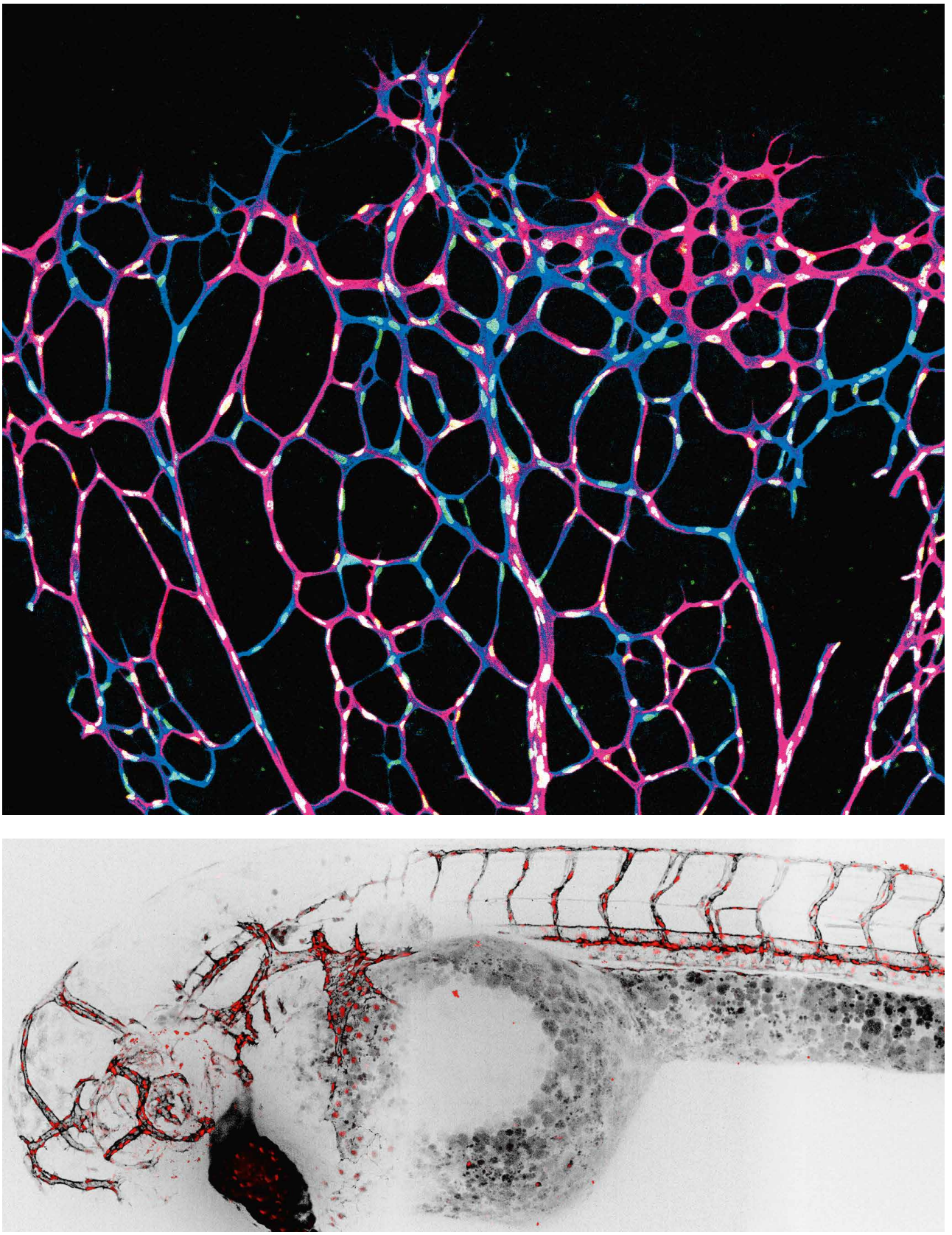
Understanding the growth and function of blood vessels

As spokesperson for the Focus Area »Translational Vascular Biomedicine,« Gerhardt has overseen its establishment and is delighted about the appointment of his colleague Michael Potente, who has been strengthening the Focus Area since August 2020. The newly appointed BIH professor is mainly interested in the influence of metabolism on blood vessels. »We want to understand how metabolic processes control the growth, remodeling and function of blood vessels,« says Potente, who previously led a lab at the Max Planck Institute for Heart and Lung Research in Bad Nauheim. For example, a lack of oxygen and nutrients can lead to the formation of new blood vessels in tumors. Similar processes also play a central role in eye diseases like wet macular degeneration, which leads to blindness if left untreated. »In this case, therapeutic interventions are already possible thanks to the use of inhibitors that suppress the abnormal growth of the blood vessels,« Potente reports.

In other disorders, such as chronic ischemic heart disease or peripheral artery disease of the legs, blocked vessels also cause a shortage of oxygen and nutrients in the tissue; however, unlike in tumors, this often doesdiseasenot lead to the sufficient formation of new blood vessels. »We would hope for new, functional →



This bone is very well supplied with blood (top).
Small branches sprout from the larger blood vessels (bottom).



The branching structures of the finest blood vessels can be studied particularly well in the retina of the eye (top) and in transparent fish embryos (bottom).

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Michael Potente

vessels to grow that would restore the supply – but here, the underlying disease prevents that from happening,« Potente explains. »If it were possible to specifically promote the growth of new blood vessels, this would have great therapeutic value.« Unfortunately, previous attempts to do so have not achieved long-term success.

Differing endothelia in different organs

Potente and his colleagues therefore intend to study how blood vessels differ across organs – in particular how the organ-specific environment affects the function of blood vessels. Their main focus here will be on the endothelium. Endothelial cells not only line the inside of all blood vessels, but are also responsible for stimulating their growth. »Interestingly, endothelial cells look very different in different organs,« Potente reports. »In the brain, for example, they are particularly tightly interconnected and form the blood-brain barrier; in the liver, the endothelium is permeable, enabling the organ's filter function.« These organ-specific functions are disrupted in many diseases. In diabetics whose blood glucose levels are consistently above normal, endothelial cells change over time and can lose specific properties, contributing to the common vascular problems associated with this widespread condition.

In order to discover the molecular and cellular mechanisms behind these differences, Potente was awarded a €2 million ERC Consolidator Grant from the European Research Council in 2017. It was also at this time that he came to Berlin regularly as a BIH Visiting Professor. Stiftung Charité supported this collaboration, which has been fundamental for the appointment, through its Private Excellence Initiative Johanna Quandt. He was invited by BIH Professor Holger Gerhardt. »I know very few scientists like Michael Potente who carry out innovative research at the highest level with such enthusiasm, curiosity and a keen sense of the most important issues,« Gerhardt says. »His work is constantly uncovering new connections and has a lasting impact on our understanding of the fascinating biology of blood vessels. I am hugely looking forward to working with him to further advance the translation of these findings into clinical practice.« From March 2021, the two scientists will team up with other colleagues to study »endothelial dysfunction,« as the improper functioning of the small blood vessels is known in medical jargon. The research will take place at the new Käthe Beutler Building on Campus Berlin Buch, which is scheduled to be completed by then. »Our vision is a university-based vascular outpatient clinic,« Gerhardt says, looking ahead to the future.

The aesthetics of blood vessels

As a cardiology specialist, Potente hopes to contribute his experience working at the interface between basic research and patient care – and thus strengthen the Focus Area »Translational Vascular Biomedicine.« »I am fascinated by the aesthetics of blood vessels and the principles behind their formation and, of course, by the possibility of one day making basic research applicable in the diagnosis and treatment of disease,« he says. This is a sentiment fully in line with the BIH's mission of turning research into health. •

Deubiquitinase USP10 regulates Notch signaling in the endothelium.
Science. 2019 Apr

Lim R, Sugino T, Nolte H, Andrade J, Zimmermann B, Shi C, Doddaballapur A, Ong YT, Wilhelm K, Fasse JWD, Ernst A, Kaulich M, Husnjak K, Boettger T, Guenther S, Braun T, Krüger M, Benedito R, Dikic I, Potente M. 364(6436):188-193. doi: 10.1126/science.aat0778