MetaSystems White Paper

Colony Finding with Metafer MSearch

Introduction

Because of mosaicism among embryonic cells it is usually required to analyze a relatively high number of amniotic cells in prenatal cytogenetic studies, thus increasing probability that metaphases from all *clones* are inspected. A common method to overcome this obstacle is the analysis of *in-situ* slides with various colonies (each representing a single *clone*). The sample is grown in a highly potent medium, so that cells divide quickly and form colonies containing a considerable number of genetically identical metaphases. With this method the researcher gains information about the number of *clones* present and can assign analyzed metaphases to the respective *clone*.

Preparation of clone slides can be principally done in two ways:

1. Cells are grown in culture dishes or flasks on coverslips (usually made of plastic to allow for better cell adherence). Coverslips are subsequently mounted onto a standard glass slide.
2. Cells are grown in dedicated culture chambers (e.g. Lab-Tek™ from Thermo Scientific). For preparation of the slide the side walls of the chamber can be removed, so that the bottom of the slide can be used as slide for microscopy.

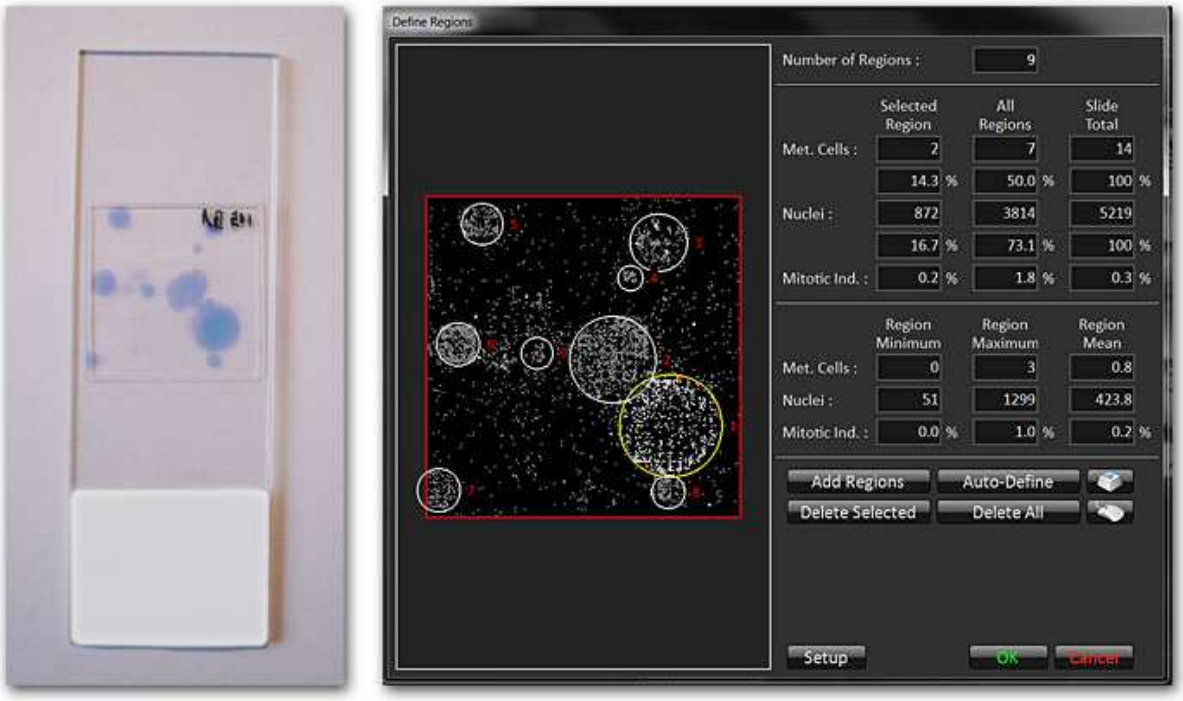

Fig. 1: Slide with coverslip and *clones* of amniotic cell culture (left). The right panel shows the results of coverslip detection, metaphase finding, and automated region detection. Results for each region can be displayed separately. In this dialogue window also the parameters of automated region detection can be tested and adapted.

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Functionality

Independently of the preparation method there are certain requirements for analysis of clone slides. If an automated metaphase finder is used, functionality to cover these requirements should be present. The automated metaphase finder **Metafer MSearch** includes the following tools to help for clone slide analysis:

1. Automated Detection of Coverslips
   Location and orientation of the coverslip is automatically determined by locating its rims, and the search window is adapted to these findings.
2. Automated Metaphase Finding
   Metaphases are detected automatically, and their positions on the slide are stored. Additionally gallery images of detected metaphase are created.
3. Region (Colony) Detection
   Regions are detected and receive a unique identifier. Colonies can be detected either based on the nucleus distribution or based on the metaphases. The algorithm accepts regions of different sizes. Target regions are defined by parameters such as the min. nucleus or metaphase count (relative or absolute), or the min. relative nucleus density.
4. Quality Ranking of Metaphases
   Each metaphase receives a quality score based on user preferences.
5. Acquisition of Best Metaphases per *Clone*
   Based on the quality rank, a pre-defined number of (best) metaphases per *clone* is automatically acquired at high magnification (with **AutoCapt** software).
6. Acquisition of Outlying Metaphases
   Metaphases which are not part of a *clone* can also be acquired by **AutoCapt** and exported to **Ikaros** karyotyping systems. Outlying metaphases automatically receive a '0' as *clone* identifier.
7. Transfer to Analysis Stations
   Metaphase images are automatically transferred to any **Ikaros** karyotyping system in the network. After export the metaphases are immediately ready for analysis, even if other slides of the same case are still being scanned. The *clone* identifier and the total number of clones are transferred with the image.
8. Convenient Review Functionality
   Metaphase images in the gallery of **Metafer MSearch** can be selected or sorted based on the region number. It is therefore easily possible to review metaphases *clone* by *clone*.

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