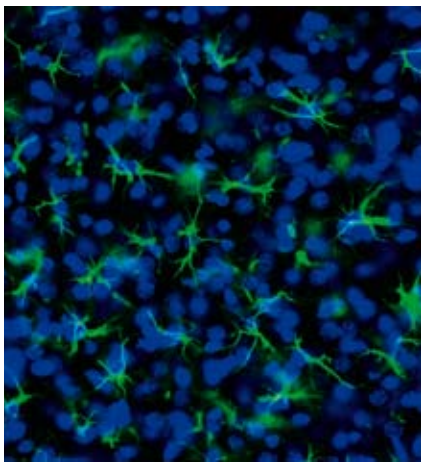
The Direction of Research – a Perspective

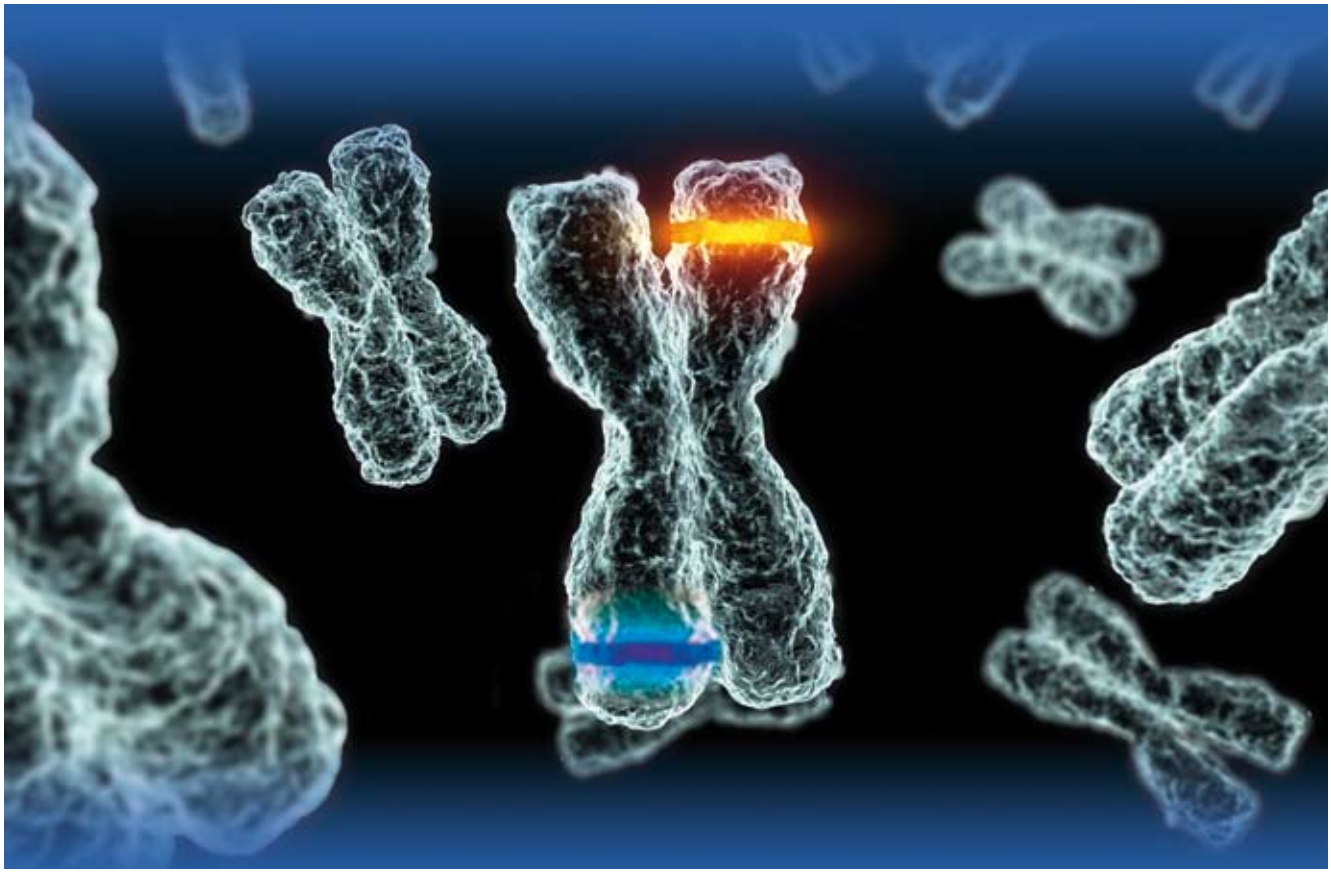
Strictly speaking, molecular imaging is not a new area of research. Nuclear physicians have been using scintigrams for decades to search for inflammation processes and tumors. For example, a patient can be injected with radioactive iodine that is exclusively concentrated by the cells of the thyroid. Using a suitable camera, the radiation can be rendered visible, thus providing information on the metabolism in the affected area.

However, those who search for the term "molecular imaging" in the Pubmed professional article database will notice a remarkable development. The first article containing this phrase appears in the year 1986 and describes a crystallographic analysis of the tobacco mosaic virus. In 2002, shortly after the publication of the "rough draft" of the human genome, 161 articles about the topic were published and in 2007 this number rose to 650. No wonder: molecular imaging is booming.

Enormous economic importance. This is also true from an economic perspective. Molecular imaging offers a wealth of new approaches for research and industry. And often the two areas overlap. An example: Nobel Prize recipient Prof. Manfred Eigen from Göttingen was originally interested in finding out how the reaction speed for very fast chemical processes can be determined. From this he developed an optical process to verify individual molecules. Together with a spin-off of the Göttingen-based Max Planck Institute, the Hamburg-based company Evotec and Carl Zeiss, the first commercially available fluorescence correlation spectrometer *ConfoCor* (see page 25, "The details") was manufactured in 1995. Since then, it has become possible to use this process to automatically filter out active ingredient candidates for a new medication from a quantity of substances. This is also due in part to the *ultra high throughput screening (uHTS)* method developed by Carl Zeiss. The original basic research turned into application research, which has enormous economic significance to pharmaceutical research. And this is only a new starting point for the broad field of medical and pharmaceutical research. If you consider the demographic development in industrialized nations and the new tasks for medicine that stem from this development, enormous growth potential emerges. This can also be gathered from the "Study regarding the Situation of Medical Technology in Germany Compared to Other Countries," which was published by the German Federal Ministry for Research in 2005. The study's authors estimate that the worldwide demand for medical products increased by 8.5 percent between 1991 and 2001. Within one decade, the global trade volume more than doubled from $30.1 billion to $67.7 billion.



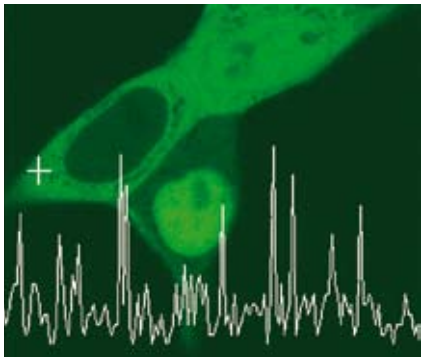
Brain cross-section (multichannel image with ApoTome).



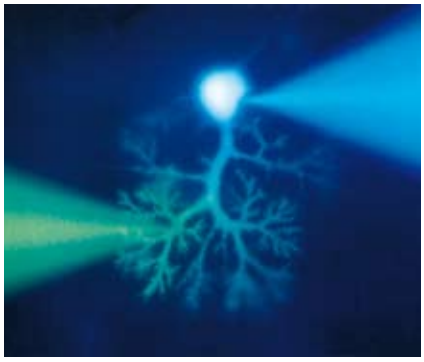
CAD view of complete chromosomes.

Many experts are convinced that the lion's share will fall upon molecular imaging. Market research company Kalorama Information estimates that an application-suitable PET label for the amyloid plaques of Alzheimer patients would have a market value of around $1.8 billion – during the patent-protected phase alone. Such perspectives have startled companies and research institutes around the globe.

High-pressure research. It is not a coincidence that the Center for Molecular Imaging Research (CMIR) was founded at Harvard University in Boston in 1994, for example. Based on the square footage of its laboratories, it has experienced equally explosive growth since that time. Several years after the founding of the CMIR, competition came from California in the form of the Molecular



Fluorescence fluctuation analysis



Neuron in the cortex of the brain, fluorescence

Imaging Program at Stanford (MIPS). Both centers are financed not only with public funds, but also draw on monies provided by industry. Intense research is also being carried out in Japan, Korea and Singapore.

It could seem belated that five leading companies, among them Carl Zeiss, established the German "Innovation Alliance of Molecular Imaging" in 2007 together with the Federal Ministry for Research. Perhaps that ship has already set sail? Michael Schäfers from the University of Münster does not think so at all. He believes that Germany is essentially well-positioned in the molecular imaging area.

"Although the American centers are very capable when it comes to basic research, our advantage still lies in our comprehensive clinical expertise."

Michael Schäfers

It is exactly this intensive cooperation between research and practice that is a not-to-be-underestimated advantage in making the leap to medical application.

A long wish list. However, clinicians would have to work closely together with their colleagues from other disciplines, says Schäfers: "It is not enough to have a medical issue. We also need the tools to work on this issue." And this is where industry comes in. The wish list of practitioners like Michael Schäfers or Berlin researcher Andreas Wunder is long: for example, suitable animal models had to be found, ligands and labels had to be synthesized and the required detection techniques had to be developed. And then, of course, there is the need for a software system so that the collected data can be visualized and analyzed. Then, German research in the area of molecular imaging will reclaim its rightful place: at the top of the winner's podium

The details

Search for active ingredients on the fast track

Ferreting out active ingredients for medications was still extremely costly several years ago. The objective was to filter out from large quantities of molecules those specific substances that might be able to form the basis for the development of new active ingredients.

Thanks to ultra high throughput screening (uHTS), today more than 100,000 samples can be examined daily. In so-called microtiter plates with a few microliters of sample volume, protein structures that play a key role in a disease can be systematically examined. They are tested for their interaction with potential active ingredients. As with molecular imaging in medicine, fluorescent probes also play a central role here. If they dock on to the sought molecules, weak luminescence can be measured. This occurs at lightning speed and can be precisely quantified. For example, an innovative uHTS process was developed by Carl Zeiss in Jena together with pharmaceutical company Roche and then sold to Hamburg company Evotec in 2005.