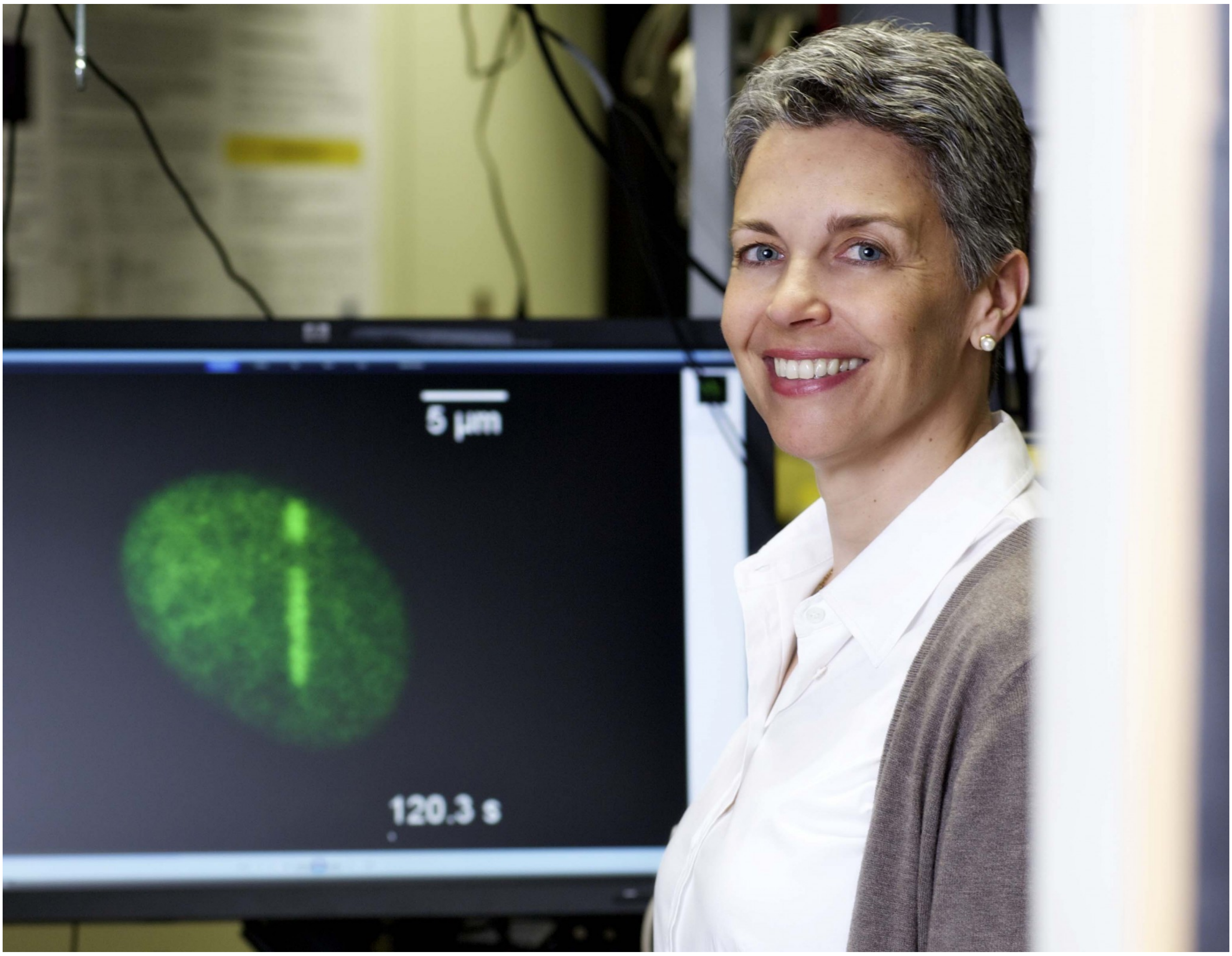
Elisa May: a sharp, microscopic look at DNA damage

DNA damage is part of our everyday life. Every day, tens of thousands of DNA single-strand breaks occur in every cell, but we have a variety of sophisticated genome maintenance mechanisms to protect ourselves against such problems. However, serious diseases can result in cases where the cellular repair system fails. Amongst other things, there is a close relationship between the failure of DNA repair mechanisms and the development of cancer. Professor Elisa May, director of the Bioimaging Center at the University of Konstanz, carries out research on living cells to find out how DNA damage is eliminated.



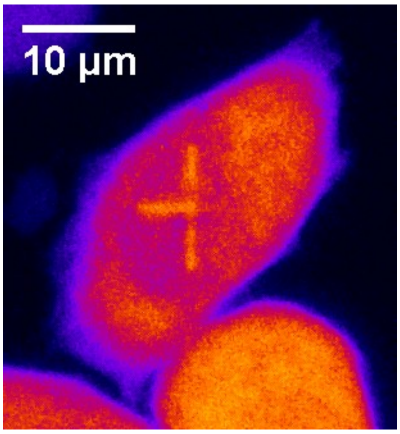
Elisa May, director of the Bioimaging Center at the University of Konstanz, uses confocal microscopes to study DNA repair processes.

DNA damage can have various causes: exogenous factors such as UV and other types of radiation or endogenous factors such as age-related decline in DNA repair capacity may lead to irreparable DNA damage. “DNA damage affects the primary structure of the double helix. Damage can affect either one strand, or both. In whichever case, DNA damage causes the DNA strands to split in two, which results in broken chromosomes. “DNA double-strand breaks lead to chromosomal rearrangements, i.e. deletions and translocations. A deletion occurs when a chromosome breaks and some of the genetic material is lost. A translocation is an abnormality that occurs when part of a chromosome breaks off and becomes attached to another chromosome,” May explains. Translocations are a frequent phenomenon of cancer cells.

Special microscope enables selective DNA damage

May and her team of researchers are studying the mechanisms associated with the repair of DNA damage in living cells. They study human cell lines under a so-called confocal scanning laser microscope. “The use of living cells has the huge advantage that DNA repair can be closely studied and analysed in real time,” said May. The excellent optical resolution of confocal microscope images is largely due to the technical capacities of confocal microscopes. In addition to the light source that all microscopes use to illuminate the sample under examination, confocal microscopes use point illumination to eliminate out-of-focus light. The lens guides the laser beam, which consists of ultra-short light packages (femtosecond pulses), through a pinhole so that the laser only illuminates one point in the sample at a time. May uses this laser beam to selectively damage the cell nucleus at specific sites. This is a major progression from previous investigation methods which have often damaged the entire cell.

Fluorescence-labelled molecules provide information about repair mechanisms



The photo shows DNA damage in the nucleus of a human tumour cell. The cross-shaped damage, which was caused by a laser, is visualised using fluorescence-labelled antibodies.
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In order to study DNA repair mechanisms, May labels certain proteins, i.e. DNA repair factors, with a fluorescent dye. These proteins are homogeneously distributed in cells with no DNA damage. Damaged DNA leads to the accumulation of the DNA repair factors at the site of damage, which is easily discernible from the fluorescent labels. The confocal image series can also be used for making diagrams that provide quantitative information about the activity of the repair factors.

Elisa May has put confocal microscopes to a completely new use: applying femtosecond laser pulses to selectively damage DNA, May was the first to show that it was possible to break DNA strands selectively using specific laser wavelengths. She was also able to show that there was a clear link between abnormal DNA repair mechanisms and the development of certain diseases. One of May's projects was carried out with researchers from the University of Zurich and focussed on XPC, a DNA damage recognition factor that plays a key role in the repair of UV-induced DNA damage. Children with moonlight disease have an abnormal XPC variant, which makes them very sensitive to sunlight. "Our investigations have shown that the way the variant repairs DNA damage is very different from that of the wild-type factor," said May.

Working with companies gives her access to the relevant research techniques and devices

Her research was made possible through cooperation with different companies. She initially worked with the company Zeiss, which supported her research by providing her with a suitable microscope. Currently, May is working with Rapp OptoElectronic GmbH from Hamburg in order to test new technologies for guiding laser beams across her samples. "Using conventional methods, the laser beam can only illuminate areas in the cell nucleus one after another," said May explaining the problem. "With Rapp OptoElectronic's help, we are aiming to couple an illumination device that is able to induce DNA damage simultaneoulsy at multiple locations to a microscope," May said.

May also works with other researchers from Konstanz University including a group of researchers led by Professor Alfred Leitenstorfer, a world-renowned specialist in elementary dynamic processes in matter and femtosecond laser technologies and head of the Department of Physics at Konstanz University. These projects are being carried out under the auspices of the Centre for Applied Photonics (CAP) in Konstanz. May's work is also supported by funding acquired by the University of Konstanz under the German Excellence Initiative which made it easier for her to purchase the expensive equipment she needed. It appears that the necessary conditions for obtaining new insights into the repair of DNA damage are now all in place.

About:
About: Elisa May studied biochemistry at the University of Tübingen and did her doctorate on photoreceptors in archaebacteria at the Max Planck Institute for Biochemistry in Munich. She habilitated at the University of Konstanz in 2005, carrying out research in the fields of cell biology and molecular toxicology. She has been the director of the Bioimaging Center (BIC) since 2008.

Further information:
Prof. Dr. Elisa May
Bioimaging Center
University of Konstanz
Tel.: (+49) 07531 88-4054
E-mail: Elisa.May(at)uni-konstanz.de