American Journal of Pathology, Vol. 148, No. 2, February 1996

Correlation between Clinicopathological Features and Karyotype in Lipomatous Tumors

A Report of 178 Cases from the Chromosomes and Morphology (CHAMP) Collaborative Study Group

Christopher D. M. Fletcher,* Mans Akerman,† Paola Dal Cin,‡ Ivo de Wever,‡ Nils Mandahl,† Fredrik Mertens,† Felix Mitelman,† Juan Rosai,§ Anders Rydholm,† Raf Sciot,‡ Giovanni Tallini,‖ Herman van den Berghe,‡ Wim van de Ven,‡ Roberta Vanni,¶,‡ and Helena Willen†

From St. Thomas's Hospital, London, United Kingdom; the University Hospital,† Lund, Sweden; the University of Leuven,‡ Leuven, Belgium; Memorial Sloan-Kettering Cancer Center,§ New York, New York; Yale University School of Medicine,‖ New Haven, Connecticut; and the University of Cagliari,¶ Cagliari, Italy*

Soft tissue tumors commonly show cytogenetic abnormalities, some of which are tumor specific. Lipomatous tumors represent the largest category of soft tissue neoplasms, and numerous karyotypic aberrations have been identified. However, clear-cut correlation between morphology and karyotype has not been undertaken on a systematic basis in a double-blind setting. The morphological features and histological diagnosis of 178 lipomatous neoplasms were reviewed independently without knowledge of the clinical data. The consensus diagnoses were then correlated with the clinical findings and compared with the tumors' karyotypes, using G-banded preparations from short-term cultures. The data were collated by a multicenter collaborative group of pathologists, geneticists, and surgeons. Clonal chromosomal abnormalities were identified in 149 cases studied (84%) and, to a large extent, the karyotype correlated with the morphological diagnosis. Specifically, 26 (96%) of 27 myxoid liposarcomas and its poorly differentiated variants showed a t(12;16); 29 (78%) of 37 atypical lipomatous tumors (including 5 dedifferentiated cases) showed ring chromosomes; 74 (80%) of 93 subcutaneous and intramuscular lipomas had karyotypic aberrations affecting mainly 12q, 6p, and 13q; 7 of 8 spindle cell and pleomorphic lipomas had aberrations of 16q; 3 lipoblastomas showed 8q rearrangements; and 2 hibernomas showed 11q abnormalities. We conclude that cytogenetic abnormalities are common in lipomatous tumors, correlate reliably with morphological subtype in many cases, and can be of diagnostic value in histologically borderline or difficult cases. (Am J Pathol 1996, 148:623–630)

Among solid tumors as a whole, cytogenetic analysis over the past decade has revealed a remarkably high incidence of tumor-specific chromosomal aberrations in soft tissue neoplasms (for reviews see Refs. 1–4). Such aberrations have proved to be frequent in both benign as well as malignant mesenchymal tumors,[1–5] thus disproving the formerly held notion that structural chromosomal abnormalities were confined to malignant lesions. In the same way as was first realized in leukemias two decades ago, demonstration of specific karyotypic aberrations may play a valuable role in solid tumor diagnosis[1–7] and is becoming established as an integral part of the diagnostic work-up in, for example, the small round cell tumors of childhood.[8,9]

Supported by the Swedish Cancer Society, EC Medical and Health Research Program BIOMED 1 (BHM1-CT92–0156 Molecular cytogenetics of solid tumors), and Belgian Interuniverstity Poles of Attraction program (initiated by the Belgian State, Prime Minister's Office, Science Policy Programming).

Accepted for publication November 1, 1995.

Address reprint requests to Dr. Christopher D. M. Fletcher, Division of Surgical Pathology, Department of Pathology, Brigham and Women's Hospital, 75 Francis Street, Boston, MA 02115.

One of the largest groups of soft tissue tumors in clinicopathological terms are lipomatous (or fatty) lesions, ie, neoplasms that, to a varying degree, show primary differentiation toward fat-forming cells (adipocytes or brown fat cells), sometimes accompanied by other connective tissue elements (such as blood vessels or fibrous tissue) that are most often stromal in nature. As a consequence of their comparative ubiquity, lipomatous neoplasms, in numerical terms, have also represented the largest subset of connective tissue tumors that have been studied by cytogenetic analysis.[3] Previously published studies have encompassed a variety of histological types of fatty tumor, often without clearly defined clinicopathological correlation. However, tantalizing results have emerged[10–17] that suggest that karyotypic analysis of this group of tumors potentially may play an important diagnostic role and, at the same time, reveal insights into the relationships between these various tumor types. For these reasons, an international collaborative group, incorporating cytogeneticists from two major centers along with surgeons and pathologists, was established in an attempt to objectively correlate karyotype with morphology and clinical features in a large number of lipomatous tumors.

Materials and Methods

A group of 178 lipomatous tumors that had been karyotyped successfully in Lund and Leuven over the preceding 6 to 8 years were selected for study to reflect the principal cytogenetic subgroups recognized among fatty neoplasms. Selection criteria were 1) all successfully karyotyped fatty tumors of any type other than simple subcutaneous lipoma; 2) all subcutaneous lipomas with an abnormal karyotype, and 3) 50% (selected randomly) of subcutaneous lipomas with a normal karyotype. After disaggregation with collagenase, all tumors were characterized, after short-term culture, by standard chromosome G-banding. In each of these 178 cases, all of the paraffin blocks were recut and 4-μm hematoxylin and eosin (H&E)-stained sections were re-examined histologically by three of the group members (J. R., G. T., and C. D. M. F.) without any knowledge of the clinical or karyotypic data. Diagnoses based solely on morphological pattern recognition were formulated and recorded, using conventional diagnostic criteria.[18–20] Based on previously reported chromosome aberrations in adipocytic tumors, the following designations were used (see also Table 2) to delineate cytogenetic subgroups: t(12:16), simple or complex translocations involving recombination between bands 12q13 and 16p11; ring, supernumerary ring chromosomes and/or giant marker chromosomes; 12q, aberrations involving chromosome segment 12q13–15; 13q, aberrations involving any part of the long arm of chromosome 13; 6p, aberrations involving any part of the short arm of chromosome 6; 16q, aberrations leading to loss of any part of the long arm of chromosome 16q; 11q, aberrations involving chromosome segment 11q13–21; 8q, aberrations involving chromosome segment 8q11–13; other, aberrations not falling into any of the groups listed above; N, normal karyotype.

All of the karyotypic and clinical data were retrieved and collated by the cytogenetic and surgical members of the group, respectively. In May 1994 the collaborative group members (henceforth referred to as the chromosomes and morphology (CHAMP) group) met in Sardinia, where the morphological, karyotypic, and clinical data in each case were compared and correlated. To simplify the recording of clinical attributes, patient age was listed by decade; anatomic location was divided into extremities, trunk, retroperitoneum, other, and unknown; and lesional depth was classified as superficial to fascia, deep to fascia, and unknown.

Table 1. *Histological Classification of 178 Adipocytic Tumors Studied*

Tumor type	Number
Ordinary Lipoma	93
Subcutaneous	55
Subfascial	32
Intramuscular	6
Angiolipoma	5
Hibernoma	2
Lipoblastoma	3
Spindle cell/pleomorphic lipoma	8
Atypical lipomatous tumor*	37
LL	28
LL plus sclerosing	4*
With dedifferentiated areas	5*
Other	1
Myxoid liposarcoma	27
Classical low grade	6
With round cell areas	17
With spindle cell areas	4
Pleomorphic liposarcoma	2
Mixed-type liposarcoma	1
Total	178

* Note that some tumors showed more than one pattern. LL, lipoma-like.

Results

The breakdown of the 178 cases by histological diagnosis is shown in Table 1. Overall, 149 of 178

Table 2. *Correlation of Histological Type with Karyotypic Aberrations in 178 Adipocytic Tumors Studied*

	Total cases	t(12;16)	Ring	12q	13q	6p	16q	11q	8q	Other	N
Ordinary lipoma	87		3	35	6	8			1	21	19
Intramuscular lipoma	6			2	1				2	2	
Angiolipoma	5										5
Hibernoma	2							2			
Lipoblastoma	3								3		
Spindle cell/pleomorphic lipoma	8		1		6	1	7				
Atypical lipomatous tumor*	37		29	1	2	3	2			1	2
LL	(28)		(23)	(1)	(2)	(3)	(2)			(1)	(1)
LL plus sclerosing*	(4)		(3)*								(1)
with dedifferentiated areas*	(5)		(4)*							(1)	
other	(1)		(1)								
Myxoid liposarcoma	27	26						1			1
Low grade	(6)	(6)						(1)			
With round cell areas	(17)	(17)									
With spindle cell areas	(4)	(3)									(1)
Pleomorphic liposarcoma	2										2
Mixed-type liposarcoma	1		1								
Total	178	26	34	39	15	12	9	3	6	24	29

N, normal; LL, lipoma-like.
Note that some cases showed more than one karyotypic aberration.
*Note that some tumors showed more than one pattern.

cases (84%) showed clonal karyotypic abnormalities. Among all of the cases studied, only 1 (a subcutaneous lipoma) showed a double minute chromosome, and homogeneously staining regions were never seen. Correlation between histological diagnoses and the most frequent characteristic aberrations is shown in Table 2.

Ordinary Lipomas

Eighty-seven cases were classified histologically as ordinary subcutaneous benign lipomas. Age range was from the second through eighth decades, with a peak in the fifth and sixth decades. Fifty-one patients were male and thirty-six were female. Anatomic distribution was as follows: extremities, forty-four cases; trunk, thirty-two cases; other sites, eight cases; and unknown, three cases. Fifty-five cases were subcutaneous and thirty-two were subfascial.

Sixty-eight cases (78%) had an abnormal karyotype, most often in the form of aberrations affecting 12q (thirty-five cases, mainly translocations), 6p (eight cases, mainly translocations), and 13q (six cases, mainly deletions). Seven cases demonstrated abnormalities of more than one of these three chromosome regions. Three cases showed ring chromosomes, of which two were subfascial and had been published previously as examples of atypical lipoma.[17] Twenty-one cases showed a wide variety of other less frequent aberrations affecting a variety of chromosomes. Nineteen cases had a normal karyotype.

Intramuscular Lipoma

Six cases were classified as intramuscular lipoma of ordinary benign type. Five affected adults in the fifth to seventh decades and one occurred in a 3-year-old child. Four patients were female and two were male. All cases arose in the extremities. Karyotypically, two cases each showed aberrations affecting 8q and 12q; one of the latter was combined with a 13q abnormality. The remaining two lesions showed aberrations affecting other chromosomes. The childhood case was one of those with an 8q abnormality. None had a normal karyotype.

Angiolipoma

Five cases were classified as angiolipomas. All occurred in males in the second to sixth decades and all were subcutaneous. Three patients had multiple lesions. Three tumors arose on the extremities and two on the trunk. All five cases had a normal karyotype.

Hibernoma

Two cases were classified as hibernoma. Both arose in males in the fourth decade, one being subfascial in the lower limb and the other subcutaneous in the buttock. Both showed abnormalities of 11q.

Lipoblastoma

Three cases were classified as lipoblastoma. All presented in the first decade, affecting two boys and one girl. Two were located on the trunk and the third arose in the retroperitoneum. One was subcutaneous and two were deep-seated. Histologically, two cases were extremely mature and were only recognizable initially by their markedly lobular architecture and increased vascularity. All three cases showed rearrangements affecting 8q.

Spindle Cell/Pleomorphic Lipoma

Eight cases were classified as spindle cell or pleomorphic lipoma. Three showed morphological features focally that overlapped with atypical lipoma or spindle cell liposarcoma[21] and one showed extensive myxoid change such that it might easily have been designated myxolipoma if the spindle cell foci had been missed. All arose in adults (five males and three females) between the fourth and eighth decades. Seven were subcutaneous and in the eighth the depth was unknown. Five arose in the neck, one on the trunk, and two in the extremities.

All cases had an abnormal karyotype. Seven cases showed unbalanced aberrations involving 16q (resulting usually in monosomy 16 or partial loss of 16q), in five cases combined also with unbalanced aberrations of 13q, and in one of the latter there was also a 6p abnormality. One case (which was morphologically classical) showed a combination of a 13q abnormality and a ring chromosome.

Atypical Lipomatous Tumors

Included in this category were thirty-seven tumors that fulfilled morphological criteria either for traditional well differentiated liposarcoma (lipoma-like or sclerosing) or for atypical lipoma (with or without lipoblasts) characterized by variation in adipocyte size, atypical adipocyte nuclei, and bizarre, often multinucleate stromal cells. There is convincing evidence that these lesions form a histological continuum with identical clinical behavior, albeit with greater mortality when located in the retroperitoneum.[22–26] All arose in adults (24 males and 13 females), predominantly in the fifth to seventh decades. Twenty-eight tumors presented in the extremities, six in the retroperitoneum and three at other sites. Six cases arose in superficial soft tissue, whereas thirty-one were deep-seated (twenty-five intramuscular or subfascial and six retroperitoneal). In terms of histological subclassification, twenty-eight cases were purely lipoma-like, four were lipoma-like plus sclerosing (of which one case each showed spindle cell and dedifferentiated areas), four were extensively dedifferentiated (of which one had myxoid spindle cell areas), and one was lipoma-like with myxoid spindle cell areas.

Thirty-five cases (95%) showed karyotypic abnormalities, characterized in twenty-nine cases by the presence of a ring chromosome (one of which was also associated with a 16q abnormality). Ring chromosomes were common at all anatomic sites. Among the other six cases, three showed abnormalities of 6p (associated with a 13q aberration in one case), one showed aberrations of both 13q and 16q, one showed a 12q abnormality, and one had a giant marker chromosome. Among the six subcutaneous cases, two had ring chromosomes, two had 6p aberrations (one associated with a 13q abnormality), one had a 16q aberration (also associated with a 13q abnormality), and one had a normal karyotype. Among the lesions with a ring chromosome, there were three lesions in which the cytological atypia was so focal or subtle that not all of the pathologists had consistently identified this feature initially. In fact, among the whole group of thirty-seven lesions, five had been published previously as ordinary lipomas[12,17] and one as a hibernoma.[27] Of the five tumors with dedifferentiated areas, four had ring chromosomes and one showed a complex karyotype with multiple aberrations, several of which involved 12q.

Myxoid Liposarcoma

Twenty-seven cases were classified as myxoid liposarcoma, of which six were conventional low grade type, seventeen were more poorly differentiated with round cell areas, and four were poorly differentiated with spindle cell areas (mimicking myxofibrosarcoma). Two cases had areas of well differentiated lipoma-like tumor, distinguishable from atypical lipoma only by the absence of fibrous septae or bizarre stromal nuclei. All patients were adults (21 males and 6 females) equally distributed in the third through eighth decades. Twenty-three cases arose in the extremities, two on the trunk, and two in the retroperitoneum. Three of four non-extremity lesions were soft tissue metastases from previous limb primaries. All tumors except two were deep-seated.

Twenty-six cases (96%) showed the reciprocal translocation t(12;16)(q13;p11), in one case associated with an 11q aberration. One case had a normal karyotype. Cases with round cell, poorly differentiated spindle cell, or lipoma-like areas showed no cytogenetic differences from the group as a whole.

Other Types of Liposarcoma

Two cases were classified as pleomorphic liposarcoma. Both occurred in adult females (in the fourth and fifth decades) and arose in the axilla and chest wall, respectively. Both had a normal karyotype. One additional case was classified as mixed liposarcoma, comprising an equal combination of well differentiated lipoma-like liposarcoma and myxoid liposarcoma with poorly differentiated spindle cell areas. This tumor arose in the retroperitoneum of a male in the sixth decade. Cytogenetic analysis in several areas revealed a ring chromosome as the sole anomaly.

Discussion

It is clear that the majority of lipomatous tumors, irrespective of histological type, show cytogenetic aberrations. Although a variety of karyotypic abnormalities may be identified in this group of tumors as a whole, it is equally clear that these correlate to a significant extent with histological classification (Table 2). Some of these findings have been previously documented,[1–7,10–17,27–31] but to our knowledge, this is the first study to systematically correlate morphology with karyotype in a double-blind setting, thereby providing an objective assessment of the potential value and specificity of cytogenetic analysis in the diagnosis of fatty tumors.

Perhaps one of the most important outcomes was the fact that the pathologists in the CHAMP group rapidly became aware, during the correlative group meeting, that in a variety of difficult or arguable diagnostic settings (see below) the tumor karyotype might facilitate a consensus diagnosis. The main category in which there was occasional discordance among the pathologists was the accurate recognition of atypical lipomatous tumors. Bearing in mind that all of the pathologists involved in this study reasonably could be claimed to be experienced in soft tissue tumor diagnosis, then it seems likely that the diagnostic (or at least problem-solving) potential of cytogenetic analysis would be even greater in a nonspecialist setting.

Although the majority of common subcutaneous lipomas pose no diagnostic problem, occasionally, differentiation is necessary from hibernoma with a high content of mature adipocytes, from lipoblastoma (or lipoblastomatosis) that has largely matured, and perhaps most importantly, from atypical lipomas in which variation in adipocyte size and nuclear atypia may be sufficiently subtle as to be beyond a consensus diagnosis. In each of these circumstances, distinction can be aided in most cases by the consistent finding of 11q13–21 abnormalities, 8q11–13 aberrations, and ring chromosomes, respectively, albeit these karyotypes are not absolutely specific. The ring chromosomes that are so distinctive in atypical lipomatous tumors have previously been shown to derive from the 12q13–15 region.[16] The presence of such a ring in the present study was highly predictive of atypical lipoma when compared with all benign lipomatous tumors ($P < 0.001$). By the same token, hibernomas with a small number of multivacuolated cells could be distinguished from atypical lipoma (lipoma-like liposarcoma), a not uncommon diagnostic problem. These points were demonstrated amply in those few cases for which some pathologists in the group had diagnosed a lipoma as atypical and, after the finding of a ring chromosome, histological review by those in doubt confirmed the diagnosis.

Similarly, in two cases composed of almost entirely mature adipose tissue, the presence of marked lobulation prompted the pathologists in the group to suggest a possible diagnosis of mature lipoblastoma, which was then confirmed by the disclosure of young patient age and an 8q11–13 aberration. The presence of an 8q rearrangement in the only intramuscular lipoma arising in a child might also suggest maturation in a lipoblastoma, but in the absence of morphological clues to such a diagnosis and in view of the presence of 8q abnormalities in two adult cases of ordinary lipoma (one subcutaneous and one intramuscular), it is not possible to be certain.

It was interesting to note that there were no consistent cytogenetic differences between subcutaneous, subfascial, and intramuscular lipomas of ordinary type, confirming that there do exist a small group of deep-seated fatty tumors that lack both histological atypia and ring chromosomes. The important corollary of this finding is that the majority of deep-seated well differentiated fatty tumors are histologically atypical and most have a ring chromosome. Given the greater tendency of such lesions to recur locally (and potentially to dedifferentiate), then the karyotype might be a valuable prognostic marker, especially in histologically arguable cases.

Turning to the spindle cell and pleomorphic lipoma group, some authors have suggested that these lesions be co-classified with atypical lipoma[24,25] although others have resisted this idea on the grounds that spindle cell and pleomorphic lipomas have little or no tendency to recur and no capacity to dedifferentiate.[32] Cytogenetic analysis supports the latter view as spindle cell and pleomorphic lipomas have consistent loss of 16q material (often in association with 13q aberrations) and usually lack

the ring chromosome of atypical lipoma. An interesting corollary was the finding of 13q and 16q aberrations in three subcutaneous lesions that resembled spindle cell and pleomorphic lipoma except for the presence of more diffuse nuclear atypia and pleomorphism and frequent lipoblasts, raising the alternative diagnoses of atypical lipoma or spindle cell liposarcoma.[21] These lesions, however, had a benign clinical course and it seems possible (subject to confirmation in larger long-term studies) that the karyotype might be utilized to predict this and to avoid overdiagnosis of malignancy. Although clinically less crucial, spindle cell and pleomorphic lipomas with only very small or inconspicuous spindle cell areas could be distinguished from usual subcutaneous lipomas in which 16q aberrations so far have never been detected.

With regard to myxoid liposarcoma, the high frequency and specificity of the previously well documented t(12;16) translocation[7,13,28,33] has been confirmed in this series, which is the largest reported to date. The consistent presence of the same aberration in lesions with high grade (round cell) areas of variable extent confirms that they form a single tumor type, as also has been verified recently at the molecular level.[34] From the viewpoint of differential diagnosis, demonstration of this translocation in the (less frequent) poorly differentiated myxoid liposarcomas with mainly spindle cell appearance facilitates distinction from myxofibrosarcoma (myxoid malignant fibrous histiocytoma). At the opposite end of the biological spectrum, it is well recognized that some lipoblastomas may be histologically almost indistinguishable from myxoid liposarcoma,[35] but clear-cut cytogenetic differences between these lesions have now emerged from this and other studies.[30,36] There also exist infrequent atypical lipomatous tumors that have extensive myxoid areas (often in recurrences) that generally lack delicate vessels but nevertheless may mimic myxoid liposarcoma; two such cases in the present study demonstrated their true nature by the presence of a ring chromosome as the sole aberration.

Lastly, there are two types of fatty neoplasm that are morphologically high grade spindle-celled or pleomorphic neoplasms: pleomorphic liposarcoma and dedifferentiated liposarcoma, the latter requiring the co-existence (or previous demonstration) of a well differentiated atypical lipomatous tumor with higher grade nonlipogenic tumor.[25,37] The two cases in this study of pleomorphic liposarcoma, which is relatively rare, both had a normal karyotype quite likely reflecting the outgrowth of non-neoplastic stromal cells rather than tumor cells in the tissue cultures. However, previously reported cases[28] have shown multiple nondistinctive complex cytogenetic abnormalities, in line with the anaplastic nature of pleomorphic malignant fibrous histiocytoma-like tumors as a whole.[7,38] Available results to date have provided no evidence to suggest that pleomorphic liposarcoma represents the anaplastic end-stage of preceding well differentiated or myxoid tumors. Dedifferentiated liposarcoma, by contrast and despite its at least partly higher grade and often pleomorphic morphology, most often seems to retain the ring abnormality of its well differentiated progenitor, and only in one of five cases was a more complex karyotype observed. This finding not only underlines the close biological relationship between well differentiated and dedifferentiated liposarcomas but might also contribute, at least in part, to explaining why morphologically high grade dedifferentiated liposarcomas do not behave as aggressively as other pleomorphic sarcomas,[37] the latter usually being associated with much more complex and numerous chromosomal abnormalities.[2,3,7]

In summary, this large collaborative study confirms and expands previous data demonstrating that karyotypic aberrations are common in adipocytic neoplasms. It also demonstrates that many of these chromosomal abnormalities are sufficiently (albeit not entirely) specific and sensitive that they can play a significant role in reaching a diagnosis, particularly in the context of cases with borderline morphological features. In the long term, such karyotypic data also may prove to have a prognostic role. When circumstances and facilities permit, we actively encourage surgeons and pathologists to include cytogenetic analysis as part of the diagnostic evaluation of soft tissue tumors.

Acknowledgments

The authors are grateful to the following for their support of various aspects of this project: Rector of the University of Cagliari, Professor G. Faa, Professor R. Gambarella (University of Cagliari), Ente Sardo Insustrie Turistiche, Sardinia, and Ente Provinciale Turismo, Sardinia.

References

1. Heim S, Mitelman F: Cancer Cytogenetics, ed 2. New York, Wiley-Liss, 1995
2. Sandberg AA, Bridge JA: The Cytogenetics of Bone and Soft Tissue Tumors. Austin, TX, RG Landes Co, 1994
3. Mitelman F: Catalog of Chromosome Aberrations in Cancer, ed 5. New York, Wiley-Liss, 1994

4. Sreekantaiah C, Ladanyi M, Rodriguez E, Chaganti RSK: Chromosomal aberrations in soft tissue tumors: relevance to diagnosis, classification, and molecular mechanisms. Am J Pathol 1994, 144:1121–1134
5. Sreekantaiah C, Sandberg AA: Clustering of aberrations to specific chromosome regions in benign neoplasms. Int J Cancer 1991, 48:194–198
6. Fletcher JA, Kozakewich HP, Hoffer FA, Lage JM, Weidner N, Tepper R, Pinkus GC, Morton CC, Corson JM: Diagnostic relevance of clonal cytogenetic aberrations in malignant soft-tissue tumors. N Engl J Med 1991, 324:436–442
7. Molenaar WM, DeJong B, Buist J, Idenburg VJS, Seruca R, Vos AM, Hoekstra MJ: Chromosomal analysis and the classification of soft tissue sarcomas. Lab Invest 1989, 60:266–274
8. Scrable H, Witte D, Shimada H, Seemayer T, Wang-Wuu S, Sonkup S, Koufos A, Houghton P, Lampkin B, Cavenee W: Molecular differential pathology of rhabdomyosarcoma. Genes Chromosomes & Cancer 1989, 1:23–25
9. Downing JR, Khandekar A, Shurtleff SA, Head DR, Parham DM, Webber BL, Pappo AS, Hulshof MA, Conn WP, Shapiro DN: Multiplex RT-PCR assay for the differential diagnosis of alveolar rhabdomyosarcoma and Ewing's sarcoma. Am J Pathol 1995, 146:626–634
10. Mandahl N, Heim S, Johansson B, Bennet K, Mertens F, Olsson G, Rooser B, Rhydholm A, Willen H, Mitelman F: Lipomas have characteristic structural chromosomal rearrangements of 12q13–14. Int J Cancer 1987, 39:685–688
11. Sreekantaiah C, Leong SPL, Karokousis CP, McGee DL, Rappaport WD, Villar HV, Neal D, Fleming S, Wankel H, Herrington PN: Cytogenetic profile of 109 lipomas. Cancer Res 1991, 51:422–433
12. Mandahl N, Heim S, Arheden K, Rydholm A, Willen H, Mitelman F: Three major cytogenetic subgroups can be identified among chromosomally abnormal solitary lipomas. Hum Genet 1988, 79:202–208
13. Turc-Carel C, Limon J, Dal Cin P, Rao U, Karakousis C, Sandberg AA: Cytogenetic studies of adipose tissue tumors. II. Recurrent reciprocal translocation t(12;16)(q13;p11) in myxoid liposarcomas. Cancer Genet Cytogenet 1986, 23:291–300
14. Heim S, Mandahl N, Kristoffersson U, Mitelman F, Rooser B, Rydholm A, Willen H: Marker ring chromosome: a new cytogenetic abnormality characterizing lipogenic tumors? Cancer Genet Cytogenet 1987, 24:319–326
15. Heim S, Mandahl N, Rydholm A, Willen H, Mitelman F: Different karyotypic features characterize different clinicopathologic subgroups of benign lipogenic tumors. Int J Cancer 1988, 42:863–867
16. Dal Cin P, Kools P, Sciot R, DeWever I, Van Damme B, Van de Ven W, Van den Berghe H: Cytogenetic and fluorescence *in situ* hybridization investigation of ring chromosomes characterizing a specific pathologic subgroup of adipose tissue tumors. Cancer Genet Cytogenet 1993, 68:85–90
17. Mandahl N, Hoglund M, Mertens F, Rydholm A, Willen H, Brosjo O, Mitelman F: Cytogenetic aberrations in 188 benign and borderline adipose tissue tumors. Genes Chromosomes & Cancer 1994, 9:207–215
18. Enzinger FM, Weiss SW: Soft Tissue Tumors, ed 3. St Louis, CV Mosby, 1995
19. Rosai J: Ackerman's Surgical Pathology, ed 7. St Louis, CV Mosby, 1989 s
20. Fletcher CDM: Soft tissue tumors. Diagnostic Histopathology of Tumors. Edited by CDM Fletcher. Edinburgh, Churchill Livingstone, 1995 pp 1043–1096
21. Dei Tos AP, Mentzel T, Newman PL, Fletcher CDM: Spindle cell liposarcoma, a hitherto unrecognized variant of liposarcoma: analysis of six cases. Am J Surg Pathol 1994, 18:913–921
22. Evans HL, Soule EH, Winkelmann RK: Atypical lipoma, atypical intramuscular lipoma and well differentiated retroperitoneal liposarcoma: a reappraisal of 30 cases formerly classified as well differentiated liposarcoma. Cancer 1979, 43:574–584
23. Kindblom L-G, Angervall L, Fassina AS: Atypical lipoma. Acta Pathol Microbiol Scand A 1982, 90:27–36
24. Azumi N, Curtis J, Kempson RL, Hendrickson RM: Atypical and malignant neoplasms showing lipomatous differentiation. Am J Surg Pathol 1989, 11:161–183
25. Evans HL: Liposarcomas and atypical lipomatous tumors: a study of 66 cases followed for a minimum of 10 years. Surg Pathol 1988, 1:41–54
26. Weiss SW, Rao VK: Well-differentiated liposarcoma (atypical lipoma) of deep soft tissue of the extremities, retroperitoneum and miscellaneous sites: a follow-up study of 92 cases with analysis of the incidence of "dedifferentiation". Am J Surg Pathol 1992, 16:1051–1058
27. Mertens F, Rydholm A, Brosjo O, Willen H, Mitelman F, Mandahl N: Hibernomas are characterized by rearrangements of chromosome bands 11q13–21. Int J Cancer 1994, 58:503–505
28. Sreekantaiah C, Karakousis CP, Leong SPL, Sandberg AA: Cytogenetic findings in liposarcoma correlate with histopathologic subtypes. Cancer 1992, 69:2484–2495
29. Mandahl N, Mertens F, Willen H, Rydholm A, Brosjo O, Mitelman F: A new cytogenetic subgroup in lipomas: loss of chromosome 16 material in spindle cell and pleomorphic lipomas. J Cancer Res Clin Oncol 1994, 120:707–711
30. Dal Cin P, Sciot R, De Wever I, Van Damme B, Van den Berghe H: New discriminative chromosomal marker in adipose tissue tumors: the chromosome 8q11-q13 region in lipoblastomas. Cancer Genet Cytogenet 1994, 78:232–235
31. Meloni AM, Spanier SS, Bush CH, Stone JF, Sandberg AA: Involvement of 10q22 and 11q13 in hibernoma. Cancer Genet Cytogenet 1994, 72:59–64
32. Fletcher CDM: Soft tissue tumours: an update. Recent Adv Histopathol 1992, 15:113–139
33. Aman P, Ron D, Mandahl N, Fioretos T, Heim S, Arheden K, Willen M, Rydholm A, Mitelman F: Rearrangement of the transcription factor gene CHOP in myxoid

liposarcomas with t(12;16)(q13;p11). Genes Chromosomes & Cancer 1992, 5:278–285
34. Knight J, Renwick PJ, Dal Cin P, Van Den Berghe H, Fletcher CDM: Translocation t(12;16)(q13;p11) in myxoid liposarcoma and round cell liposarcoma: molecular and cytogenetic analysis. Cancer Res 1995, 55:24–27
35. Mentzel T, Calonje E, Fletcher CDM: Lipoblastoma and lipoblastomatosis: a clinicopathological study of 14 cases. Histopathology 1993, 23:527–533
36. Fletcher JA, Kozakewich HP, Schoenberg ML, Morton CC: Cytogenetic findings in pediatric adipose tumors: consistent rearrangement of chromosome 8 in lipoblastoma. Genes Chromosomes & Cancer 1993, 6:24–29
37. McCormick D, Mentzel T, Beham A, Fletcher CDM: Dedifferentiated liposarcoma: clinicopathologic analysis of 32 cases suggesting a better prognostic subgroup among pleomorphic sarcomas. Am J Surg Pathol 1995, 18:1213–1223
38. Fletcher CDM: Pleomorphic malignant fibrous histiocytoma: fact or fiction? A critical reappraisal based on 159 tumors diagnosed as pleomorphic sarcoma. Am J Surg Pathol 1992, 16:213–228.