

Contents

1	Introduction	1
1.1	General introduction	1
1.2	Interphase and metaphase chromosome structure	1
1.2.1	The organization of DNA in the nucleus	1
1.2.2	Eu- and heterochromatin	3
1.2.3	Chromosome banding and nomenclature	3
1.3	Karyotypic analysis of chromosomes	4
1.3.1	Changes in ploidy and numerical chromosomal aberrations	4
1.3.2	Structural chromosomal aberrations	5
1.4	Tools in molecular genetics	7
1.5	Non-radioactive <i>in situ</i> hybridization	9
1.5.1	The development of non-isotopic <i>in situ</i> hybridization	9
1.5.2	The sensitivity and application of ISH	10
1.5.3	Novel methods in ISH: Comparative genomic hybridization	13
2	Methodological aspects of <i>in situ</i> hybridization	14
2.1	Isolated nuclei vs tissue sections	14
2.2	Types of DNA probes	16
2.2.1	Repetitive DNA probes	16
2.2.2	Library DNA probes	19
2.2.3	Unique regional DNA probes	20
2.3	Types of labels for DNA probes	20
2.4	Pretreatment of the specimen	21
2.4.1	Fixation of the tissue	21
2.4.2	Slide preparation	23
2.4.3	Permeabilizing treatments	23
2.5	Denaturation and hybridization	24
2.6	Visualization of hybridization signals	25
2.7	Evaluation of ISH signals	27
2.7.1	Evaluation of ISH signals	27
2.7.2	Statistical analysis	31
3	Cytogenetic aberrations in solid tumors	31
3.1	General aspects	31
3.1.1	Cytogenetic changes in human cancer	31
3.1.2	Oncogenes and tumor suppressor genes	32
3.1.3	Cytogenetic analysis of solid tumors	33
3.2	Urinary system	34
3.2.1	Kidney cancer	34
3.2.2	Bladder cancer	35
3.3	Gastrointestinal system	39

3.3.1	Esophageal cancer	39
3.3.2	Gastric cancer	41
3.3.3	Colorectal cancer	41
3.4	Hepatobiliary system and pancreas	45
3.4.1	Liver cancer	45
3.4.2	Pancreatic cancer	47
3.5	Endocrine system	47
3.5.1	The MEN1 syndrome	47
3.5.2	The MEN2a, MEN2b, and FMTC syndrome	48
3.5.3	Thyroid gland cancer	50
3.6	Male reproductive system	51
3.6.1	Testicular cancer	51
3.6.2	Prostatic cancer	53
3.7	Female reproductive system and breast	56
3.7.1	Ovarian cancer	56
3.7.2	Cervical cancer	57
3.7.3	Endometrial cancer	59
3.7.4	Breast cancer	60
3.8	Nervous system	63
3.8.1	Gliomas	64
3.8.2	Meningiomas	66
3.8.3	Neurofibromas/schwannomas	67
3.9	Respiratory system	68
3.9.1	Lung cancer	68
3.9.2	Malignant mesotheliomas	71
3.10	Skin	71
3.10.1	Basal cell carcinomas	71
3.10.2	Squamous cell carcinomas	72
3.10.3	Melanomas	72
3.11	Head and neck	74
3.11.1	Upper aerodigestive tract cancer	74
3.11.2	Salivary gland cancer	75
3.11.3	Nasopharyngeal cancer	76
3.12	Skeletal and soft tissues	76
3.12.1	Osteosarcomas	76
3.12.2	Ewing sarcomas	77
3.12.3	Chondrosarcomas	78
3.12.4	Rhabdomyosarcomas	78
3.12.5	Smooth muscle tumors	79
3.12.6	Synovial sarcomas	79
3.12.7	Fat cell tumors	80

3.13	Pediatric tumors	80
3.13.1	Tumors of the central nervous system	80
3.13.2	Neuroblastomas	81
3.13.3	Retinoblastomas	82
3.13.4	Pediatric tumors of the kidney	82
3.14	Lymphoid system	83
3.14.1	Hodgkin's lymphomas	83
3.14.2	Non-Hodgkin's lymphomas	84
4	Concluding remarks	85
4.1	The utility of interphase cytogenetics	85
4.2	Prospects in interphase cytogenetics	86
4.2.1	Developments in DNA probe technology	86
4.2.2	Developments in visualization histochemistry	87
4.2.3	Developments in computer assisted evaluation	87
	References	90
	Subject index	135