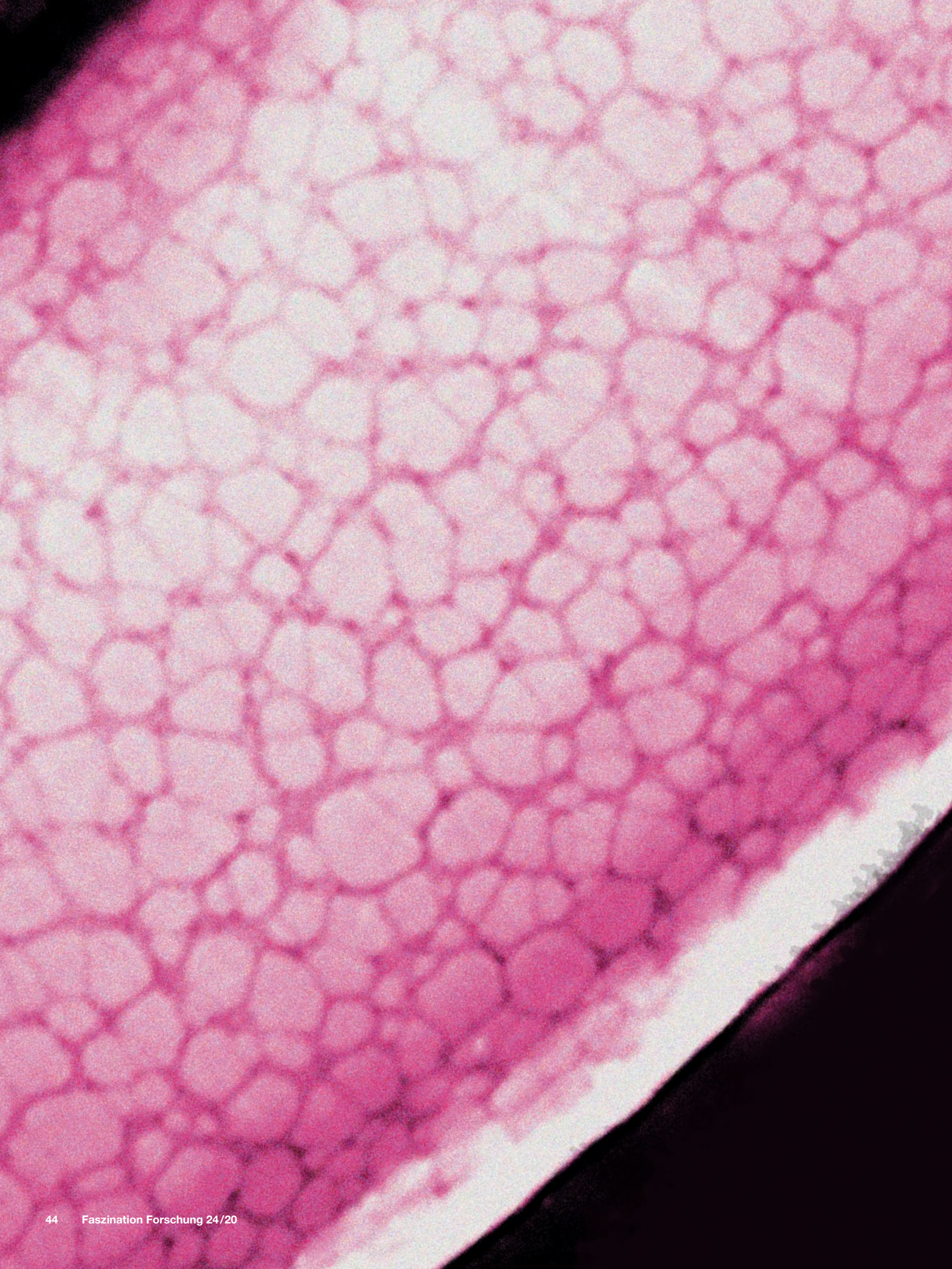
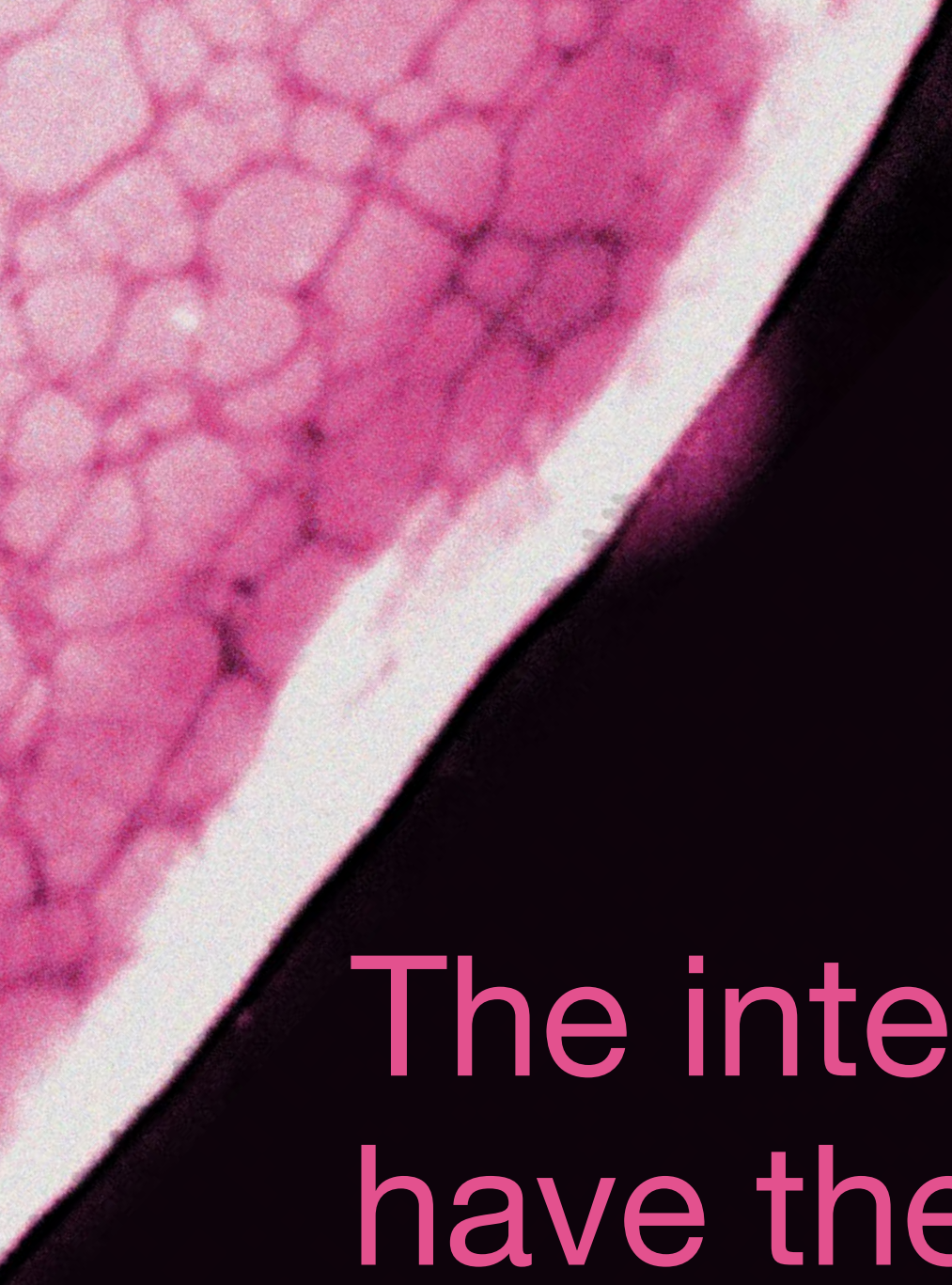
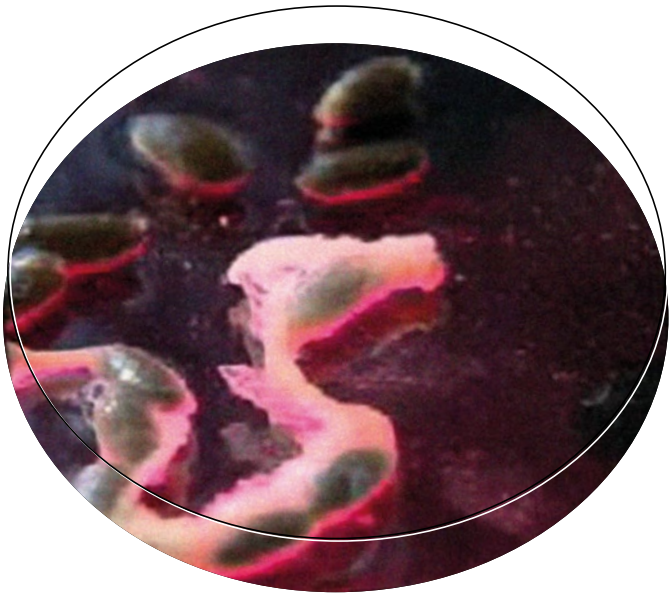




The intestines have their **own “brain”**

Prof. Michael Schemann has spent almost his entire career in research studying the “little brain in the gut” which autonomously controls the movements of our intestines. New methods from his working group have helped to finally identify the cause of some organic intestinal diseases. The challenge now is to turn these findings into benefits for patients.

Picture credits: Michael Schemann



An intestinal specimen is capable of moving outside the body. It performs regular muscle contractions, which researchers refer to as the "peristaltic reflex". This enables the intestine to move contents distally in a coordinated fashion (see fig. above and below).

The man has an urgent need to get some more ideas off his chest. Michael Schemann holds the Chair of Human Biology at TUM Weihenstephan and is one of this country's rare experts on an organ whose ideally silent performance we all have a decided appreciation for, but which we otherwise regard as somewhat unseemly: the intestines. Or to state it more accurately: Schemann conducts research into the intestines' nervous system (officially called the enteric nervous system), the "little brain in the gut" – although the scientist puts great emphasis on the quotation marks.

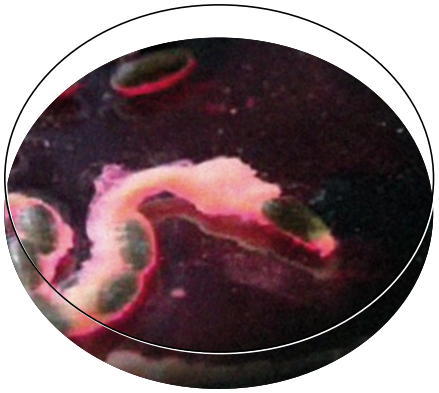
After all, it is obvious that the intestines can't think. Pain, emotions, intelligence – all the preserve of the large brain in our head. And we only feel pain in our gut if certain centers in the brain receive so many signals from the sensory pathways leading from the intestines that they make us aware of pain. But by strictly scientific criteria, the intestines also have their own small brain, he states.

You need proof? Schemann jumps up and hurries to his PC screen. He shows a film of a kind of sea cucumber twisting around in a petri dish and constantly contracting in different places. We are viewing a highly magnified, isolated intestinal specimen – and one that is clearly very much alive. Specimens, sections of animal or human intestines – whether the large or small intestine – can be preserved in culture for at least a week and perform their peristaltic movements there day and night with which they otherwise slowly carry chunks of food through the organism, from front to back and from top to bottom.

Uniquely autonomous organ

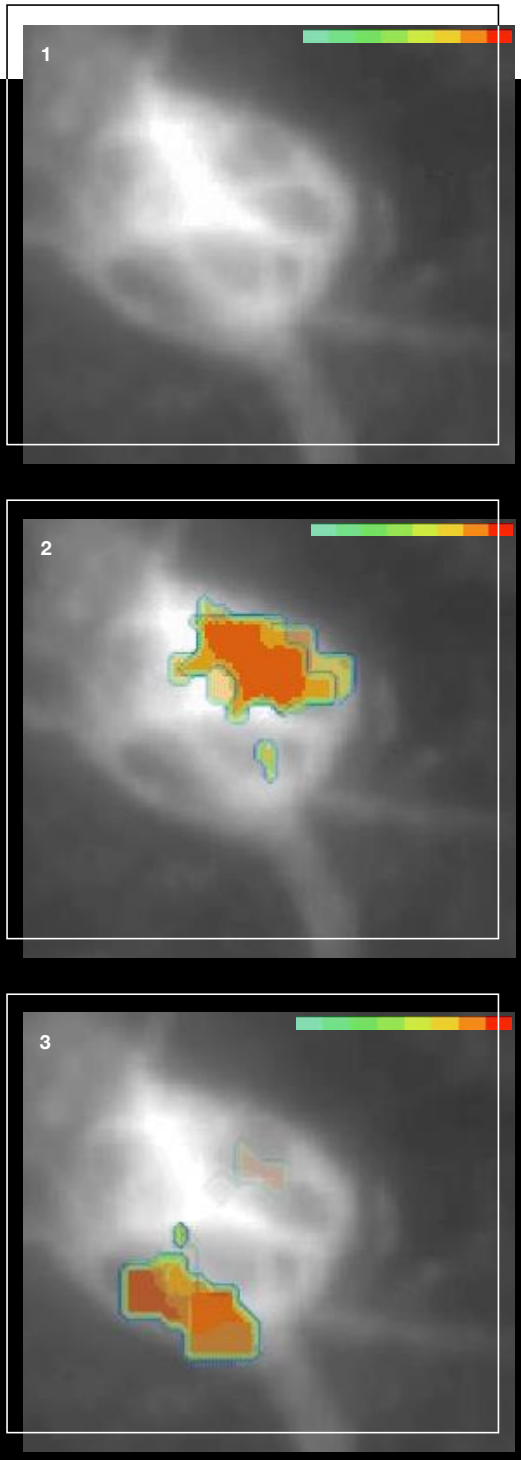
No other human organ can perform such autonomous movements when separated from the rest of the body and left to its own devices, as Schemann emphasizes. If you were to cut the nerve pathways from the heart, diaphragm or skeletal muscles to the spinal cord and brain, all activity would cease, he explains. But even in the smallest intestinal specimen – held in isolation – an autonomous nervous system continues to direct its movements. Schemann informs us instructively that a nervous system acting autonomously like this is called a brain in biology. Anatomically, the "little brain in the gut" is distributed across several nerve plexuses.

Schemann's group has developed new methods which enable the network to be identified for the first time. For many years, scientists were unable to access stimulus and information pathways in human intestines. It was not possible to capture the weak electrical signals from the "intestinal brain" with electrodes as is possible with many peripheral nerves and in the brain. "The network of nerves in the intestines is very delicate, and above all, the cells are in constant motion – which is not the case in the brain. You can't get near them with electrodes, they quickly break off," the scientist explains.



Making cells shine

Neuroimaging renders the work of nerve cells visible. Each activity is associated with a change in voltage. By using special voltage-sensitive dyes – the color of which changes in a flash – it is possible to view this process in ultra-slow motion and high magnification. This reveals which nerve cells are active and when.



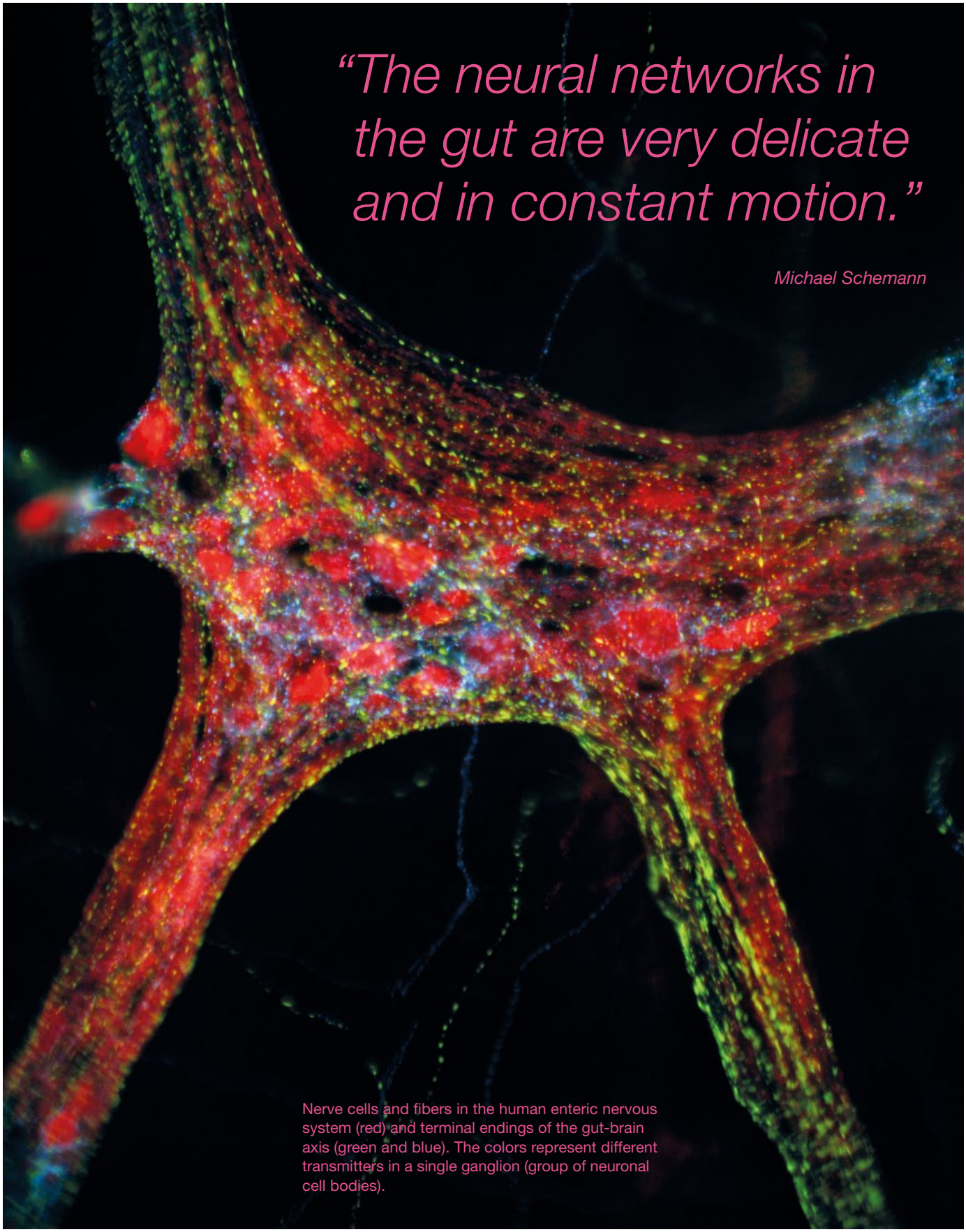
At the end of the 1990s, his staff developed an alternative. They adapted the method of neuroimaging in such a way that it could also be used in the intestines. To do so, the scientists place special dyes on the nerve cell membranes, the color of which changes in a flash if the voltage changes. The change of color when the nerve is stimulated only lasts a few milliseconds and can only be detected by the human eye at ultra slow motion and high magnification. Consequently, a high-resolution camera is used to film the experiments.

Understanding intestinal disorders such as irritable bowel syndrome

Drawing on such methods, Schemann's group was also the first to identify the foundations for understanding intestinal disorders which are clearly related to malfunctions in the "little brain in the gut" – e. g. irritable bowel syndrome. According to estimates, ten percent of the population in this country experience puzzling, intermittent over- or under-activity in the intestines: diarrhea or constipation. Inflammation is not the cause. But what are the reasons? There is a lack of diagnosis and causal treatment.

In 2009, Schemann's team succeeded for the first time in proving that false stimuli in the enteric nervous system play a key role in this syndrome. If you bring nerves in the "intestinal brain" into contact with substances secreted from the mucosa of irritable bowel syndrome patients, this triggers a whole storm of action potentials. And indeed, we can see the occasional red flash in the videos which Schemann now calls up on the monitor. "Every red flash reflects the activation of a single nerve cell," the researcher explains. However, if the mucosal supernatants originate from healthy people, the enteric nervous system remains calm and quiet. ▷

Picture credits: Michael Schemann



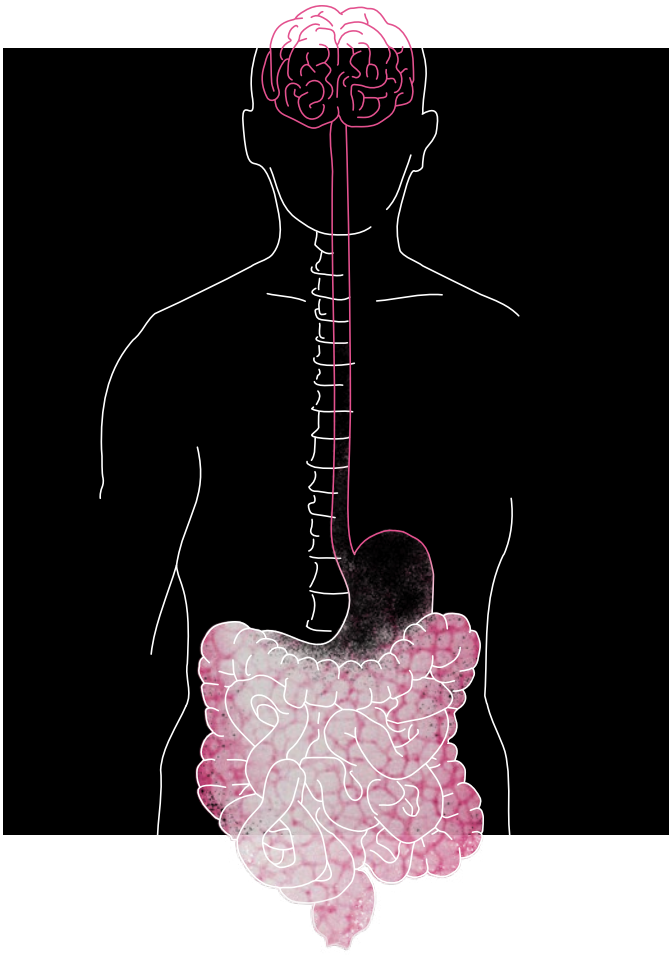
Nerve cells and fibers in the human enteric nervous system (red) and terminal endings of the gut-brain axis (green and blue). The colors represent different transmitters in a single ganglion (group of neuronal cell bodies).

The search has also been narrowed down to a few possible miscreants. The neurotransmitter serotonin, the immunomodulator histamine and above all some digestive enzymes that break down protein, so-called proteases, which can stimulate nerve cells via their own receptors, occur in such volumes in patients with irritable bowel syndrome that they lead to permanent overactivity of the "little brain in the gut". These are scientific findings that have attracted worldwide attention. However, concerted interdisciplinary cooperation is now required to ensure that we capitalize on this breakthrough. "We must combine the clinical data of many patients with such physiological tests on biopsies and intestinal specimens; then we will have a chance of developing reliable diagnostic markers and effective drugs against the disease," Schemann believes. But as he also points out, "It will be up to others to do that work." In less than three years, Schemann will be retiring. But as we said, the man is in a hurry to get some more ideas off his chest.

Bernhard Epping

Prof. Michael Schemann

Michael Schemann was born in Cologne in 1956. Identifying as a genuine native of the Rhineland, he studied agricultural biology in Stuttgart-Hohenheim – and obtained his doctorate there in 1985. As from 1989, this was followed by three postdoc years at the Ohio State University in Columbus, Ohio, USA. It was then and there that Schemann encountered the guru of research into the enteric nervous system: Jackie Wood. His habilitation in Hohenheim in 1990 was followed by two years at the MPI for Physiological and Clinical Research in Bad Nauheim, and in 1994 Schemann moved on to the University of Veterinary Medicine Hannover. Since 2002, he has held the Chair for Human Biology at TUM in Weihenstephan. Michael Schemann has won numerous prizes for his work. He is married and has one daughter.



The autonomous "little brain in the gut" is connected to the brain in the head via the spinal cord as well as the vagus and pelvic nerves, and can exchange information.

Picture credits: Michael Schemann, Astrid Eckert/TUM; Graphics: ediundsepp