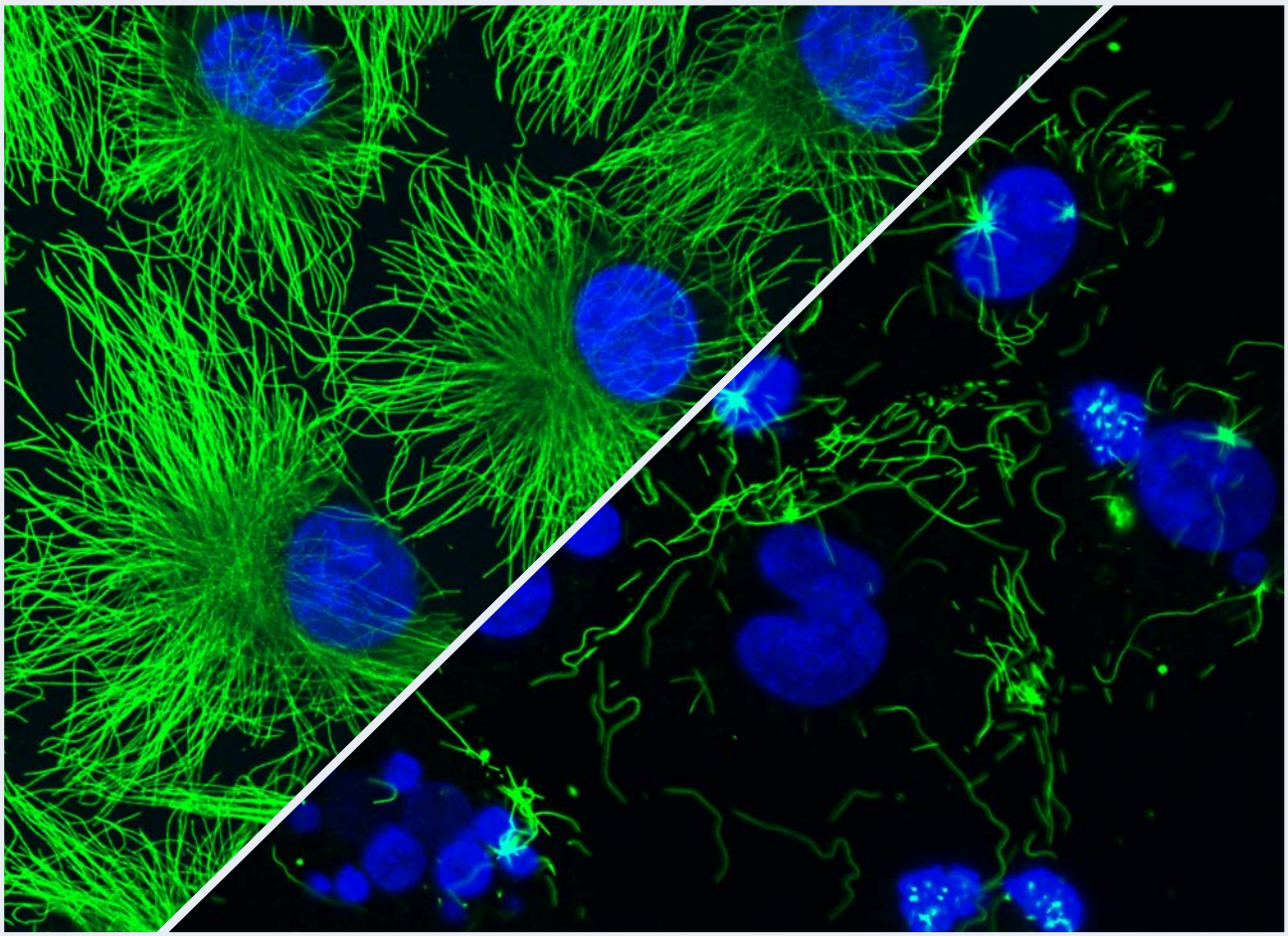
OTTO BAYER AWARD FOR PROFESSOR DIRK TRAUNER

Light switches for molecules

Professor Dirk Trauner, a pioneer in photopharmacology, has found a way of equipping molecules with a switch that specifically activates a cell's biological processes by exposure to light – a method that could help in cancer therapy, for example. The biochemist's research work has led to major advances in the field of optogenetics, an achievement for which he was recently honored with the 2016 Otto Bayer Award.

At present it is still science fiction, but it could soon be science fact: switching biochemical processes in the body on and off like a light switch, or specifically activating drugs only after they have reached their actual site of action. This would allow doctors to develop cancer chemotherapies that only target tumors, with almost no side effects. What sounds like wishful thinking could soon be reality. A team headed up by biochemist Professor Dirk Trauner from Ludwig-Maximilians-Universität Munich has succeeded in developing a molecular switch that can be controlled with light. These photoswitches change their chemical structure depending on the wavelength of the light to which they are exposed. In darkness, the light-sensitive hybrid molecules are inactive, but when exposed to short-wave UV light, the switch is flipped and activates the molecule. When exposed to long-wave light, the switch then returns to



Cell cultures treated with photostatins: when unexposed to light (left), microtubules (green) and cell nuclei (blue) are intact and clearly recognizable. Exposure to blue light (right) destroys the microtubules. The cells die and the cell nuclei start decomposing.

its inactive state. In a way, Trauner has taught molecules how to see. "Our retinas likewise have a switch that is flipped on exposure to light, which is what makes it possible for us to see things in the first place," explains the biochemist. In recognition of his research work, the 49-year-old recently received the 2016 Otto Bayer Award from the Bayer Science & Education Foundation. The award, endowed with EUR 75,000, has been awarded regularly since 1984 to scientists who have conducted pioneering research in the fields of chemistry and biochemistry.

Photostatins could revolutionize modern cancer therapy in the future

Trauner has been Professor of Chemical Biology and Chemical Genetics at Ludwig-Maximilians-Universität Munich since 2008. One concrete application for his photoswitch is cancer treatment. To this end, Trauner and his team have developed what are known as photostatins. These molecules are based on colchicine, a toxin that naturally occurs in the autumn crocus, to which a photoswitch has been added. Colchicine inhibits microtubule formation even before cell division. Microtubules, together with other proteins, are responsible for organizing intracellular movement and transport mechanisms. If the microtubules are inhibited, the cell is no longer able to divide. "So colchicine would be a good chemotherapy agent," says Trauner. However, its action also impacts healthy cells. "Its side effects would be too severe. So therapeutic use of colchicine is really not feasible," he explains.

Trauner's plan was to "modify the cell toxin in such a way that it is only toxic at the place where it is switched on." With photostatins, he has achieved just that. They are only active when they are exposed to blue light, and can therefore be controlled very precisely. A molecule modified in this way is therefore able to specifically prevent tumor cell division while leaving healthy body cells unaffected by treatment. "So doctors only have to shine a light on the tumor and leave the rest of the body in the dark to exert an extremely localized toxic effect," explains Trauner.

It will take some time before that becomes reality. "At the moment, we have only succeeded in doing this on the cellular level with simple study animals such as roundworms," says Trauner. But the most important first step has been taken. Says Trauner, "This kind of cancer therapy could be used above all to treat tumors that are accessible with LEDs, such as retinoblastoma – the most common form of eye cancer in children – and skin cancer or, using endoscopy, colorectal or bladder cancer." The photoswitch has already passed studies in cells with flying colors: when activated by exposure to light, the photostatins inhibited cell division 250 times more potently than in cells that were kept in the dark. "This dramatic light-induced activation exceeds anything that has ever been seen before in photopharmacology," says Trauner. It was made possible by a new method that he and his team used to incorporate the light-activated switch, which makes it possible to increase the activity particularly strongly.

Award: Werner Baumann, Chairman of the Board of Management of Bayer AG (left), and Professor Ernst-Ludwig Winnacker, Chairman of the Foundation's Board of Trustees (right) present the Otto Bayer Award to Professor Dirk Trauner.

Photoswitches can regulate microtubules temporally and spatially

But the opportunities offered by these photoswitches are even greater. The scientists were able to employ photostatins in all processes in cell biology in which microtubules play a role: including for example, in addition to cell division, intracellular transport and embryonic development. Using photostatins, scientists were able for the first time to precisely regulate microtubules spatially and temporally, and repeatedly switch them on and off within a fraction of a second. "For example, we were able to halt the development of a cell at a specific point in time and then switch it back on again to observe the further development of the cell. That could help us elucidate the role of certain precursor cells during development," explains Trauner.

The microtubules were just the beginning. The opportunities presented by photoswitches are nowhere near to being exhausted. Active ingredients that can be switched on and off as required with millimeter precision could dramatically reduce the side effects of many drug products in the future. ■

The Otto Bayer Award honors pioneering research

The Otto Bayer Award has been presented by the Bayer Science & Education Foundation since 1984 to scientists who have conducted pioneering research in innovative areas of chemistry and biochemistry. It is presented in memory of its endower Professor Otto Bayer, the inventor of polyurethane chemistry. The former Head of Research at Bayer AG (no relation to the company founder) promoted intensive contact to universities and supported the academic training of young scientists.

Photos: David Ausserhofer/Bayer AG (2), Peter Himsel/Bayer AG (1), Alf Mauritius Images (2), Taras Bezpalyi (1), Jérémie Christaller (1), Getty Images (1), Dirk Trauner/LMU (1), private (2)