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Photo Glassubstrate: With „Slide A," Schott has developed a specially coated glass substrate for the immobilization of biomolecules. Pharmaceutical researchers use this substrate to compare the genetic activity of healthy and diseased cells. (Photo: Rainer Meier)

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Increasing **Efficien**

With "Schott Slide A" Schott has developed a coated substrate for microarrays that makes it possible to carry out a more reliable analysis of DNA activity.

Analyses of DNA chips play a key role in pharmaceutical research and development. They make it possible to carry out gene expression analyses of healthy and diseased tissue samples at high throughput rates. The more reliable these initial results are, the more accurate the development of appropriate drugs.

Facing new challenges

The pharmaceutical industry's search for new drugs still involves pursuing a long-drawn-out and often difficult process. Rather like the old gold diggers, who once had to wash tons of sand to stumble across a few grains of gold, chemists and biologists have to test myriads of combinations of DNA to track down one potential candidate for an active ingredient.

Currently, the heavily research-oriented industry finds itself at the beginning of a new era: the costs of developing new drugs are exploding, as are expectations that functional genomic research will reduce both the time and cost factor involved in the technological process. The objective is not only to identify a large number of potential new active ingredients, but also to speed up and rationalize the pre-clinical research process. Today, it still takes on average twelve to fifteen years from the identification of a potential active ingredient to the finished drug.

New coated substrate glasses for the immobilization of biomolecules are also available with bar codes which allow customers to trace a DNA chip from its final analysis back to the production batch.

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Within a short time frame, Schott has installed a new biological laboratory and developed coated substrate glass for DNA chips. Next to research activities, application tests can also be carried out in the new labs.

A quicker route to new pharmaceutical active ingredients

What are the possibilities of reducing these development times which would be totally unacceptable in other key technologies? In the clinical testing phase, the possibilities are quite limited due to considerations regarding patient safety. The focus has been shifted to the earliest possible stage of active ingredient research. One promising approach lies in identifying the genes responsible for the emergence of the disease in the first place.

In pharmaceutical research, one way to identify disease-relevant genes is the use of DNA microarrays. In this process, which is derived from semiconductor engineering, a specially coated glass substrate material is printed with genetic material known as the probe DNA. There are several alternative technologies available for this: e.g. contact printing, adapted inkjet printing and photolithography. Because several hundred thousand gene fragments are located on the substrate, hybridization experiments can be carried out in parallel at high throughput rates. This involves placing fluorescence marked DNA target molecules taken from cells or tissue onto the substrate. If the probe DNA immobilized on the substrate matches the target DNA originating from the sample material, the two complementary single sequences hybridize to form a DNA double sequence. The fluorescence marking makes it possible for specially developed scanners to verify the hybridized DNA molecules.

Double innovation

With the market launch of "Schott Slide A," Schott has succeeded in offering a coated substrate which makes the evaluation of gene expression experiments safer and at the same time leads to reproducible results for use in pharmaceutical research. The core of the innovation is a multi-amino-silane coating on a special Schott borosilicate glass.

In contrast to conventional products the multi-amino-silane coating achieves a stronger binding of DNA probes across a higher number of "docking points," which amounts to greater sensitivity. "In the evaluation of gene expression experiments the excellent material properties of the borosilicate glass used show up very positively," adds Dr. Dirk van den Broek, Executive Vice President of Schott's "Health" Business Segment. The glass has a very low inherent fluorescence which results in an excellent signal to noise ratio. Together with the extremely flat surface of the glass, which largely puts a stop to irregularities in printing and detection, the results of DNA microarray applications can be evaluated more reliably than before.

People involved in pharmaceutical drug discovery research are looking to increase the reproducibility of the results from all the technologies used. The reliability of the initial data is of major economic importance for the pharmaceutical industry, in order to select those active ingredient candidates with the best prospects. The early sorting out of possible "flops" will lead to more efficient drug disovery research and ultimately to cost savings running into the millions.

Schott "Slide A" glass substrates are subjected to a strict quality control in order to ensure reliability and top product quality. Above, the slides are undergoing a visual inspection.

Dr. Udo Ungeheuer, Schott Management Board member and Dr. Dirk van den Broek, "Health" Business Segment Executive Vice-President on Schott's entry into a promising market.

Becoming **Partners**

Schott's innovation offensive is getting a further boost from its new "Health" business.

What goals is Schott pursuing with its new activities?

Dr. Ungeheuer: As a technology trendsetter we are developing advanced technologies for mass production. The "Health" Business Segment, with its microarray products and services is aiming to become a reliable partner to the pharmaceutical industry for its research into active ingredients. Our motto: quicker, better, more efficient.

What makes Schott eminently suitable for this partnership?

Dr. Ungeheuer: As a special glass manufacturer we have many years of experience with laboratory glass and pharmaceutical packaging plus extensive coating know-how. At the same time we are now a leading supplier of glass substrates to microarray manufacturers.

What benefits does Schott offer its customers?

Dr. van den Broek: The pharmaceutical industry has to face increasing development costs. It can take up to 15 years for a potential active ingredient to be developed into a drug. The reason for this are long, but prescribed clinical tests. Our future products will help in the preliminary phase to identify with certainty those active ingredients that have a very high degree of probability of passing the tests. This means enormous savings and improves the efficiency of pharmaceutical research.

What is the main emphasis of your activities?

Dr. van den Broek:
The internationalization in the pharmaceutical industry calls for activity on a worldwide scale. The business segment is managed from Mainz – supported by our Research and Development department in Marienborn – and controls international sales and marketing, too. The product development for Health was done at Schott Glass Technologies in Duryea (USA). The pilot production facilities for the coating of substrate glasses is there too. The first phase of series production is planned to take place in the biotech region in Jena, Germany.

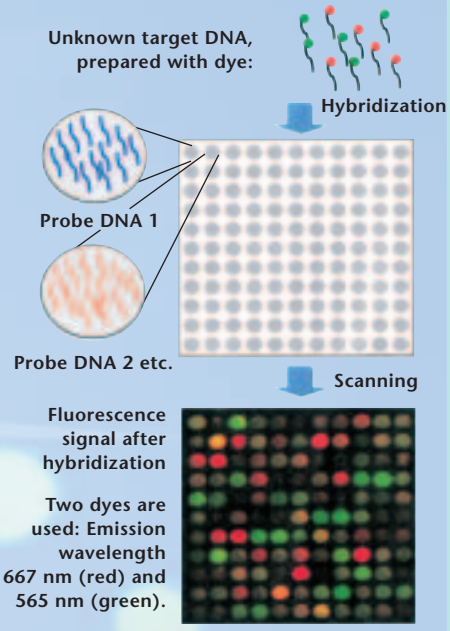
Microarrays: Ingeniously simple

The identification of a DNA sequence by hybridization appears to be relatively straightforward. But is it possible to identify a whole range of DNA sequences in a single step? The trick is to keep track of the known DNA sequences, or targets, being used.

A microarray handles this task in an elegant way: In its simplest form it is a surface with a grid. The grid is formed by the various sorts of probe DNA, rather like a chessboard. However this chessboard can fit several hundred thousand squares in the space of a square centimeter. If hybridization takes place on one square, it is possible to trace back what sequence the probe DNA on this square had and in this way the unknown target DNA can be clearly identified.

An optical process has been established to verify the hybridization. Before hybridization, the unknown DNA sequences (targets) are prepared with a dye which fluoresces when excited by a laser. After the hybridization, all target DNA that has not found a partner on the chip is rinsed off. The remaining bound target DNA produces a signal in the form of a matrix of dots in which each dot represents a different DNA sequence. The more intensively the dots light up, the more probe DNA is bound there, making it possible to determine in one step not only which sequences are present, but also how many of them.

By using two dyes it is possible to compare two different target DNA directly on one array. The signal is a multicolor matrix of dots made up of individual colors in compound tones.



What role does "Health" play within Schott?

Dr. Ungeheuer: The "Health" segment covers the production of uncoated and coated flat glass products for DNA microarrays. We are building on these, creating new products and investing in start-up companies that are developing innovative microarray technologies. The know-how obtained through this is being used to set up new businesses of our own, such as the provision of services for pharmaceutical drug discovery.

Dr. van den Broek: "Health" is a new and promising segment and an example of how we are combining existing and new competences, and thus opening up new markets. That is exactly the purpose of our innovation offensive. And with "Schott Slide A" we are now on the very brink of the market launch and in so doing are taking a major step towards setting up the whole business. Speed is one of our success factors: it has taken us less than a year to develop this product to a marketable state.

Who are the first possible customers?

Dr. van den Broek: Initially interest is being shown by the biotechnology industry, manufacturers of microarrays, pharmaceutical companies, universities and institutes. Coated substrates went on display for the first time to a broad specialist audience at the "Eurobiochips" exhibition in Berlin in June. Additionally we are training staff at Schott sales companies around the world to ensure success in major foreign markets too.

Have you received feedback from any interested parties?

Dr. Ungeheuer:
Yes, and we are especially proud of the response from a major US laboratory, which rated our products as 'among the best'. This means that our pilot production has already achieved the high standard of quality of other products in series production. ◂

The interview was conducted by Thilo Horvatitsch

Interview