IN THIS ISSUE

Comprehensive Characterization

The incidence of liver disease is continuously increasing. The study of stem cells is expected to increase our knowledge of the pathogenesis of liver disease, and to facilitate the development of novel therapeutic approaches. The liver is a complex tissue, composed by a variety of mature cellular elements deriving from different lineages. So far, these intrahepatic compartments have not been comprehensively characterized at the stem cell level. Porretti and co-workers used flow cytometry and cell culture assays to study the adult human liver samples from both healthy and diseased individuals. They demonstrated that four stem cell compartments –i.e. epithelial, endothelial, hematopoietic, and mesenchymal –are present in adult human liver, and showed how these cells can be identified on the basis of their phenotypic profile. This study provides a useful background for future experiments focusing on the role and interactions of different cell lineages in the pathogenesis of liver disease.

In this issue: page 31

Organotypic HCS

The use of angiogenesis inhibitors for cancer treatment has spurred interest in discovery-oriented chemical biology strategies to elucidate both the basic mechanisms and therapeutic opportunities afforded by the regulation of new blood vessel formation. However, physiologically relevant angiogenesis models based on primary human vascular cells are generally incompatible with high throughput-screening formats. Evensen and co-workers describe a novel imaging-based, HTS-format organotypic assay comprising early passage, primary human vascular cells that models several facets of blood vessel formation and maturation. Co-cultured primary human vascular cells self-assemble into a quantifiable network of tubular, basement membrane enveloped, capillary-like structures via heterotypic cell-cell interactions and paracrine growth factors. The authors demonstrate that automated image-based high-throughput screening of chemical libraries using this primary human cell-based assay can reveal new insights into the molecular mechanism of blood vessel formation and identify novel anti-angiogenic agents.

In this issue: page 41

Bringing cellular structure into focus

To characterize the state of a cell, its physical structure is equally important to its gene expression patterns and signaling activity, for example. In mammalian cells, the main determinant of cellular structure is the actin cytoskeleton, a dynamic system of biopolymers which determines mechanical stability and coordinates many essential spatial processes in the cell. Weichsel and co-workers now have established an automated workflow which quantifies changes in the actin cytoskeleton combining high-throughput microscopy with model-based image processing. The new approach was successfully benchmarked for pharmacological perturbations of the actin cytoskeleton and then applied to characterize the changes induced by HIV-infection. The study of Weichsel and co-workers demonstrates how cellular structure can be approached by quantitative microscopy and thus constitutes an important advance in regard to the long-term goal of achieving a systems-level characterization of cells.

In this issue: page 52

Divide and conquer - assessing image quality on a sub-image level

Automated high-throughput microscopy has developed into an indispensible screening tool for biologists. The collection of high quality image data, e.g. for single cell analysis, requires strategies that autonomously assess the quality of large numbers of images, preferably already during image acquisition rather than at the end of the image processing workflow. In this context, the analysis of subdivided instead of entire images can be advantageous because it mimics the human strategy of judging images, i.e., the overall quality of an image is probably low if parts of the image are of low quality. Such subdivided images will thus provide superior input both for image autofocusing (Cytometry A 2009;75A:781-788) and for the rapid automated quality assessment by machine learning approaches (e.g., artificial neural networks).

In this issue: page 76

Noise, Accuracy, and Resolving Power

Visual analysis of 3D fluorescent microscopy images containing many and sometimes overlapping point-like signals is a time consuming and problematic task. Automatic detection and quantification of signals is of great importance in many areas of biological research. In addition, localization of the subcellular signal position is important for many applications, as described in previous work from the Allalou and Pinidiyaarachchi groups (Cytometry A, 2009; 75:319-28). In their current offering, Allalou, Pinidiyaarachchi and Wðhlby propose a new method for robust detection and localization of signals in 3D image data. Compared to conventional methods, this method shows better robustness to noise and good ability to resolve signals that are spatially close. Tests also conclude that the method has equivalent accuracy in signal detection in comparison to visual detection by experts.

In this issue: page 86