

Editorial

Genes, chromosomes and cancer

About 70 scientists recently attended the conference on "Aneuploidy and Cancer" in Oakland, CA, which was organized by P. Duesberg and D. Rasnick from the University of California, Berkeley, and generously sponsored by philanthropist Robert Leppo. The conference explored whether aneuploidy, i.e., specific genomic imbalances, is a driving force behind the development of cancer. A century ago this theory was first suggested by the German biologist, Theodor Boveri, who hypothesized that the gain or loss of promoting and inhibiting chromosomes, respectively, results in aberrant cell division and tumorigenesis. Boveri suggested that "malignant tumors might be the result of a certain abnormal condition of the chromosomes which may arise from multipolar mitosis. Abnormal mitosis may bring about an immense number of different chromosome combinations, such combinations as would make a cell into a tumor cell *must* occasionally occur". Despite the fact that quantitative measurements of the nuclear DNA content unequivocally demonstrated that cancer genomes are frequently aneuploid, the main focus of scientific research regarding the genetic basis of cancer shifted towards the role and involvement of single, specific genes. This development was also promoted due to the emerging of molecular cloning and hence the identification of oncogenes and tumor suppressor genes. However, the identification of centrosome abnormalities in tumors, the clarification that telomere defects can result in unbalanced chromosomal translocations and genomic imbalances and the application of novel molecular cytogenetic techniques has clearly demonstrated that chromosomal aneuploidies play a central role in the genesis of epithelial tumors. Both, the successful implementation of nuclear and chromosomal aneuploidy as a molecular target for cancer diagnosis and prognostication has solidified the fundamental role of aneuploidy and rekindled research interest into its origin. Moreover, several clinical stud-

ies showed that aneuploidy played a role already at the beginning of the multistep neoplastic process, i.e. in premalignant, preinvasive dysplastic lesions. For instance, numerous studies have shown that the specific gain of chromosome 7 occurs in colonic polyps before mutational inactivation of the tumor suppressor gene p53. Similarly, in assumingly premalignant lesions of the oral mucosa, i.e. erythro- and leukoplakias, cases of aneuploidy were shown to have a 70% malignant transformation rate within 3 years and a similar mortality rate within 3 years of patients after the development of a cancer. We now know that the dynamic genomes of pre/malignancies are defined by the sequential acquisition of chromosomal aneuploidies that are specific to a particular type of tumor and that are continuously selected for under conditions of prevailing genomic or chromosomal instability. The observation that aneuploidy as an indicator of genetic instability is an early event in the process of neoplastic transformation has stimulated new interest into the biological processes that determine genetic instability. One of the goals of the conference was to discuss the relative role of aneuploidy and gene mutations for tumorigenesis, a question that was at times hotly contested. However, it should be obvious by now, that aneuploidy reflects a core genetic aberration that results in cellular immortalization and transformation. We therefore hope that future conferences specifically dedicated to this problem will continue exploring and discussing the genetic basis of aneuploidy and the translational prospect of aneuploidy when applied to cancer screening, diagnosis, prognostication and therapeutic intervention.

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