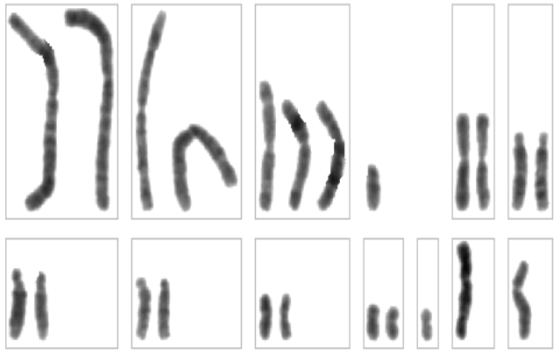
22. Juni 2013

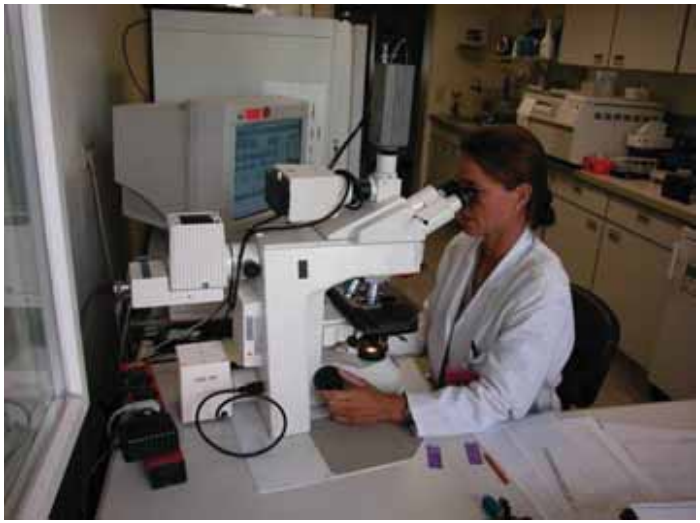
Zytogenetik bei MDS- Wie funktioniert´s und was bringt´s

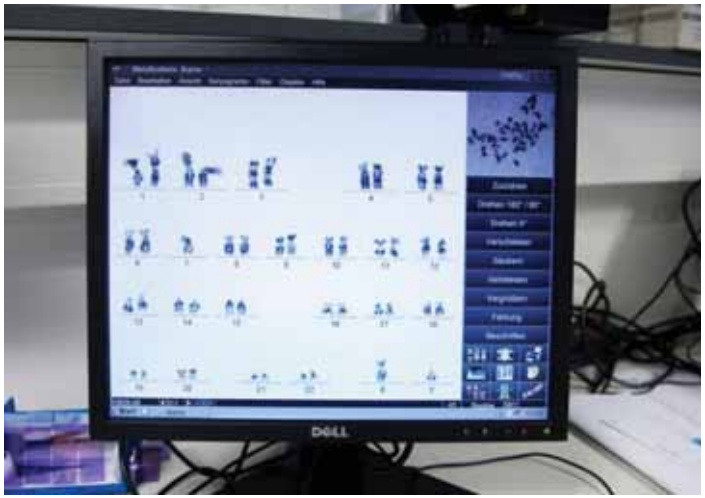
Patiententag der III. Medizinischen Klinik

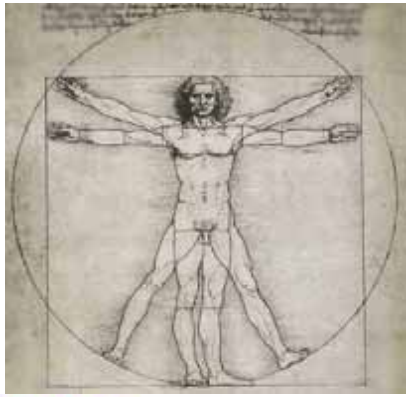
Universitätsmedizin Mannheim

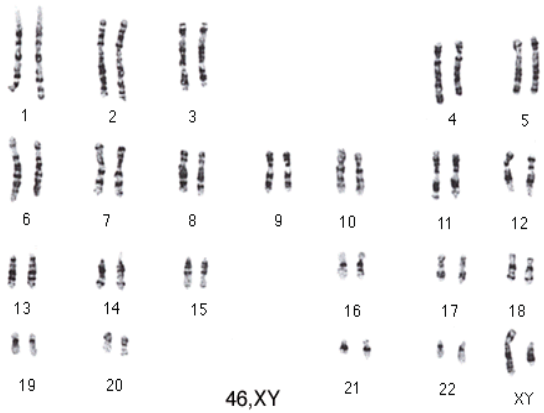
Spezies und Chromosomen



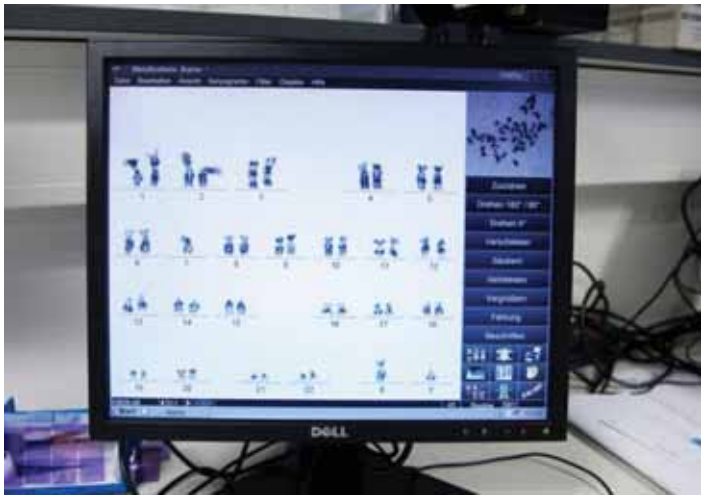








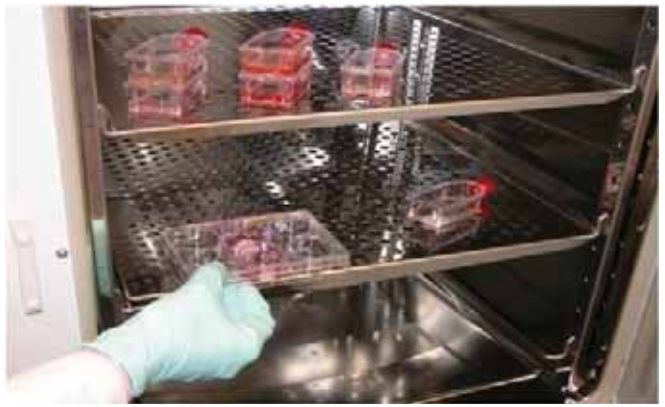
Spezies und Chromosomen



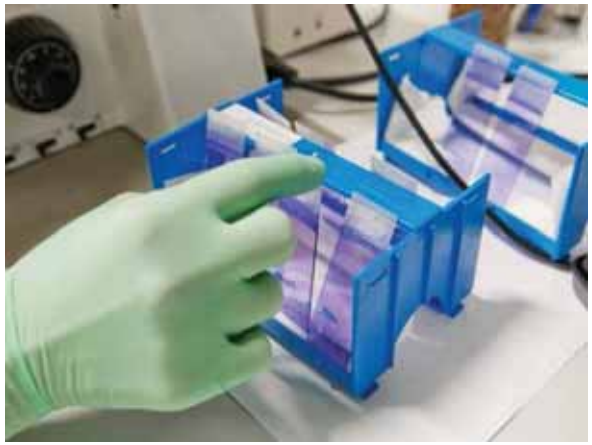
Species	Chromosomes
Human	46
Chimpanzee	48
Bat	44
Mouse	40
Golden hamster	40
Rattus norvegicus	42
Dog	78
Pig	38
Goldfish	94
Lamprey	174
Slow worm	44
Alligator	32
Chicken	78
Blackbird	80

Kultivierung und Aufarbeitung

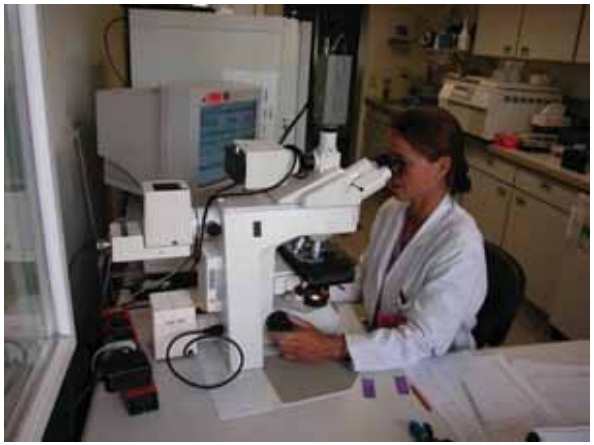
- Aseptische Bedingungen
- Kultivierung bei 37°C, 5% CO_2 und 19,7% O_2
- Direktpräparation, 24h, 48h, 72h
- Medium und Zusätze
- Colcemid
- PHA-Kulturen (72h) zur Bestimmung des konstitutionellen Karyotyps



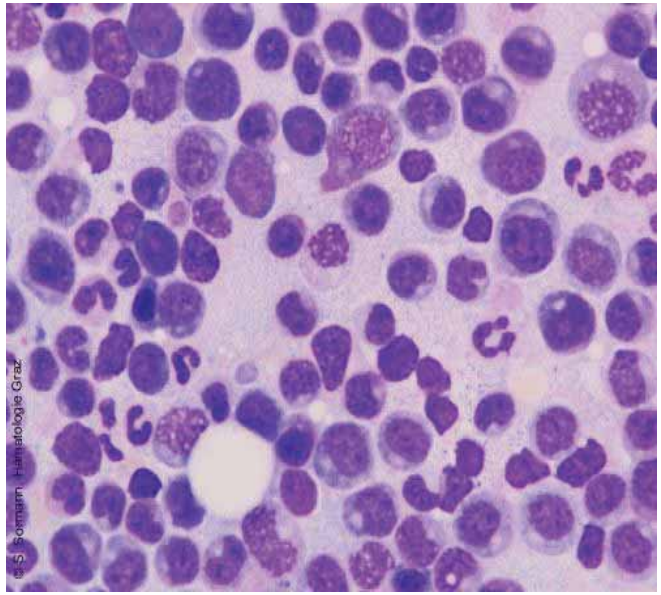
Aufarbeitung und Banding

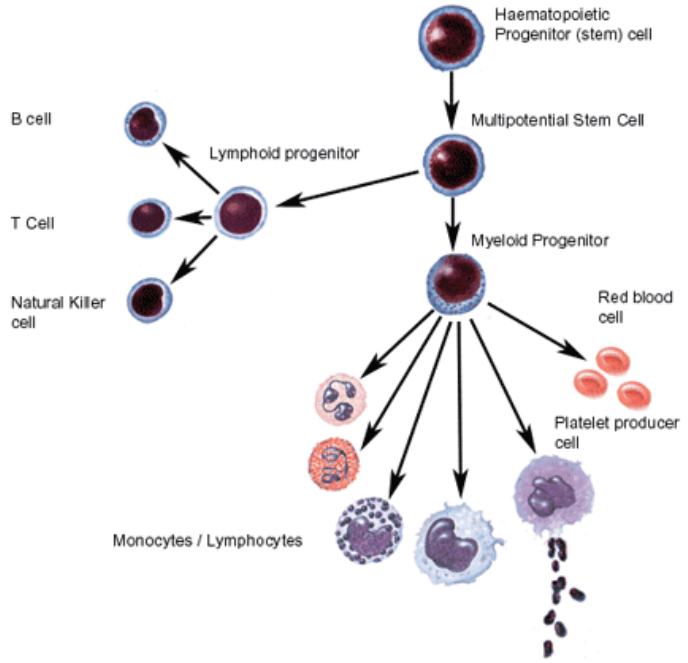


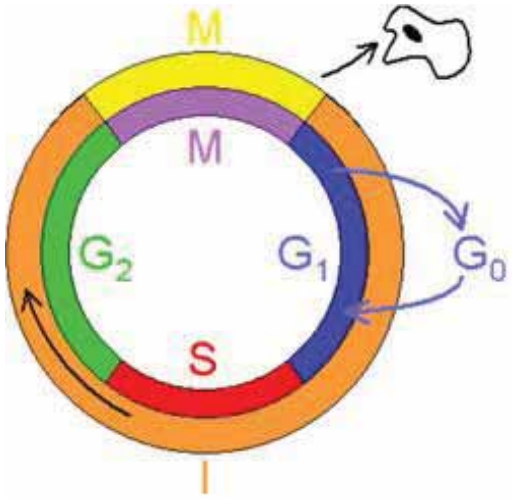
- Hypotone Behandlung (+0.075 M KCl)
- Fixation (Methanol/Essigsäure 3:1)
- Auftropfen
- Banding (Q, G, R, C, T, NOR-Banding)
- Analyse (25 Metaphasen)
- Bei Bedarf 10 PHA Metaphasen
- Erstellung des Karyotyps

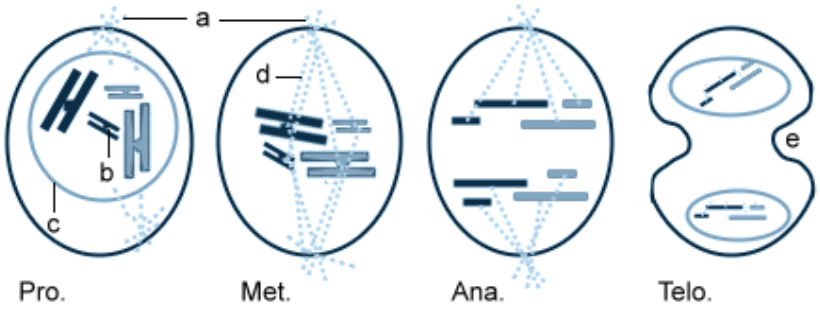


Gesunde Hämatopoese + normale Zellteilung

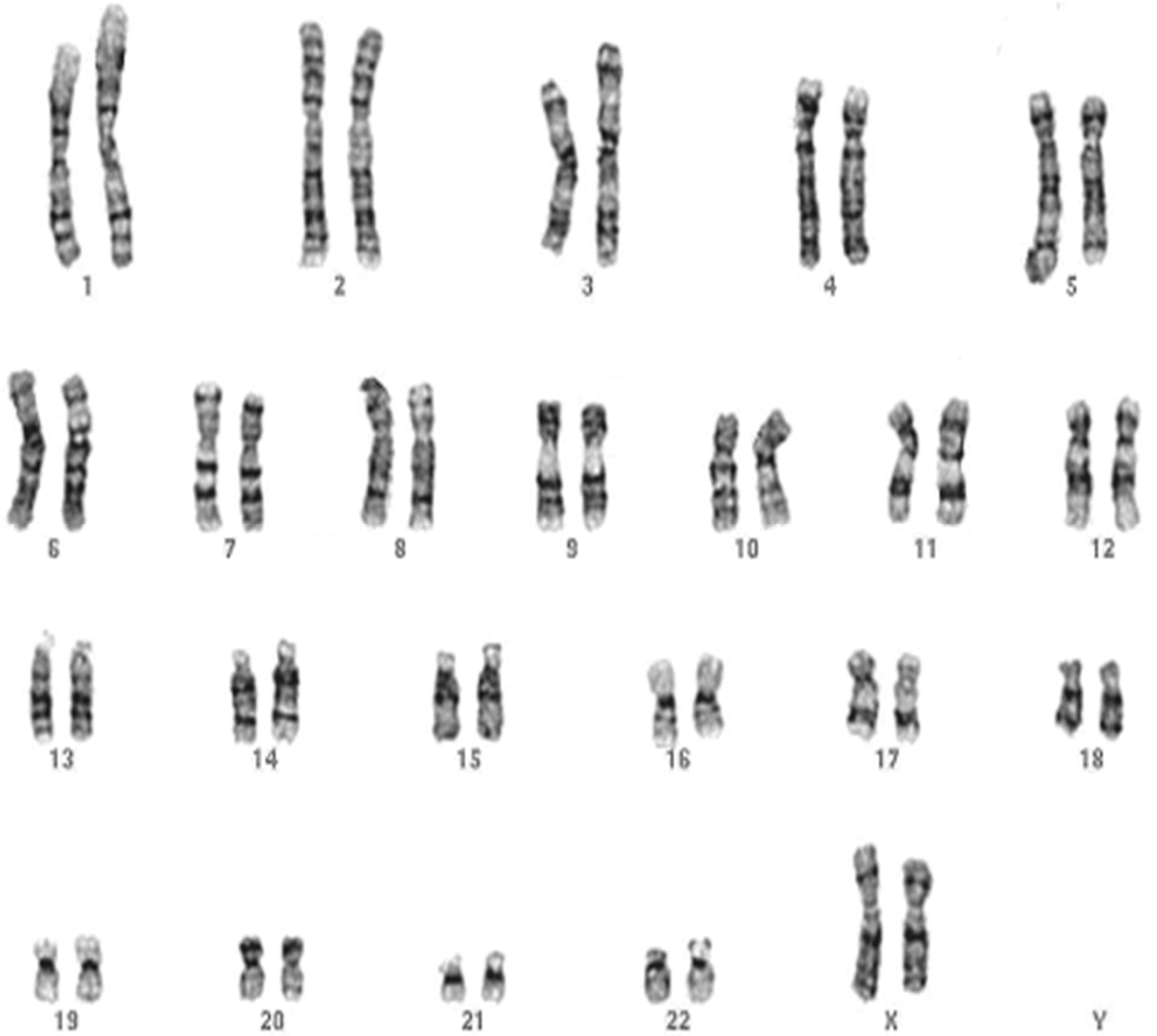




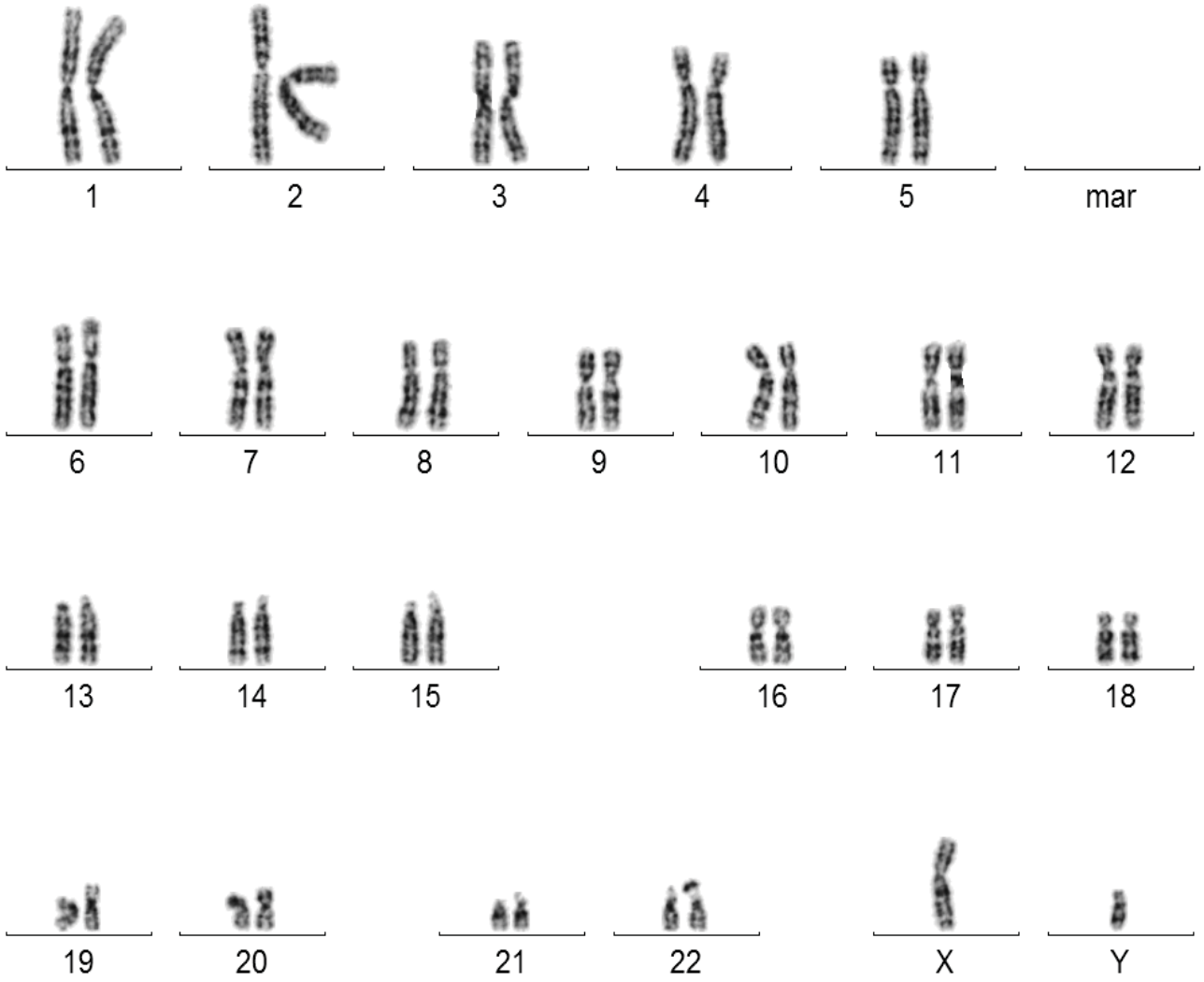




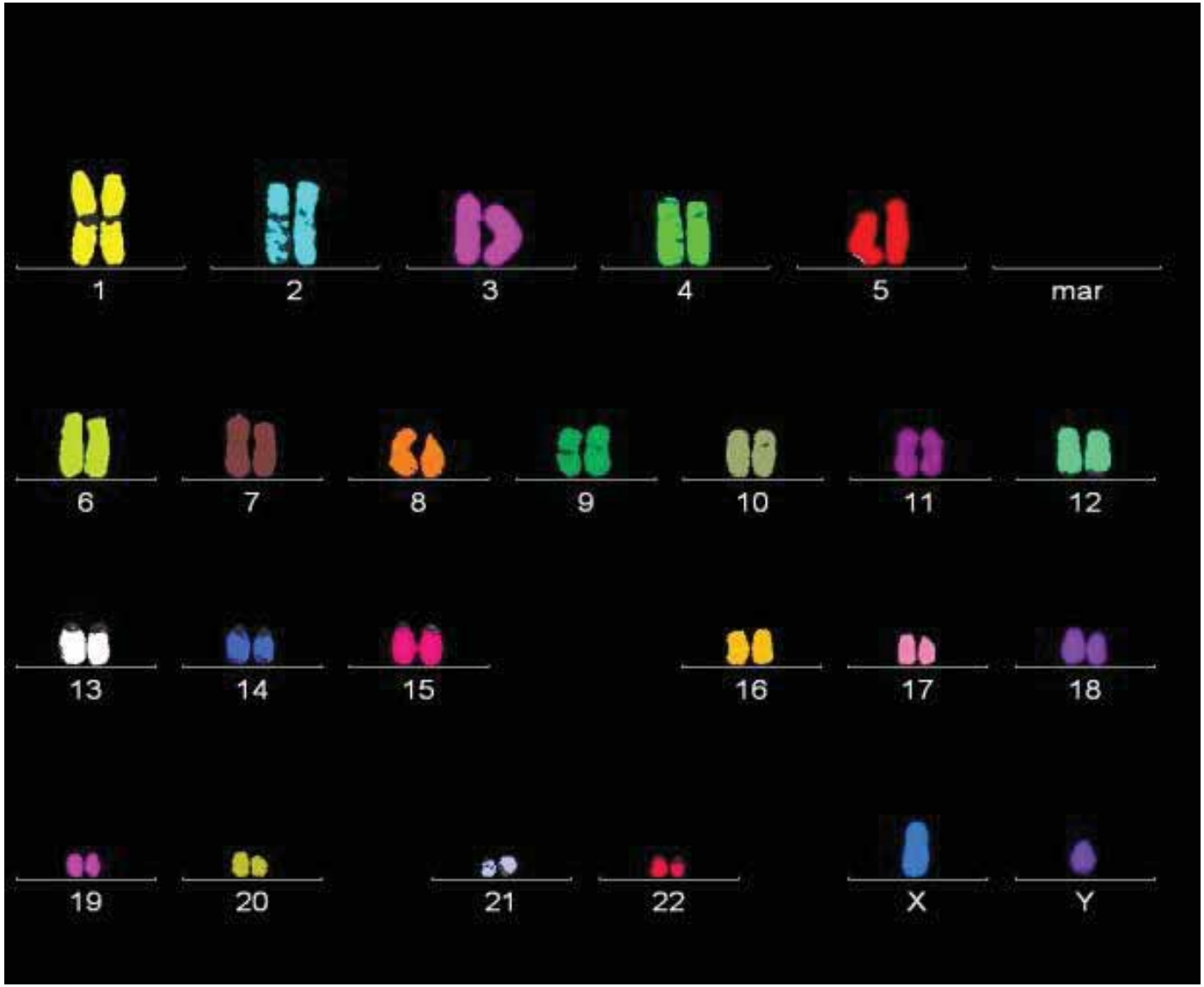
Der weibliche Karyotyp

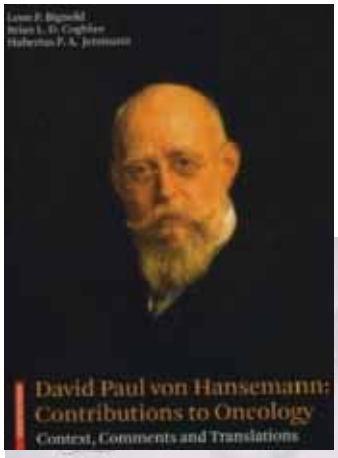


Der männliche Karyotyp

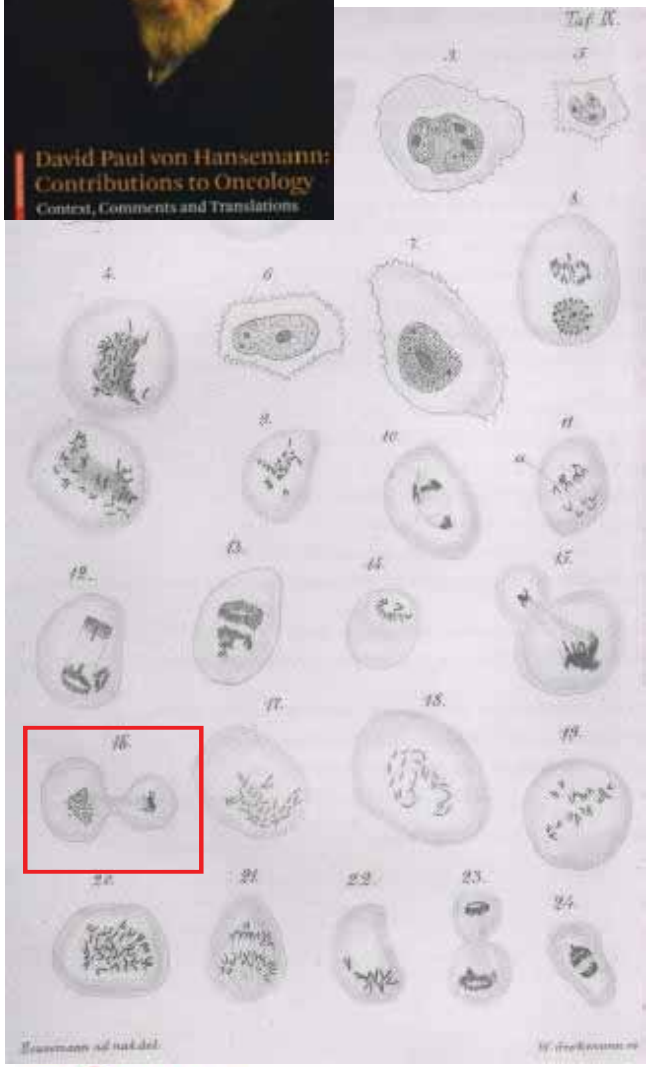


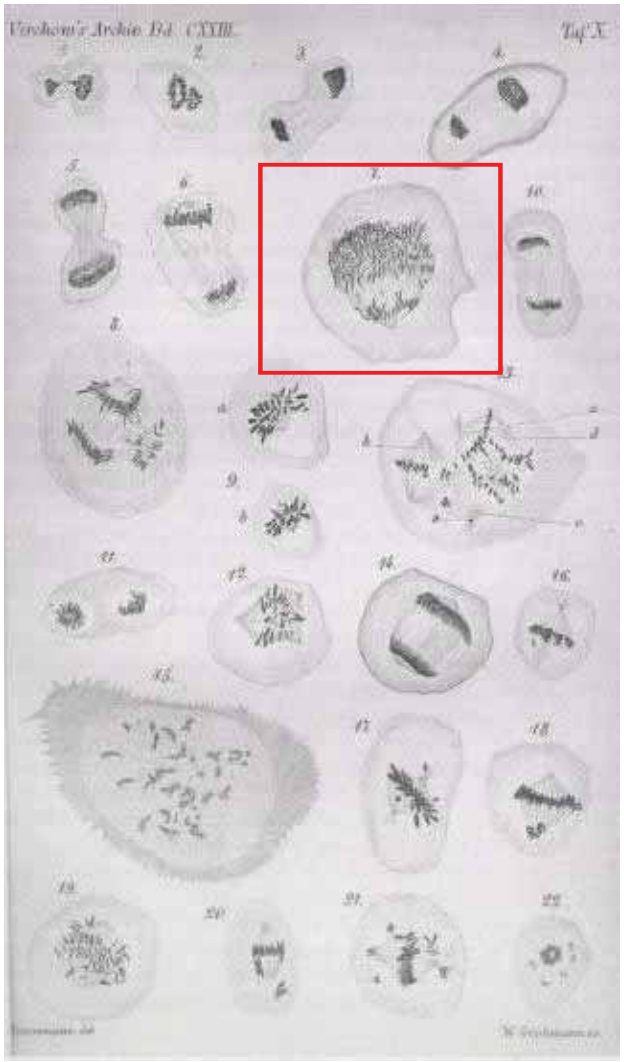
24 Farben Färbung

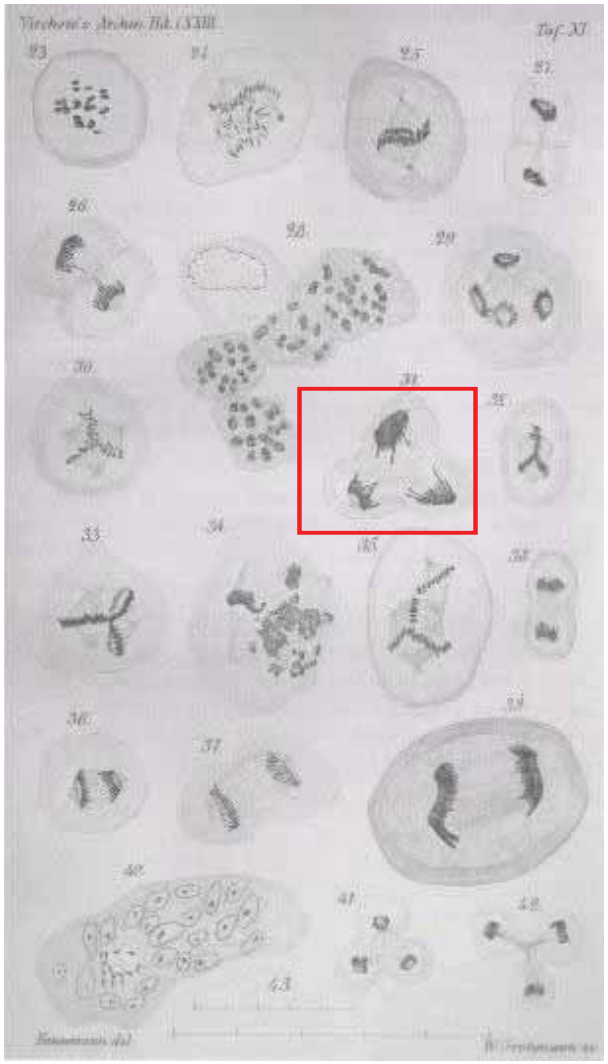




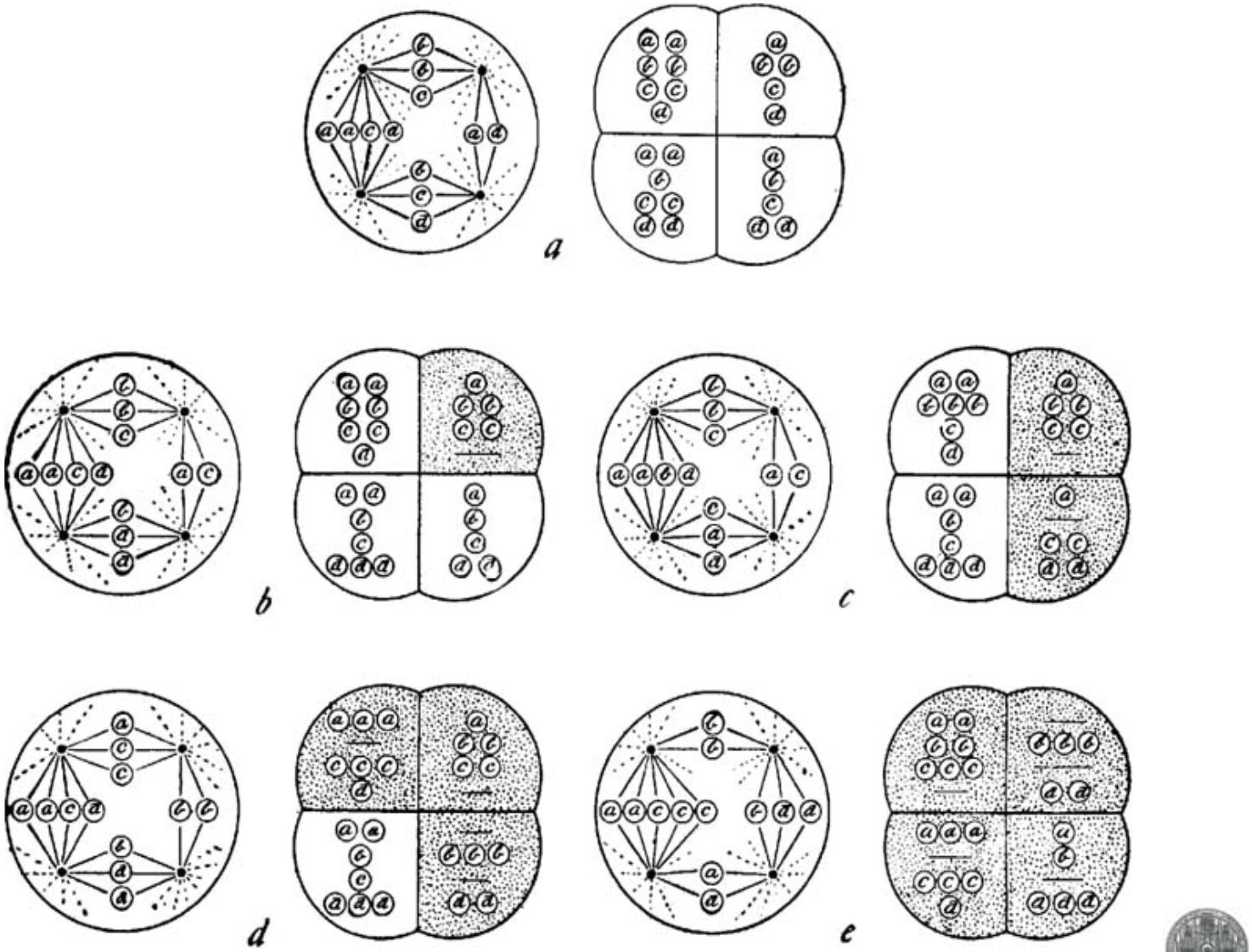
Von Hansemann, 1890
Asymmetrische Zellteilung und Krebs



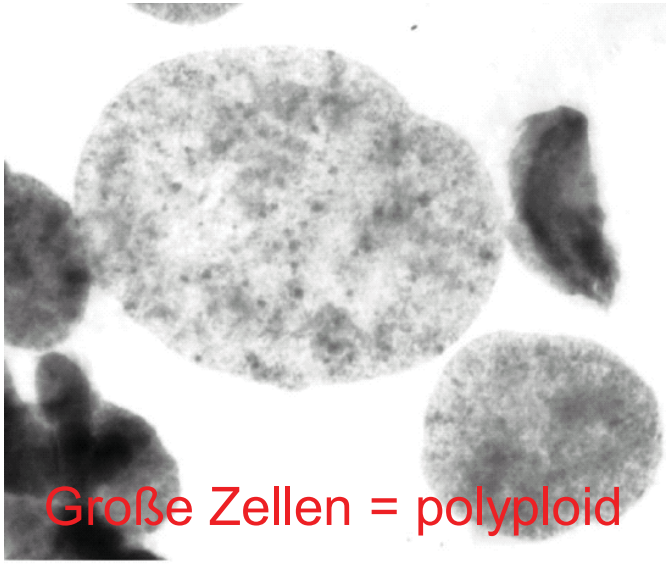




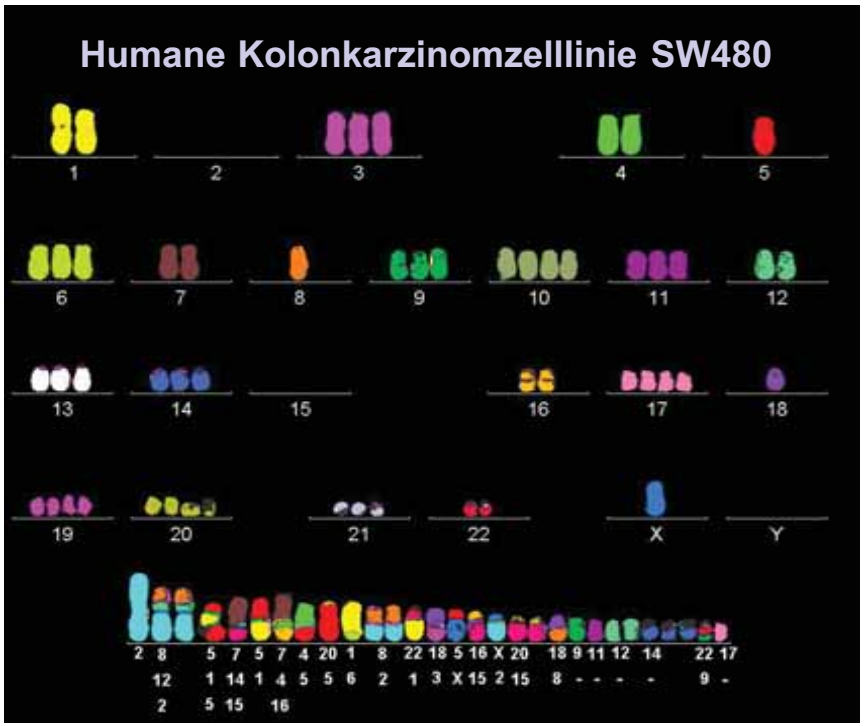
Theodor Boveri, 1914
Asymmetrische Zellteilung und Krebs

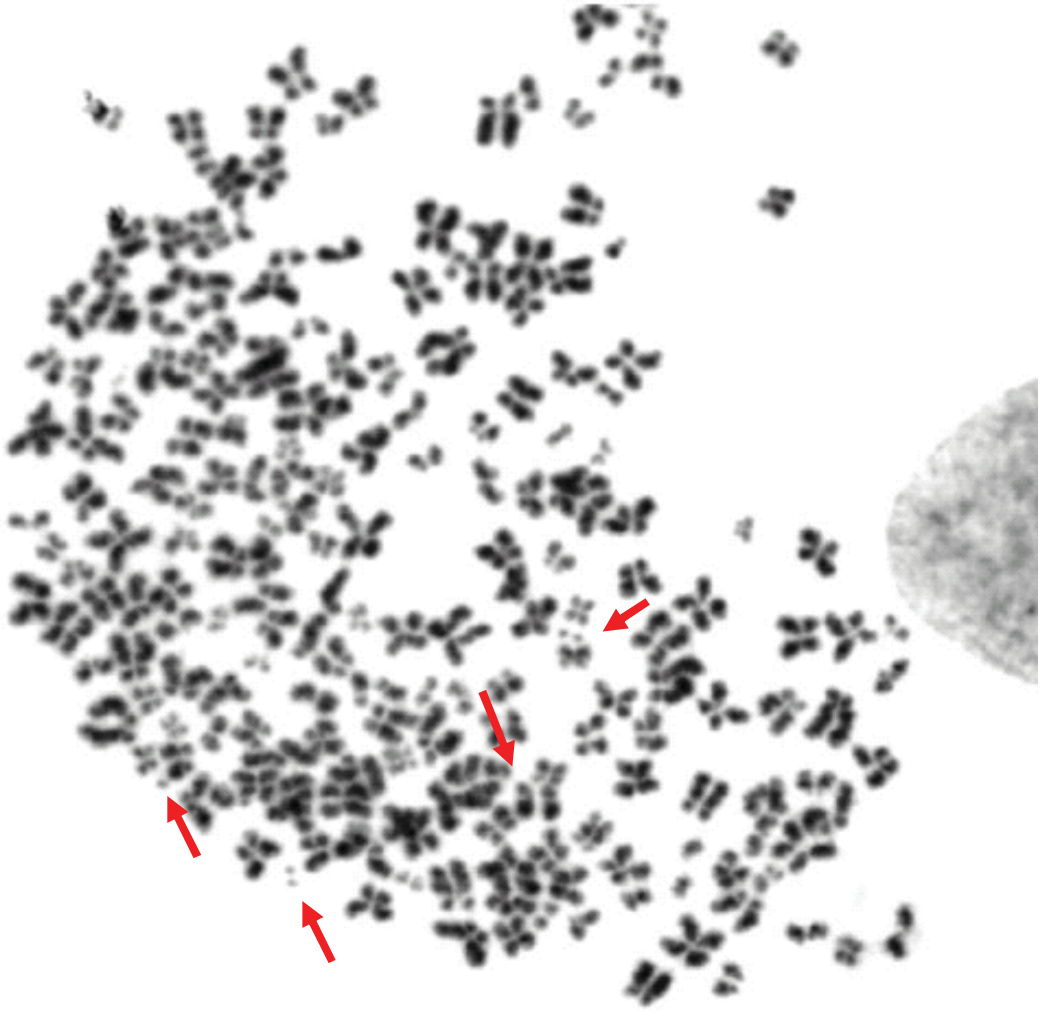


Solide Tumoren

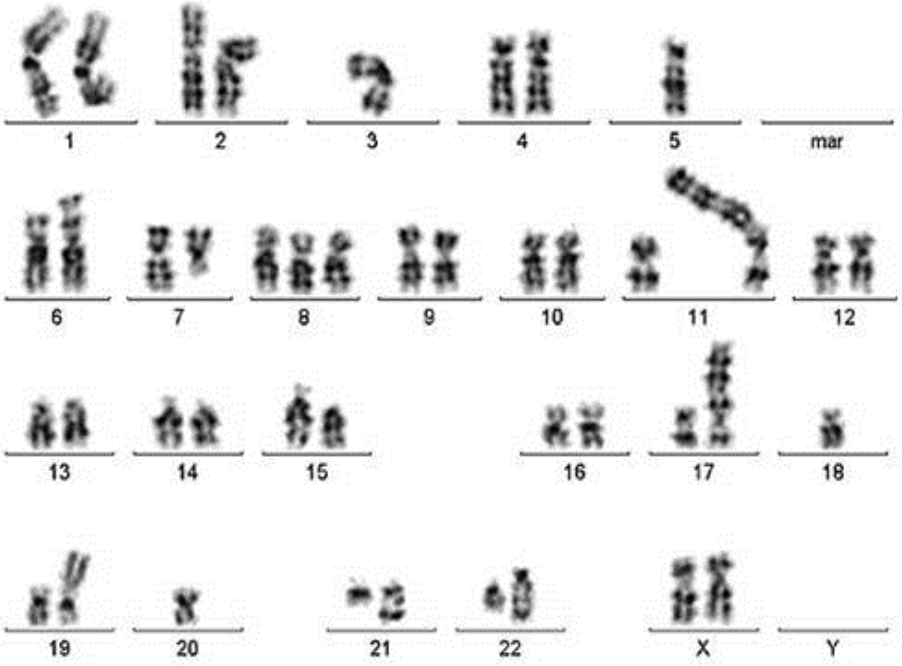


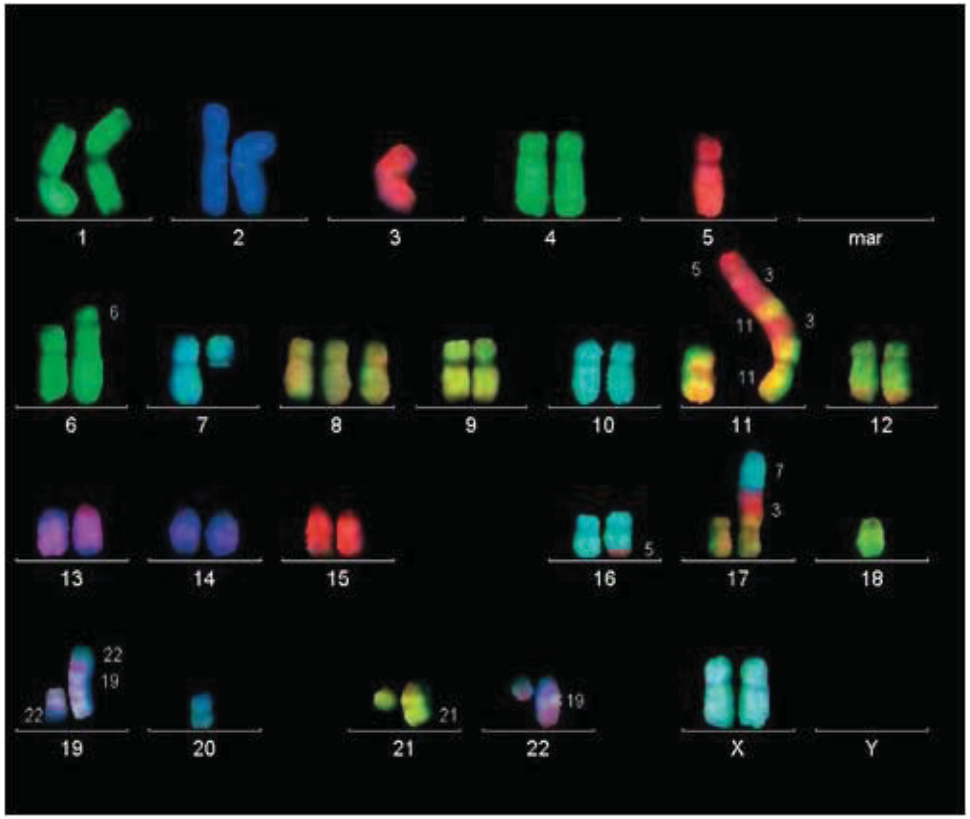
Große Zellen = polyploid





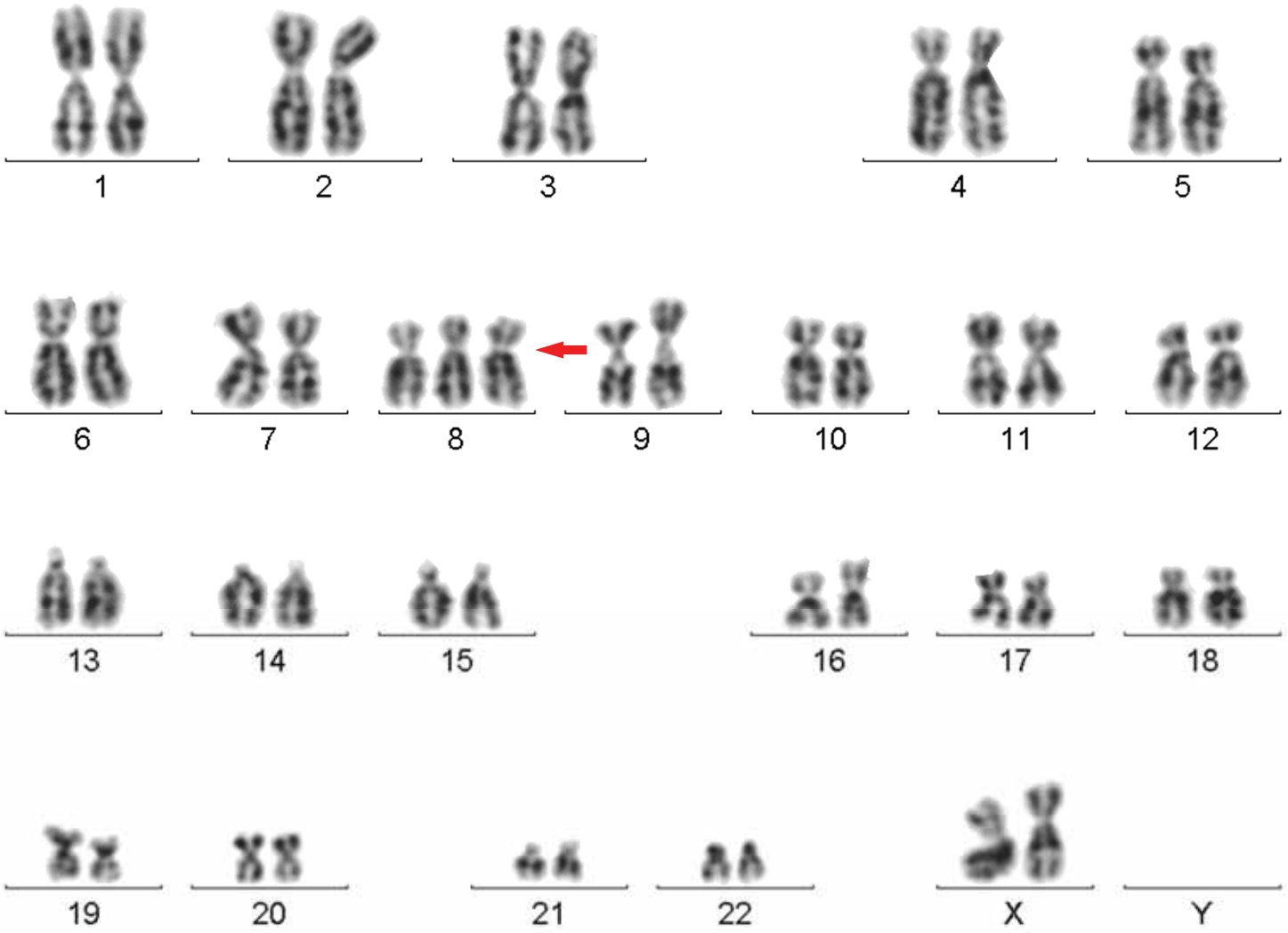
Akute Leukämie



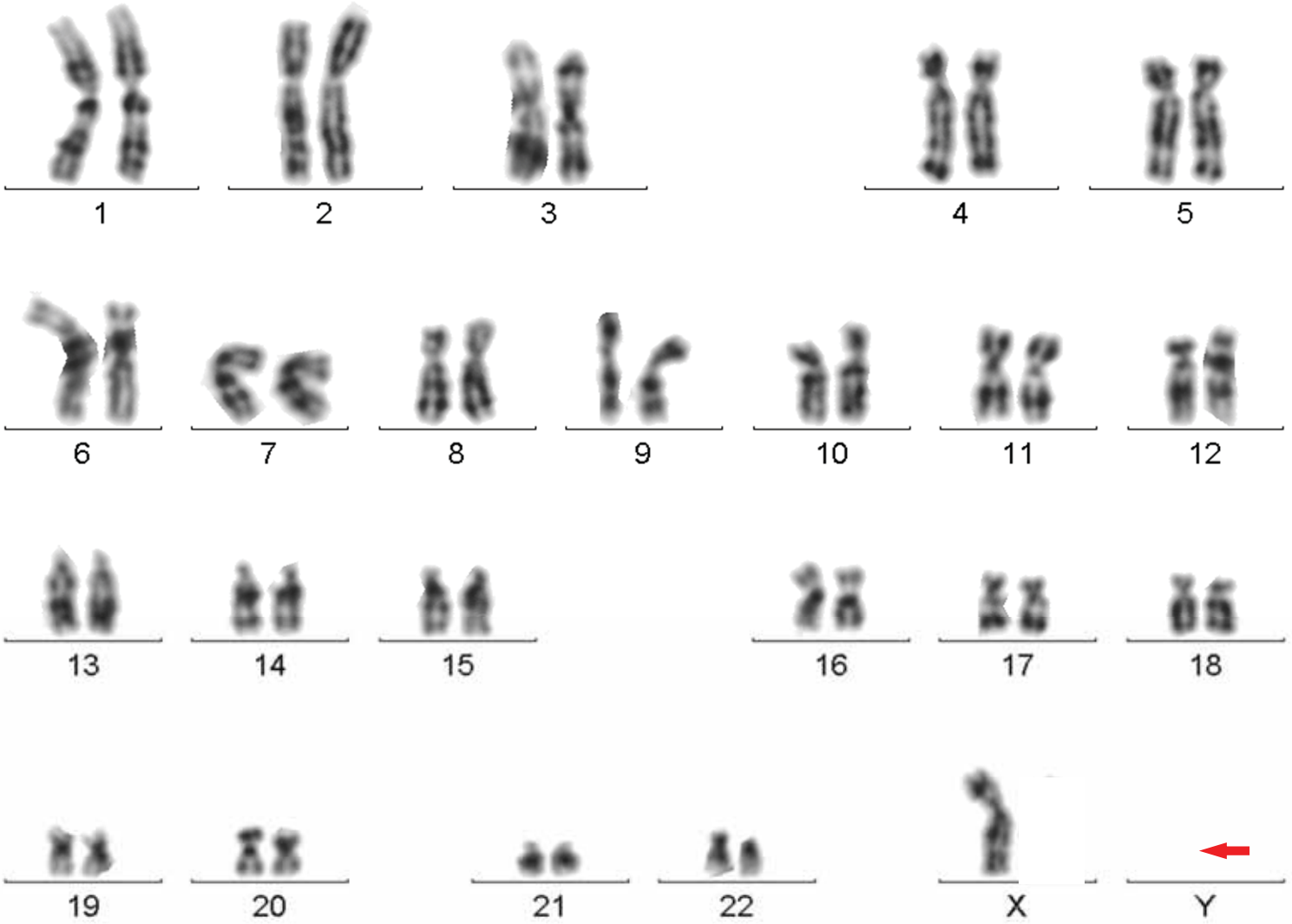


Wie sehen die Chromosomen beim myelodysplastischen Syndrom (MDS) aus?

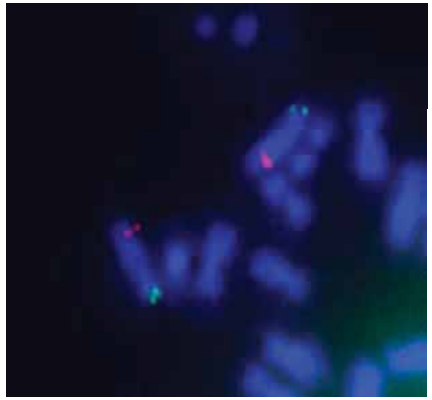
Trisomie 8 (47,XX,+8)

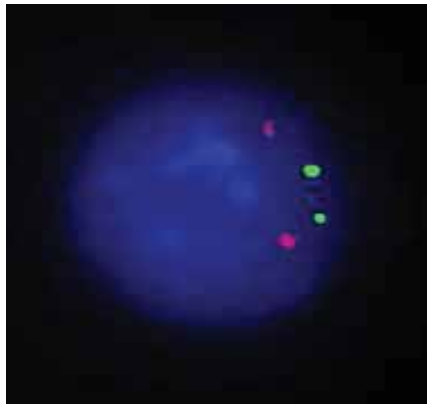


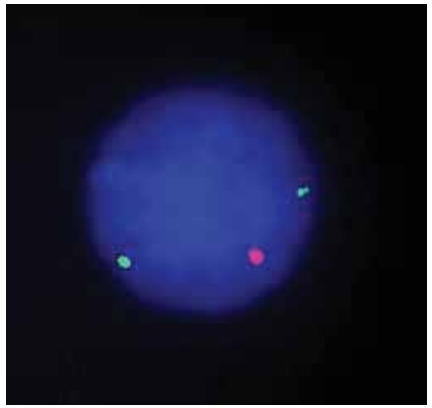
Verlust des Y-Chromosoms (45,X,-Y)

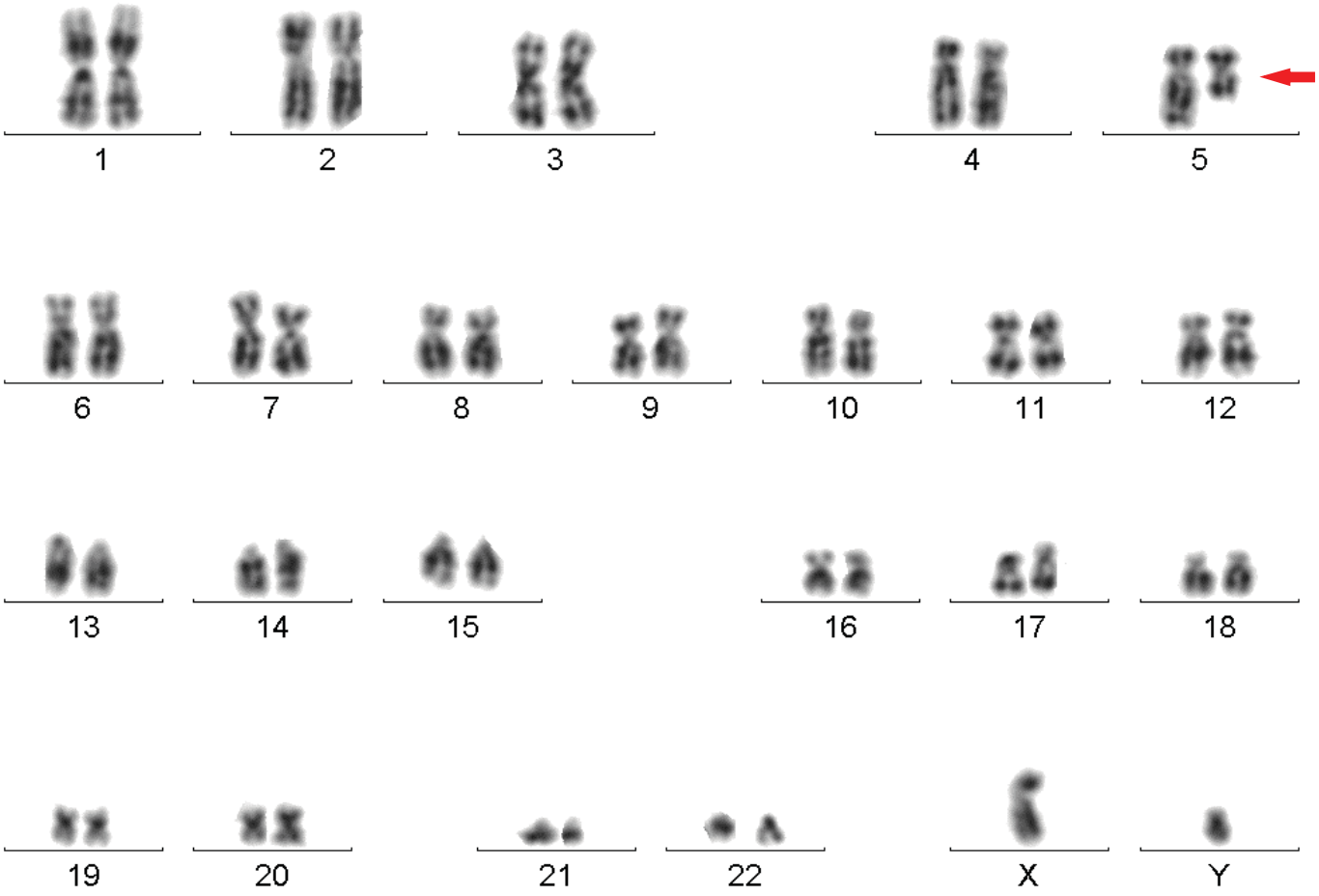


Das 5q- Syndrom
46,XX,del(5)(q13q31)

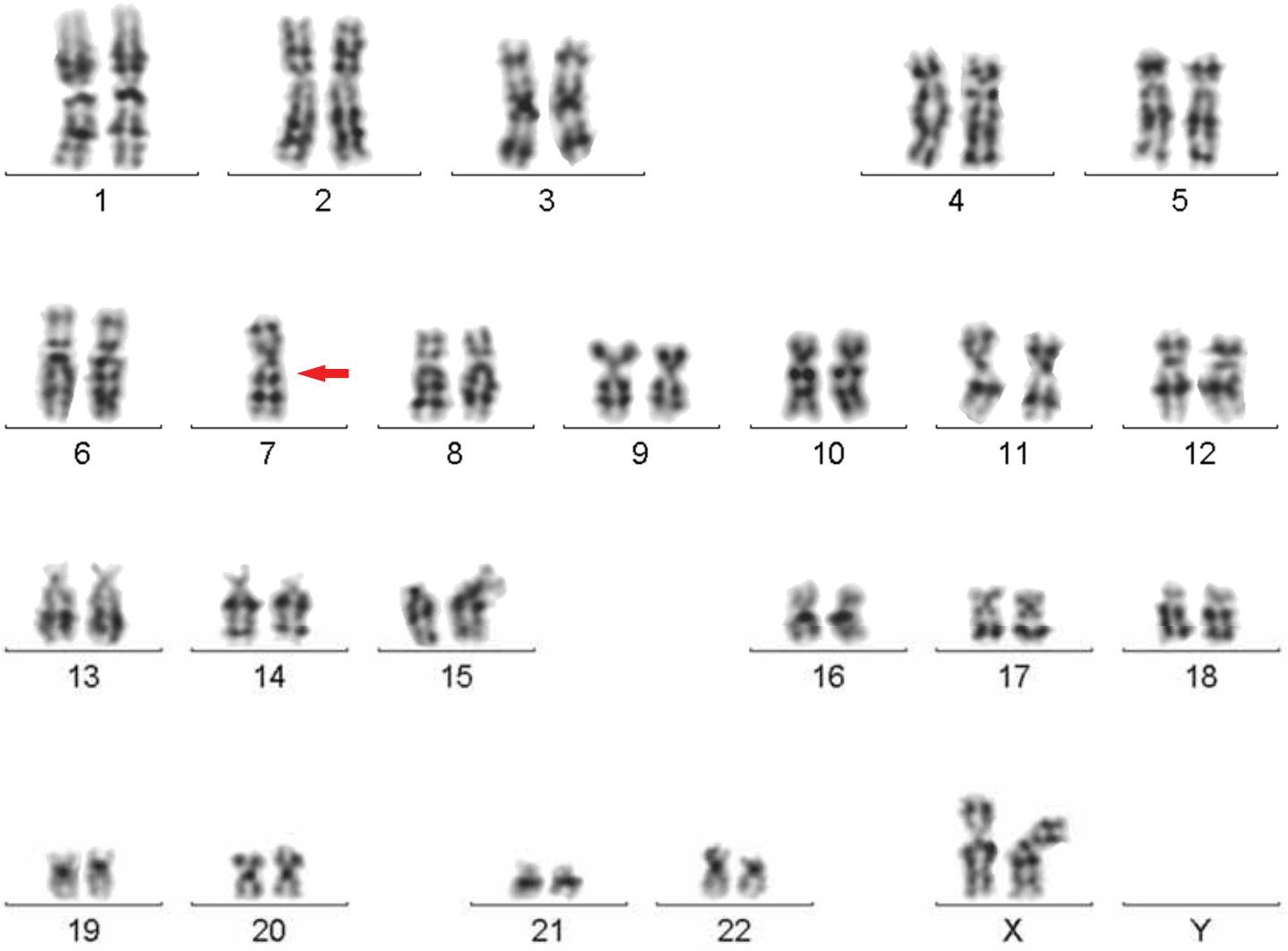




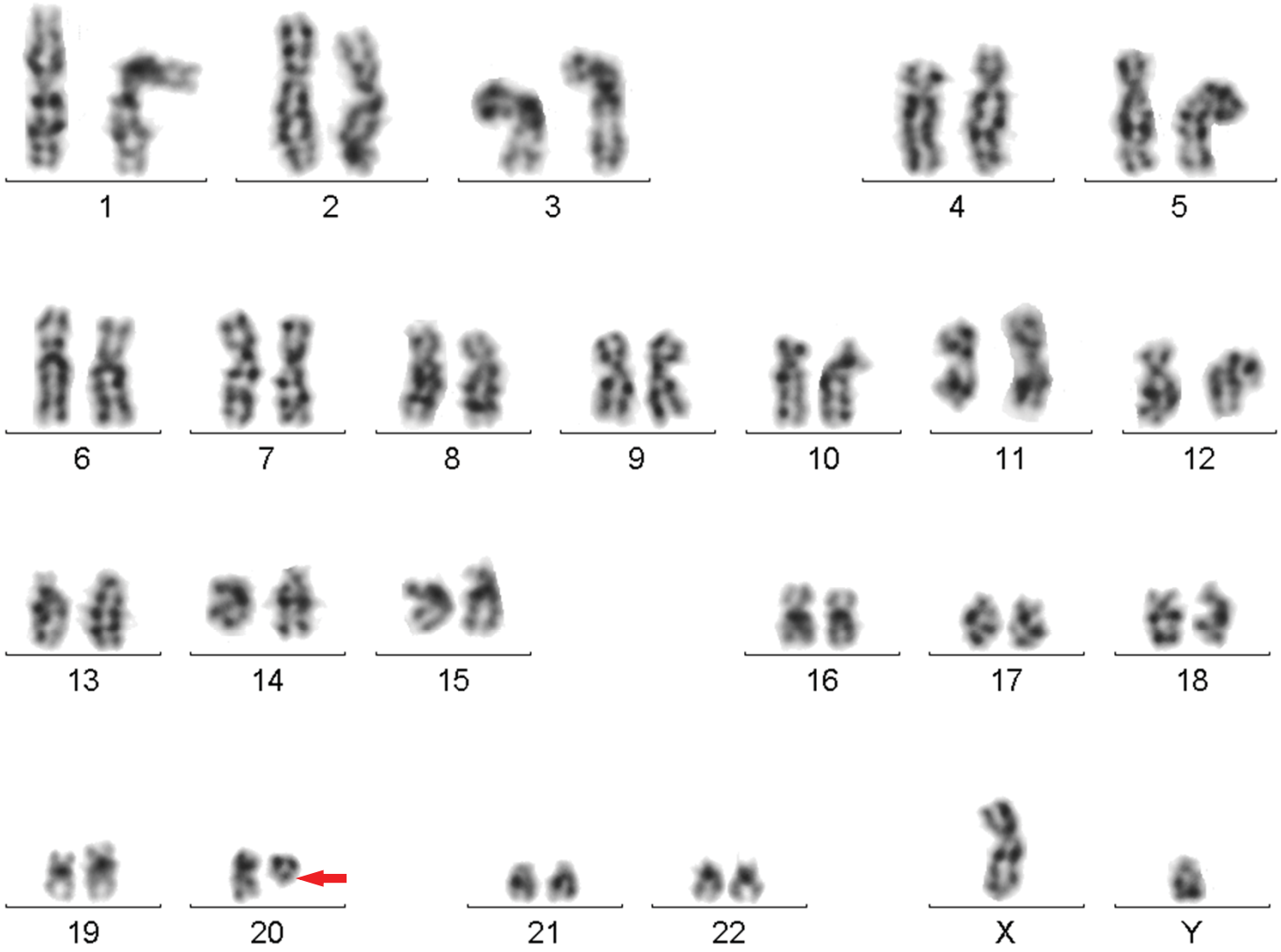




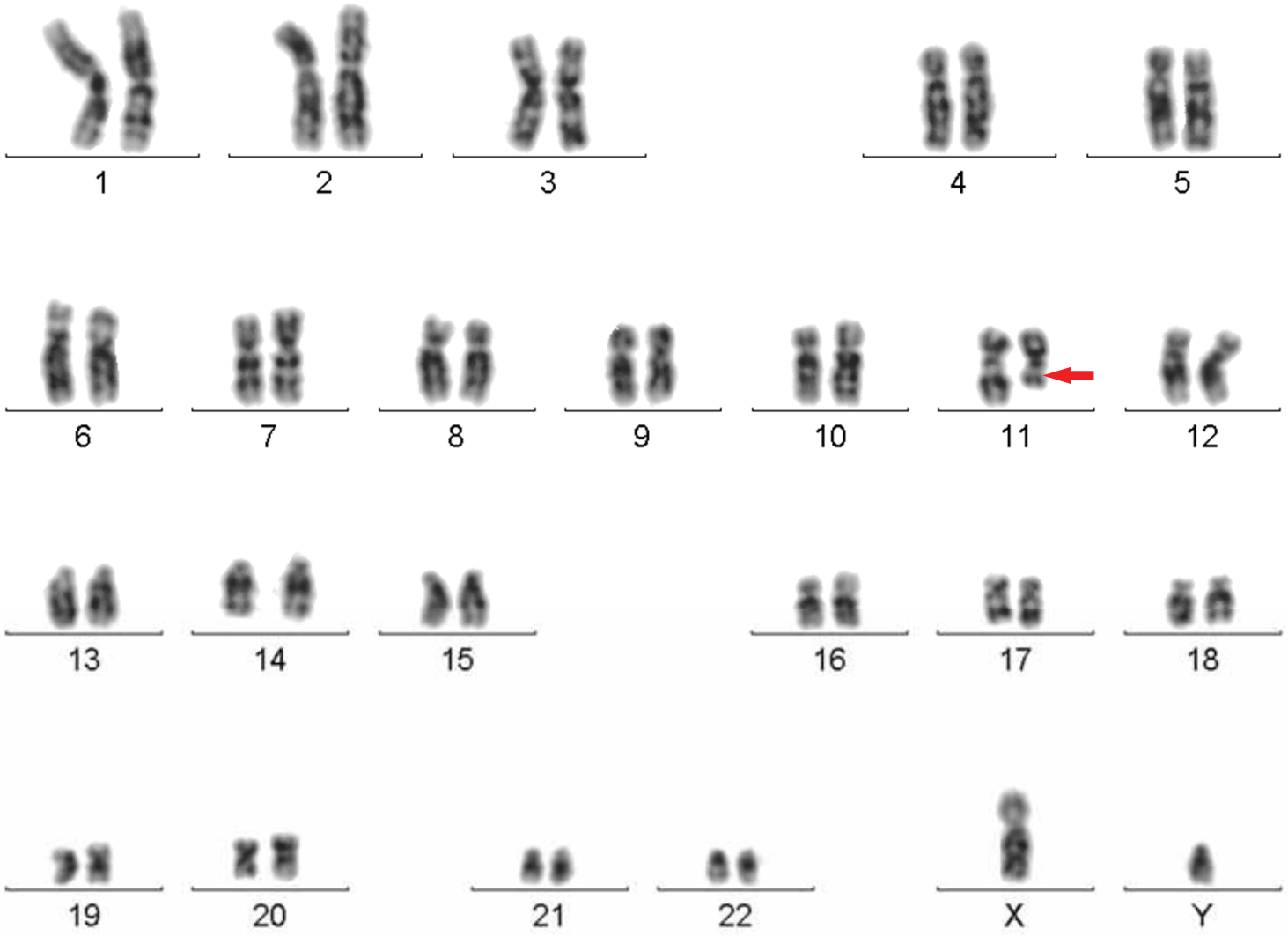
Monosomie 7: 45,XX,-7



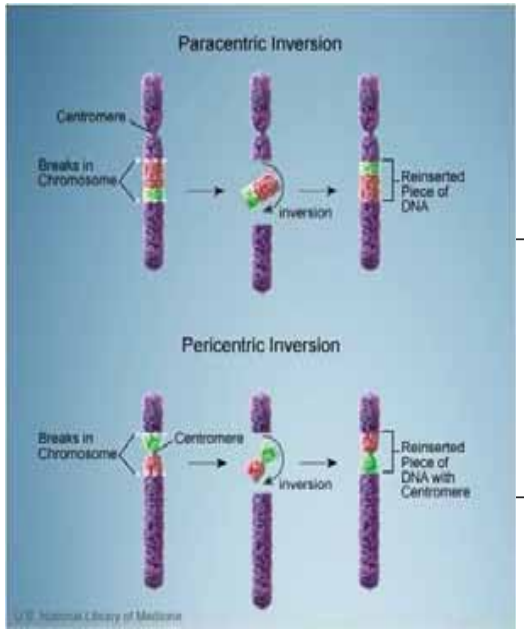
46,XY,del(20)(q11)

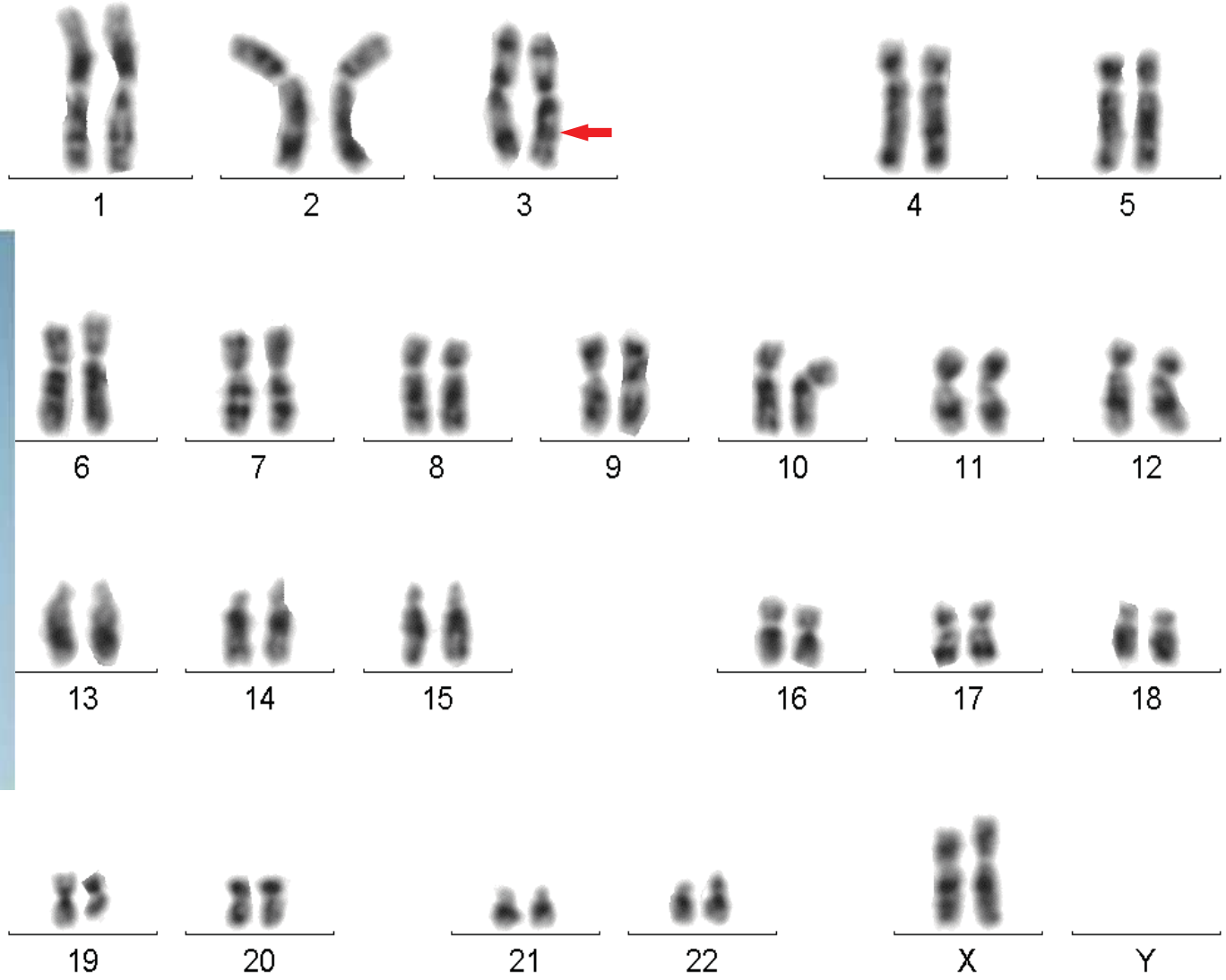


46,XY,del(11)(q14)

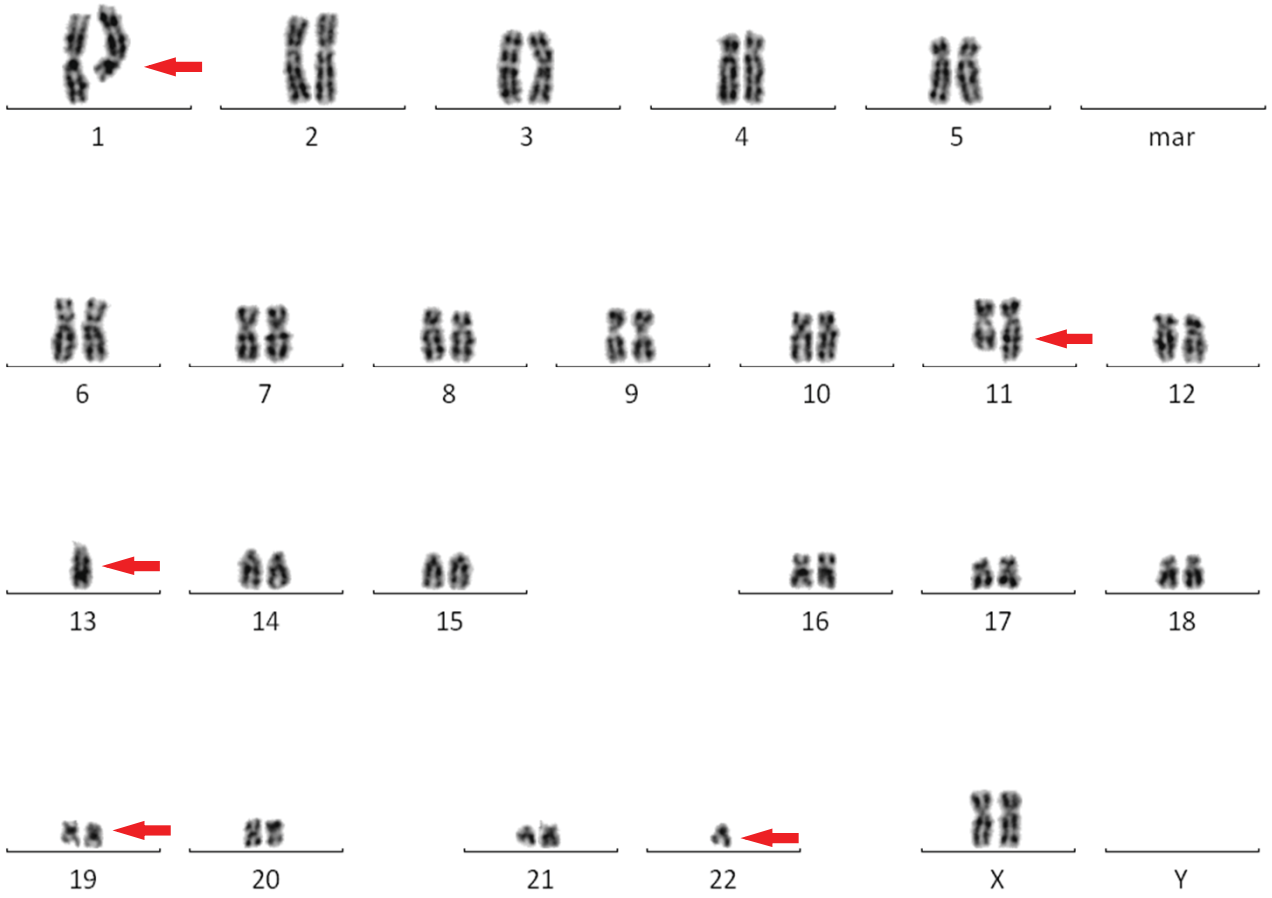


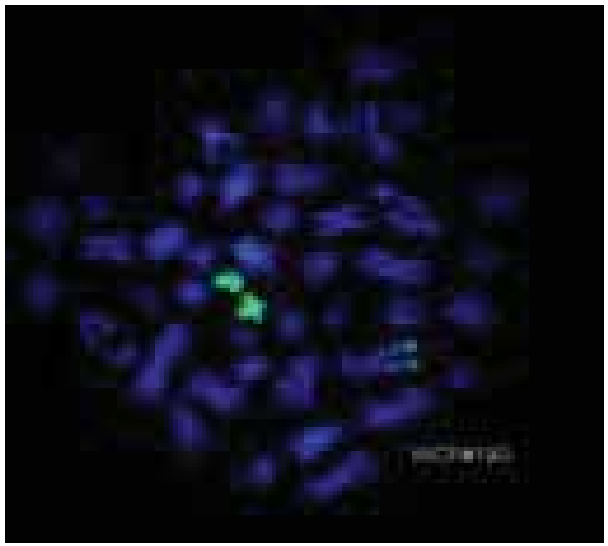
Die Inversion 3q [46,XX,inv(3)(q21q26)]

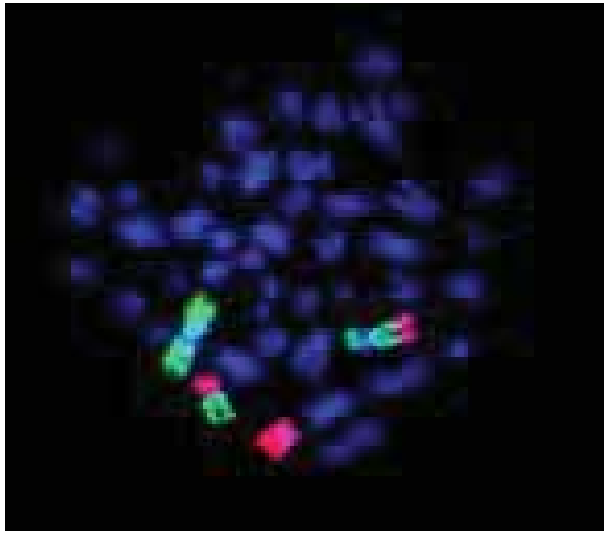




Komplex aberranter Karyotyp

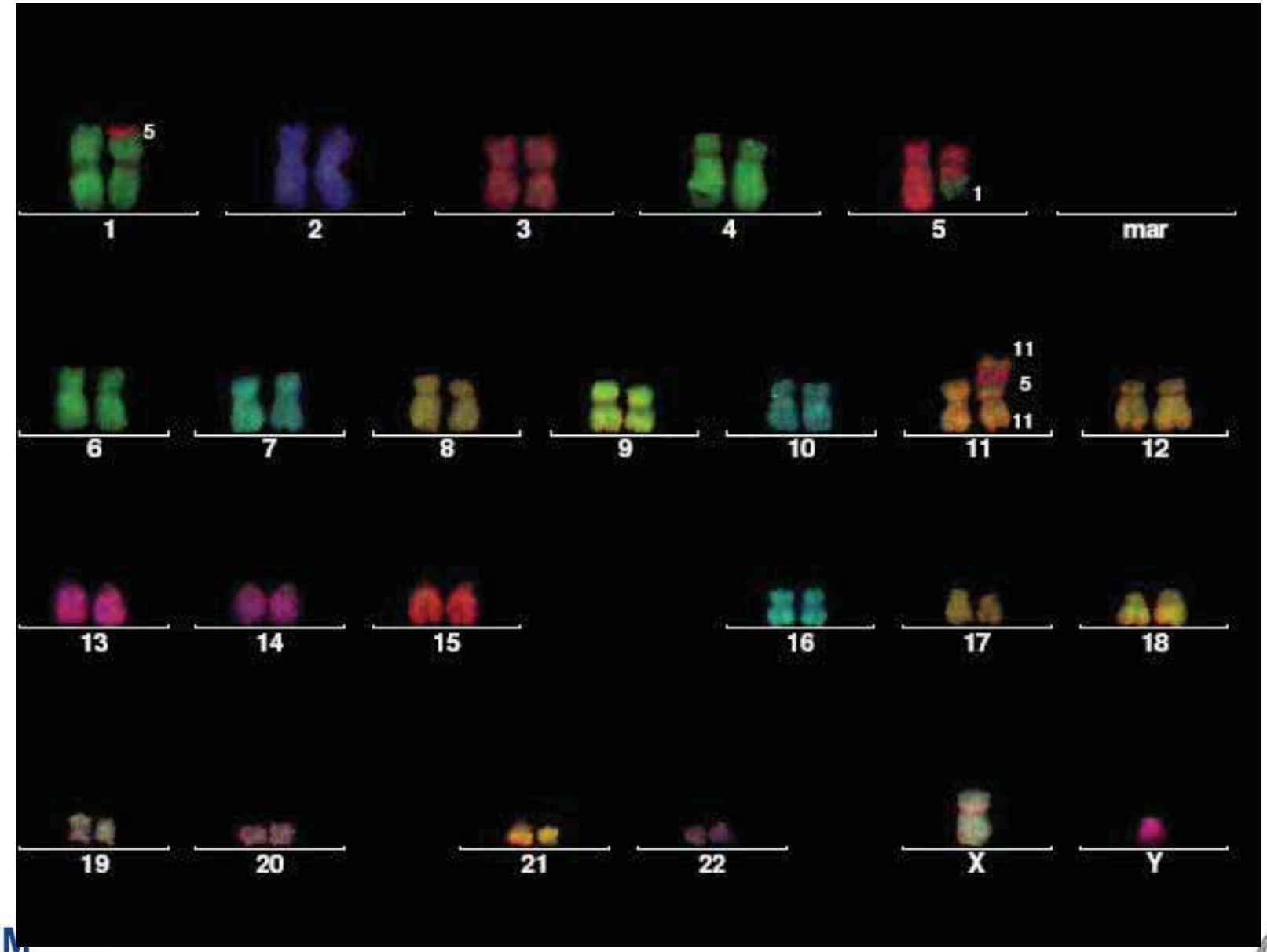






44,XX,der(1)t(1;11)(p36;q12)t(11;19)(q23;p13)del(1)(q22),der(11)t(1;11)(q22;q12),-13,der(19)t(11;19)(q23;p13),-22
Fluoreszenz-in-situ-Hybridisierung mit einer 1er und 11er Sonde bzw. mit einer 19er Sonde.

Insertion 11p



Neues Zytogenetisches „Scoring System“ für das MDS

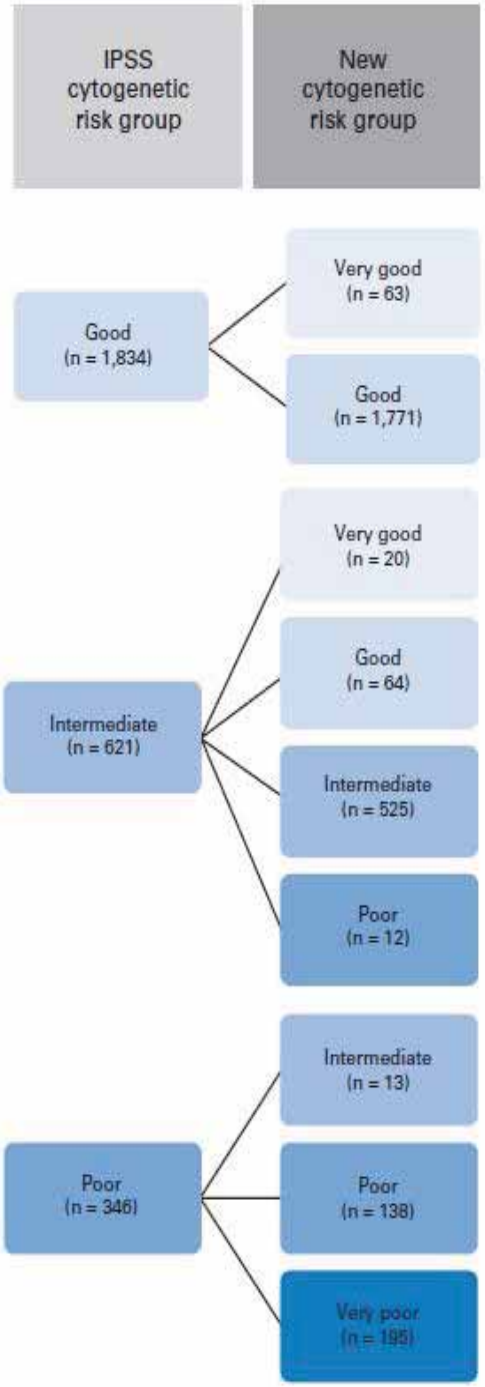


Table 3. Design of Cytogenetic Scoring System (n = 2,754)*

Prognostic Subgroup	Abnormality: No. of Patients	%	Single	Double	Complex	Overall Survival: Median (months)†	95% CI	HR	95% CI	AML Transformation: Median (months)†	95% CI	HR	95% CI
Very good	81	2.9	del(11q) −Y	—	—	60.8	50.3 to NR	0.5†	0.3 to 0.7	NR	121.2 to NR	0.5	0.2 to 1.2
Good (reference)	1,809	65.7	Normal del(5q) del(12p) del(20q)	Including del(5q)	—	48.6	44.6 to 54.3	1.0	0.9 to 1.1	NR	189.0 to NR	1.0	0.9 to 1.2
Intermediate	529	19.2	del(7q) +8 i(17q) +19 Any other	Any other Independent clones	—	26.0	22.1 to 31.0	1.6†	1.4 to 1.8	78.0	42.6 to NR	2.2†	1.8 to 2.7
Poor	148	5.4	inv(3)/t(3q)/ del(3q) −7	Including −7/del(7q)	3	15.8	12.0 to 18.0	2.6†	2.1 to 3.2	21.0	13.4 to 42.2	3.4†	2.5 to 4.6
Very poor	187	6.8	—	—	> 3	5.9	4.9 to 6.9	4.2†	3.4 to 5.2	8.2	6.4 to 15.4	4.9†	3.6 to 6.7

Abbreviations: AML, acute myeloid leukemia; HR, hazard ratio; NR, not reached.
*Patients with complete data.
†$P < .01$.

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Neues Zytogenetisches „Scoring System“

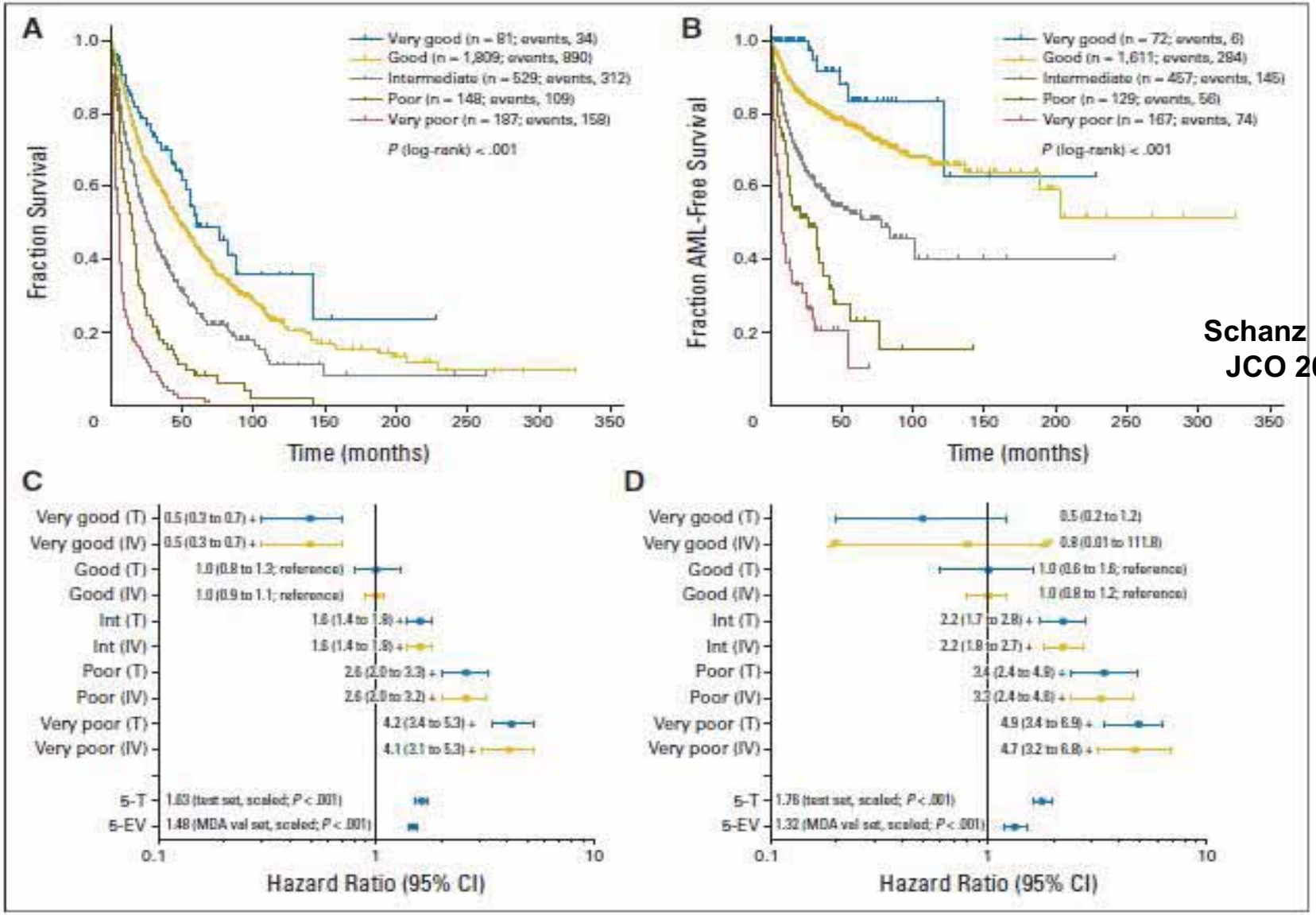

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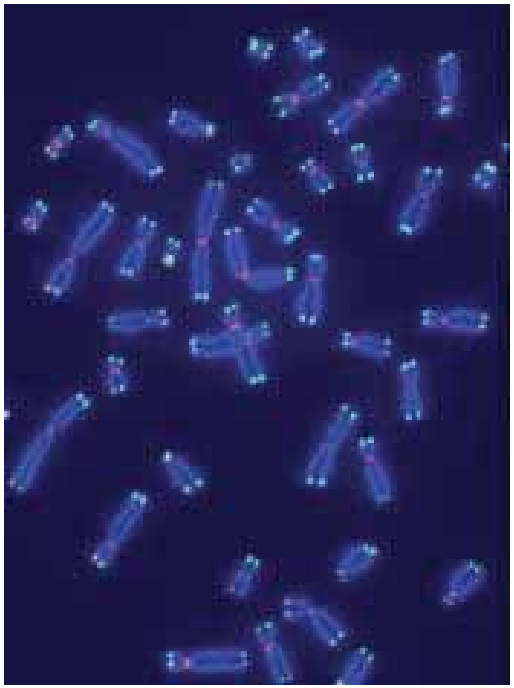
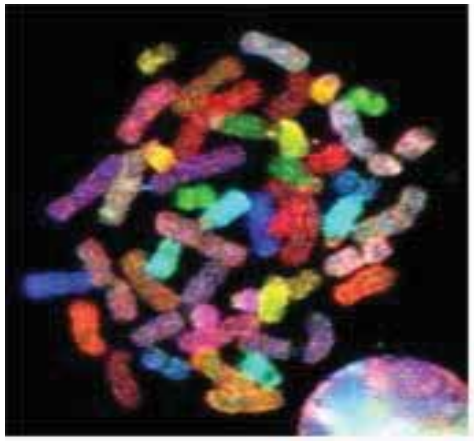
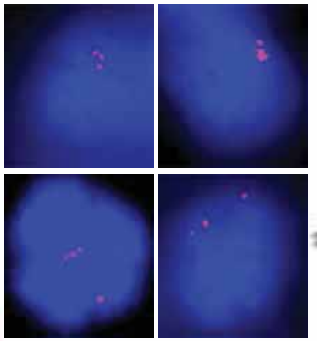
Fig 2. (A, B) Kaplan-Meier curves and (C, D) forest plots for (A, C) overall survival and (B, D) risk of acute myeloid leukemia (AML) transformation in new cytogenetic prognostic subgroups; + indicates $P < .01$ (as compared with reference category). 5-EV, external validation set (MD Anderson Cancer Center [MDA]), scaled, five groups; 5-T, test set, scaled, five groups; int, intermediate; IV, internal validation set; T, test set; val, validation.

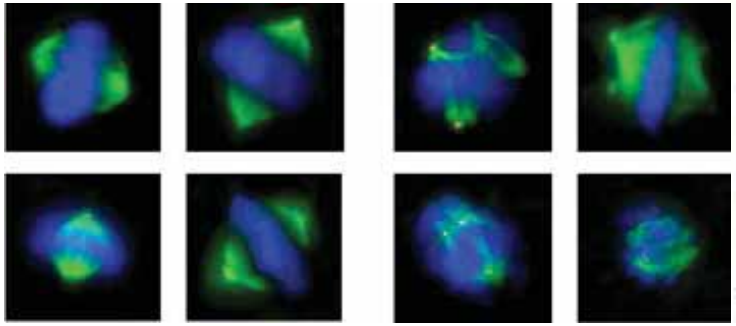
Was bringt die zytogenetische Analyse?

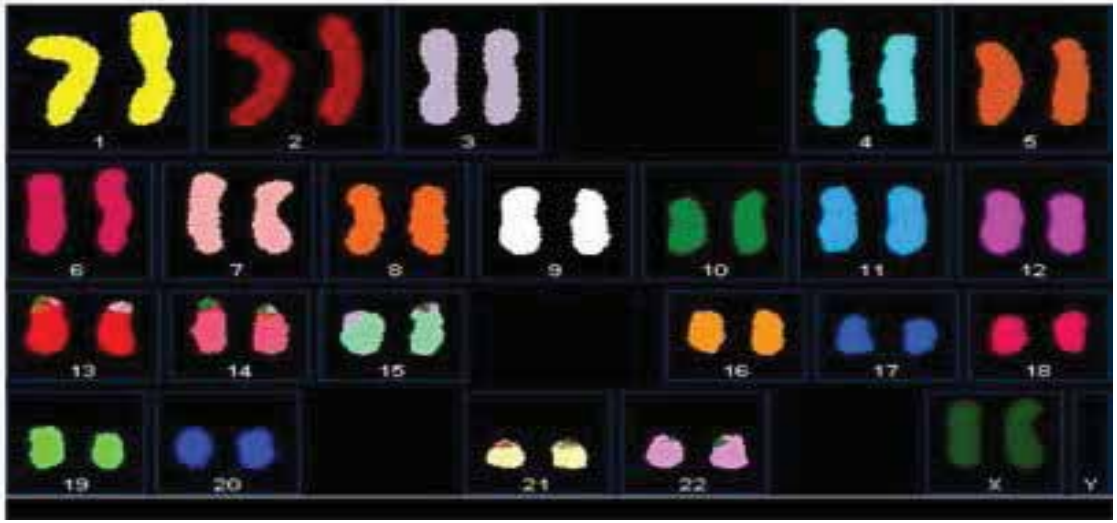
- Beim MDS wird Blut oder Knochenmark auf Chromosomenveränderungen analysiert
- Die Chromosomenstörungen beim MDS finden sich nur im Knochenmark und Blut und können nicht vererbt werden
- Ein normaler Karyotyp ist günstig
- Chromosomale Veränderungen (aberranter Karyotyp) können eine gute, mittlere oder schlechte Prognose haben
- Der Karyotyp beeinflusst die Therapie
- Für das 5q-Syndrom gibt es sehr gute, neu zugelassene Medikamente











Vielen Dank!