Screening

Background

Methods of rapid analysis and diagnostics have been investigated intensively in the past. It seems that the quantitative approach of analyzing biological systems has been especially successful. One example is the consequent development from PCR to DNA-micro arrays. Another example are the screening methods used by pharmaceutical companies. The application of screening methods is not limited to a search for cures of disease. Screening methods have entered several fields of application and have reentered the biological sciences on a different scale, like for example Proteomics. However screening is not limited to the molecular level, it is also useful on the cellular scale.

The terminology used in screening

- HTS: high throughput screening. HTS utilizes the properties single molecules and is often carried out on the interaction molecules.
- UHTS: ultra high throughput screening - more than 100 000samples / day.
- HCS: high content screening. HCS is an approach that utilizes a more complex environment than single molecules. It uses for example high-resolution fluorescence images for analysis of cell based measurements. HCS is sometimes used for lead optimization of HTS.
- Target: Investigative aim, generally a gene or protein.
- Hit: A hit is a substance with a positive result in the screening assay and therefore a possible lead.
- Lead: A lead is a hit that has proven to have specific effect on the target. Lead verification is often done in HCS.
- Hit to lead relation is a means of classifying a screening assay.

Together with combinatorial chemistry or substance libraries the number of testable substances is seemingly infinite. Combinatorial chemistry is also used for lead optimization. The screening process in the pharmaceutical industry is embedded in a line of product development that encompasses basic research via target discovery, target validation, lead verification, clinical research, and scale up production leading to launch of a product. For researchers in a university environment more or less the same is applicable with the publication of the discoveries at the stage of the clinical research.

Several quantitative techniques in fluorescence microscopy have proved their values in screening assays among these are:

- FRET: fluorescence resonant energy transfer
- FLIM: fluorescence lifetime imaging
- FCS: fluorescence correlation spectroscopy
- FRAP: fluorescence recovery after photobleaching
- Time resolve fluorescence
- FP: fluorescence-polarization or anisotropy
- Fluorescence reporters

The accuracy of the measurements depends on the understanding of the biological background on which the measurements are performed. A great variety of fluorescent labels are available for countless of applications. For a quantitative conclusion the quality of the measurements need to be validated, for example by cross checking the signal with a second reference staining.

Screening the iMIC way

- With the iMIC, TILL Photonics presents a novel fully motorized imaging platform. The iMIC provides the basis for complex, automated image acquisition and analysis tasks, has been especially designed for either quantitative or routine measurements.
- The iMIC is an automated microscope with full software control. In combination with the included Software it is the base for your fluorescence application. It is the workhorse solution for automated screening, laser scanning, or imaging, or routine microscopy.
- The standard three motorized levels allow the selection between up to 4 objective lenses with a revolver at the top level and two sliders on the two lower levels allow switching between filter sets and tube lenses. The tube lenses slider also permits output light to be switched between several detector ports. The filter sets or tube lenses can easily be replaced by hand within a few seconds.

Requirements

For optimal results a complex system is needed. TILL supplies the complete platform for image acquisition and analysis. It has to be kept in mind that several other experimental bottlenecks might arise and, for example, a pipette robot might be needed.