Preface

Human molecular cytogenetics goes multicolor

Chromosome-banding is still the gold standard for all routine techniques of clinical and tumor cytogenetics, however, the technical restrictions are well known. As chromosome morphology combined with a black and white banding pattern are the only two parameters to be evaluated, changes exclusively within the normal pattern such as size variations in a chromosomal band or the chromosome itself and changes of the centromere index can be detected. Thus, the origin of additional material in a structurally altered chromosome often remains questionable. To overcome such limitations fluorescence in situ hybridization (FISH) approaches were introduced into cytogenetics in the 1980s and the new field of 'molecular cytogenetics' was established. In recent years the main progress of this area has been the invention of multicolor-FISH (mFISH). mFISH assays are nowadays indispensable for a precise description of complex chromosomal rearrangements and research. Routine application of such techniques on human chromosomes started in 1996 with the simultaneous use of all 24 human whole chromosome painting probes in multiplex-FISH (M-FISH) and spectral karyotyping (SKY). Since then different approaches for chromosomal differentiation based on multicolor-FISH (mFISH) assays have been described. Predominantly, they were established to characterize marker chromosomes, which has high clinical impact and is a requisite condition for further molecular investigations aimed at the identification of disease-related genes.

The present themed issue of Cytogenetic and Genome Research focuses on the developments in the exciting, inspiring and continuously progressing mFISH field. It highlights the developments including their advantages, limitations and possible applications. It is divided into four sections starting with a more technically orientated part, reviewing the main mFISH-techniques. The first focus is the basic mFISH approach, which applies all human whole chromosome painting libraries as probes, and which is described as M-FISH (L. Kearney), SKY (E. Schröck) and COBRA-FISH (Raap and

Tanke). Combinations of M-FISH with other probe sets or techniques are presented in the contributions of Stewenius et al. (subtelomeric probes), Ye et al. (immunostaining) and Weimer et al. (microdissection). Several chromosome banding techniques based on mFISH, referred to as FISH-banding techniques, were recently introduced and they are summarized in the contributions of Liehr et al., Müller and Wienberg, and Kakazu and Tatsuo. Apart from FISH-probes produced by microdissection, flow-sorting or by molecular genetics (e.g. cosmid, BACs, YACs) there is a fourth group, the PNA-probes which are suitable for mFISH applications – these are summarized in the contribution of Pellestor et al. at the end of this first part of the themed issue.

The remaining three parts concentrate on mFISH applied in tumor cytogenetics, clinical genetics and three special research fields (see below). The value of mFISH approaches in the diagnostics of leukemia, of lymphoma and even of solid tumors is shown exemplarily in the contributions of Mkrtchyan et al., Adam et al. and Junker et al. As these three aforementioned contributions have already shown, in tumor cytogenetics diagnostics and research are closely related since the characterization of complex chromosome aberrations has a high impact on learning more about tumor development and progression. Thus, also the detailed mFISH characterization of cell lines, as shown for a thyroid cancer by U. Weier et al., should nowadays be a standard clinical procedure before applying them in further molecular research.

The third part of this themed issue is about mFISH in clinical genetics, and here the same holds true as for tumor (cyto)genetics: diagnostics and research can hardly be separated. mFISH is applied to detect numerical chromosomal aberrations in prenatal as well as PGD diagnostics (Stumm et al.) and in meiosis or PID-related research (Oliver-Bonet et al., F. Weier et al., Cooper et al.). Apart from detecting numerical aberrations the main problem of clinical (cyto)genetics is the characterization of structurally rearranged chromosomes, which easily can be faced by mFISH approaches. Examples for marker chromosome characterization are presented by six different contributors. Larger marker or deriva-

tive chromosomes are defined by different molecular cytogenetic approaches in the work presented by Dufke et al., Thienpont et al. and Barber et al. A special problem in clinical cytogenetics is the worldwide 2.5 million patients comprising a group of individuals with a small supernumerary marker chromosome (sSMC). This still sparsely studied cytogenetic group is represented here in three contributions, as mFISH is the method of choice to characterize sSMC (Brecevic et al., Tönnies et al. and Sarri et al.). The last paper of this section combines FISH with the newest field related to cytogenetics, i.e. comparative genomic hybridization on chip = array-CGH. The work of Kashork et al. is an example of how to combine molecular cytogenetics and array-CGH. Already now and even more in the future such studies will lead to a previously almost impossible accuracy of breakpoint characterization.

In the fourth and last section of this themed issue two special mFISH applications are presented. Rudolph et al. show that mFISH studies performed with murine probes in a mouse lymphoma allow inference on tumorigenesis in the homologous human tumor. Walter et al. show the possibilities of characterizing the human interphase nuclei by mFISH-approaches.

We wish to express our gratitude to all those who have contributed to this project. Only due to their efforts are we able to present a comprehensive and timely collection of the state of the art of Multicolour FISH in Human Cytogenetics.

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