Table S1 CGH

Reference #	1st Author & Year	Article Title	Study Type		Lesion Characteristics			Results Summary
				n	nevus	proliferation	melanoma	
1	Bastian BC 2000	Mutations and copy number increase of HRAS in Spitz nevi with distinctive histopathological features.	retrospect case series	102	102			Correlated 11p incresase to specific cytomorphologic features in Spitz nevi. 102 (Spitz)
2	Harvell JD 2002	Persistent (recurrent) Spitz nevi: a histopathologic, immunohistochemical, and molecular pathologic study of 22 cases.	case series	22	22			50% cases no abnormalities, 30% isolated 11p gain, 10% multiple losses, 10% 9p loss (w poor outcome)= 90% specific, ?90% sensitive
3	Bastian BC 2002	Genetic changes in neoplasms arising in congenital melanocytic nevi: differences between nodular proliferations and melanomas.	retrospect case series	151	23		128	Looked at nodular proliferations in large congenital nevi and compared then to typical congenital nevi and melanomas, some developing within nevi and some not associated with nevi using CGH. Found frequent aberrations in the nodular proliferations. However, the patterns of aberrations were different in comparison to melanoma. Suggest differences are responsible for behavior.
4	Bastian BC 2003	Classifying melanocytic tumors based on DNA copy number changes.	retrospect case series	186	54		132	Applied CGH to 132 melanoma and 54 benign nevi and showed that 96.2% of melanomas had some form of genetic abnormality, while none of the nevi examined, with the exception of Spitz nevi that show gains in 11p, had any abnormalities
5	Harvell JD 2004	High-resolution array-based comparative genomic hybridization for distinguishing paraffin-embedded Spitz nevi and melanomas.	retrospect case series	5	3		2	Highlighted utility of aCGH: 2/3 Spitz nevi had no aberrations. 1/3 had 11p gain, all 3 MM had multiple aberrations. Aberations: 100% sensitive, 66% specific 3 spitz, 2 melanomas
6	Namiki T 2005	Genomic alterations in primary cutaneous melanomas detected by metaphase comparative genomic hybridization with laser capture or manual microdissection: 6p gains may predict poor outcome.	retrospect case series	20			20	100% had multiple chromosomal abnormalities, 6p gains may predict poor outcome
7	Maize JC 2005	Genomic analysis of blue nevi and related dermal melanocytic proliferations.	retrospect case series	29	11	11	7	0% typical blue nevi w/ chrom aberrations. Atypical lesions: 3/11 with aberrations (ranging from 1-3 aberrations/tumor). Melanomas: 100% w multiple aberrations (avg 8/tumor), more loss 9p
8	Vincek v 2009	Comparative genome hybridization analysis of laser-capture microdissected in situ melanoma.	retrospect case series	15	5		10	3/5 melanomas with chromosomal alterations. 2/5 MIS with chromosomal alterations. 0/5 nevi. MIS: only 2 chromosomes involved. Technical limitations involving size of areas available after laser-capture microdissection. Proposed that delection of 13q may be early event in melanoma progression.
9	Gaiser T 2010	Classifying ambiguous melanocytic lesions with FISH and correlation with clinical long-term follow up.	retrospect case series	22		22		Compared aCGH with FISH. No significant differences. Cases of melanoma that developed mets showed more chromosomal aberrations detected by aCGH. Comparing the FISH results with the clinical behavior reached an overall sensitivity of 60% and a specificity of 50% ($\chi 2=0.25$; P=0.61) for later development of metastases.
10	Ali L 2010	Correlating array comparative genomic hybridization findings with histology and outcome in spitzoid melanocytic neoplasms.	retrospect case series	10	8	1	1	7/8 Spitz nevi without aberration. 1/8 w gains in 7q and 11p. 1/1 spitzoid tumors w 19p gains. Spitzoid melanoma w/ multiple abnormalities Use aCGH to evaluate 10 melanocytic neoplasms with spitzoid morphology (8 spitz nevi, 1 spitz tumor and 1 spitzoid melanoma) and correlate the aCGH findings to the clinical outcome of these cases.

11	Kutzner H 2012	Histological and genetic evidence for a variant of superficial spreading melanoma composed predominantly of large nests.	retrospect case series	27			27	Using aCGH to examine melanoma with large nests. Found they are cytogenetically similar to superfical pearding melanoma.
12	Wang L 2013	A genome-wide high-resolution array-CGH analysis of cutaneous melanoma and comparison of array-CGH to FISH in diagnostic evaluation.	retrospect case series	30	5		25	Compared aCGH analysis with FISH assay. Positive results were obtained in 72% of melanomas via the four-probe FISH assay (RREB1/MYB/CEP6/CCND1).The overall concordance in aberrations detected using the two methods was 90%.
13	Hirsch D 2013	Chromothripsis and focal copy number alterations determine poor outcome in malignant melanoma.	retrospect case series	20			20	Used cytogenetic analysis to stratify melanomas into good and bad prognosis groups and showed that melanomas associated with a good prognosis showed only a few chromosomal imbalances, whereas melanomas with poor prognosis harbored significantly more chromosomal aberrations, including aberrations associated with chromothripsis.
14	Guo R 2014	Comparative genomic hybridization in a case of melanoma that loses expression of S100, HMB45, Melan A and tyrosinase in metastasis.	retrospect case series	3			3	Used aCGH to look at paired melanoma prirmaries and mets. Found gains of 7q and loss chromosome 9p24.3-q13 and chromosome 4. Interestingly, the mets were Melan A negative and the detected loss was in the region of the Melan A gene.
15	Boi S 2014	Increased frequency of minimal homozygous deletions is associated with poor prognosis in primary malignant melanoma patients.	retrospect case series	96			96	Looked at copy number abnormalities with aCGH in melanoma and showed that deletions may be associated with a poor prognosis.
16	Magro C 2014	Deep penetrating nevus-like borderline tumors: A unique subset of ambiguous melanocytic tumors with malignant potential and normal cytogenetics.	retrospect case series	46		40	6	40 cases of DPN-like borderline tumor were identified along with 6 cases of plexiform melanoma. All 6 DPN-like borderline tumor cases tested by CGH showed normal cytogenetics, as did 7 of 9 cases tested by FISH. Of the plexiform melanomas, 4/6 patients died of disease. In 3 cases there was morphologic progression from a DPN-like borderline tumor to overt melanoma. DPN-like borderline tumors are melanocytic tumors associated with a high incidence of regional lymph node disease and exhibiting the potential for melanoma progression despite a normal cytogenetic profile.
17	Lacoste C 2015	Malignant Melanoma Arising in Patients with a Large Congenital Melanocytic Naevus: Retrospective Study of 10 Cases with Cytogenetic Analysis.	retrospect case series	10			10	Explored large congenital nevi with FISH and CGH. Melanomas that developed in thir cohort were more common on the back and trunk. Found CGH most useful in challenging leisons.
18	Mahas A 2016	Copy number variation in archival melanoma biopsies versus benign melanocytic lesions.	retrospect case series	62	21		41	Used high resolution, genome-wide single-nucleotide polymorphism arrays to perfom analysis on recurrent copy number aberrations detected by aCGH in melanoma compared with nevi (41 melanoma, 21 benign nevi)
				856	254	74	528	

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Table S2 FISH

Reference #	1st Author & Year	Article Title	Study Type		Lesion Characteristics			Patient Characteristics		Results Summary
				n	nevus	proliferation	melanoma	adult 18+	pediatric <18	outcomes of procedure
1	Bastian BC 2000	Mutations and copy number increase of HRAS in Spitz nevi with distinctive histopathological features.	molecular/cytology correlation	102	102					Showed that isolated gains in 11p (involving the locus 11p15.5) are present in roughly 20% of Spitz nevi, corresponding to the HRAS gene locus. Interestingly, in nearly two thirds of these cases an activating in the HRAS gene is also found. These aberrations have some effect on morphology as Spitz nevi with gains in 11p are often large in diameter and have an infiltrative growth pattern at the base with a pronounced desmoplastic stromal reaction. (102 Spitz)
2	Harvell JD 2002	Persistent (recurrent) Spitz nevi: a histopathologic, immunohistochemical, and molecular pathologic study of 22 cases.	retrospective	22	21		1			Examined 22 cases of persistent / recurrent Spitz nevi, 12 of which had additional analysis using dual-color FISH with probes to 11p and 11q. FISH was able to corroborate the 11p amplification in two of the three cases that were detected by CGH. (21 spitz nevi, 1 spitzoid melanoma)
3	Sauter ER 2002	Cyclin D1 is a candidate oncogene in cutaneous melanoma.	case series	137			137			amplification of CD1 in acral (44.4%) and occasional amplification in lentigo maligna melanoma (10.5%) and superficial spreading melanoma (5.6%). CD1 protein was overexpressed in all cases with amplifications and in an additional 20% of cases without amplification
4	Treszl A 2004	Extra copies of c-myc are more pronounced in nodular melanomas than in superficial spreading melanomas as revealed by fluorescence in situ hybridisation	case series	68			68			-myc copy number alterations differ in the two melanoma subtypes and are associated with the advanced stage of the disease
5	Casorzo L 2005	Fluorescence in situ hybridization (FISH) evaluation of chromosomes 6, 7, 9 and 10 throughout human melanocytic tumorigenesis.	case series	60	30		30			Analyzed 30 common nevi and 30 melanomas associated with nevi by FISh and suggested that loss of 9p21 may be a marker for progression. None of the common nevi showed chromosomal aberrations.
6	Takata M 2005	Constitutive activation of the mitogen-activated protein kinase signaling pathway in acral melanomas	case series	28			28			prominent amplification of the cyclin D1 (CCND1) gene, which is an important down-stream effecter of the MAPK pathway, in 5 of 21 (23.8%) tumors examined
7	Willmore-Payne C 2006	BRAF and c-kit gene copy number in mutation-positive malignant melanoma	case series	46			46			43 BRAF mutation-positive tumors, 26 as presumptive heterozygous, 8 indeterminent, 9 excess allele
8	Koynova DK 2007	Increased C-MYC copy numbers on the background of CDKN2A loss is associated with improved survival in nodular melanoma.	retrospective	49			49			C-MYC increased copy number changes on the background of CDKN2A deletions seem to be related to a low metastatic potential and better patients' outcome in primary NMs
9	Koynova DK 2007	Gene-specific fluorescence in-situ hybridization analysis on tissue microarray to refine the region of chromosome 20q amplification in melanoma.	case series	280			280			Applied FISH to melanomas with MYBL2, ZNF217, CYP24 and STK6 specific probes
10	Antonescu CR 2007	L576P KIT mutation in anal melanomas correlates with KIT protein expression and is sensitive to specific kinase inhibition	case series	20			20			heterozygous KIT substitution was identified in 3 case, NRAS mutation was identified in one tumor, BRAF or PDGFRA mutations identified. (**20 anal melanomas)**
11	North JP 2008	Distribution and significance of occult intraepidermal tumor cells surrounding primary melanoma	case series	19			19			melanocytes with genetic amplifications in histopathologically normal skin (field cells) were detected exclusively in the epidermis in 84% of 19 cases, with a mean extension of 6.1 mm (in situ melanomas) and 4.5 mm (invasive melanomas) beyond the histopathological margin
12	Moore SR 2008	Detection of copy number alterations in metastatic melanoma by a DNA fluorescence in situ hybridization probe panel and array comparative genomic hybridization: a southwest oncology group study	case series	19			19			Outlines the most common copy number aberrations in metastatic melanoma using a panel of 16 locus-specific FISH probes located on eight chromosomes. (**19 metastatic melanomas)**
13	Rakosy Z 2008	Characterization of 9p21 copy number alterations in human melanoma by fluorescence in situ hybridization.	case series	81			81			high frequency of 9p21 loss (84%) was found
14	Gerami P 2009	Fluorescence in situ hybridization for distinguishing nevoid melanomas from mitotically active nevi	comparative case	20	10		10			All 10 nevoid melanomas showed copy number abnormalities by FISH in either chromosome 6 or 11 while none of the 10 mitotically active nevi did. The results demonstrate that FISH targeting key chromosomal loci on chromosomes 6 and 11 can be effective in discriminating nevoid melanomas from mitotically active nevi.
15	Newman MD 2009	Chromosomal copy number changes supporting the classification of lentiginous junctional melanoma of the elderly as a subtype of melanoma	comparative case	36	17		19			Classified lentiginous nevi in the elderly as a form of melanoma as 16 of 19 cases (84%) showed sufficient copy number changes in one of the targeted chromosomal loci to meet FISH criteria for melanoma.(19 lentiginous nevi of the elderly; 17 lentiginous junctional nevi, control)
16	Pouryazdanparast 2009	Distinguishing epithelioid blue nevus from blue nevus like cutaneous melanoma metastasis using fluorescence in situ hybridization	comparative case	20	10		10			Explored the use of FISH to distinguishing epithelioid blue nevus from blue nevus like cutaneous melanoma metastasis. In this study, FISH was able to identify significant genetic aberrations in nine out of the 10 cases of blue nevus like cutaneous melanoma metastasis. None of the epithelioid blue nevi (0/10) showed evidence of significant copy number changes or met FISH criteria for a diagnosis of melanoma.
17	Newman 2009	Fluorescence in situ hybridization as a tool for microstaging in malignant melanoma	comparative case	42			42			Looked at melanoma associate with nevi and nevoid melanoma with FISH. In the cases of melanoma associated with a nevus, FISH was performed on both portions of the lesion. 78% of the melanomas were FISH positive and none of the nevi were FISH positive. All (6) of the nevoid melanomas were FISH positive.
18	Gerami P 2009	Fluorescence in situ hybridization (FISH) as an ancillary diagnostic tool in the diagnosis of melanoma	validation study	524	239	54	231			Identified the modern FISH melanoma test using a training set and an algorithm for scoring. The 4 probe FISH with the greatest sensitivity (86.7%) and specificity (95.4%) was FISH using probes targeting chromosome 6p25, 6 centromere, 6q23, and 11q13
19	Morey AL 2009	Diagnosis of cutaneous melanocytic tumours by four colour fluorescence in situ hybridisation	comparative case	40	20		20			FISH distinguished the melanomas and the nevi with a sensitivity of 90% (10/10 primary melanoma cases and 8/10 metastatic melanoma cases, respectively), and a specificity of 95%
20	Zimmermann AK 2010	FISH analysis for diagnostic evaluation fo challenging melanocytic lesions	case series	14		14				The results of FISH analysis were consistent with the conventional diagnosis in 11 of 14 small ambiguous lesions. Of the remaining 3 cases, 2 showed FISH-results close to the cut-off level. Comparison of FISH results on thin and thick sections revealed that the cut-off values have to be adapted for 2 microm destained sections
21	Gerami P 2010	Superficial melanocytic neoplasms with pagetoid melanocytosis:a study of interobserver concordance and correlation with FISH	comparative case series	24		24				Examined histologically challenging lesions with single cell pagetosis by 4 probe FISH and also by histologic concordance. The authors found strong interobserver reliability by expert judgement. None of the cases labeled as benign were FISH positive. FISH was able to identify 5 /7 cases where melanoma was judged histologically. FISH was also able to identify 2 case as melanoma that were found indeterminate by histology.

22	Gerami P 2010	Sensitivity of fluorescence in situ hybridization for melanoma diagnosis using RREB1, MYB, Cep6 and 11q12 probes in melanoma subtypes	blinded comparison	233	110		123			Overall, sensitivity was 83.0% and specificity was 94.0%. The 6p25 gain criterion had the highest sensitivity for melanoma overall and in each subtype. The assay was most sensitive in the subgroups of nodular and acral melanomas and least sensitive in the superficial spreading subtype. The 11q13 gain was more commonly seen in chronically sun-damaged skin and infrequently in non-chronically sun-damaged skin
23	Gaiser T 2010	Classifying ambiguous melanocytic lesions with FISH and correlation with clinical long-term follow up	validation study	22		22				Comparing the FISH results with the clinical behavior reached an overall sensitivity of 60% and a specificity of 50% (chi(2)=0.25; P=0.61) for later development of metastases
24	Dalton SR 2010	Use of fluorescence in situ hybridization (FISH) to distinguish intranodal nevus from metastatic melanoma		59	17		42			Looked at the ability of FISH to distinguish intranodal nevus from metastatic melanoma. Using FISH markers for three regions on chromosome 6 and one on chromosome 11 to determine the presence of chromosomal aberrations, they found that 20 of 24 (83%) cases diagnosed as metastatic melanoma showed aberrations by FISH and only one of the 17 nodal nevi (6%) showed aberrations by FISH.
25	Busam K 2010	Distinction of conjunctival melanocytic nevi from melanomas by fluorescence in situ hybridization	case series	12	4		8			Used the melanoma FISH test in conjunctival lesions (4 nevi and 8 melanomas) and showed that the test was able to discriminate between benign and malignant leisons.
26	Diaz A 2011	Pigmented spindle cell nevus: clues for differentiating it from spindle cell malignant melanoma. A comprehensive survey including clinicopathologic, immunohistochemical and FISH studies	comparative case series	46	22		24			Looked at pigmented spindle cell nevus of Reed (PSCN) and spindle cell melanoma by FISH and immunohistochemistry, including MIB-1 and survivin. They showed that FISH was positive in 1 of the 15 PSCN and negative in 4 of the 15 melanomas, resulting in a sensitivity73% and specificity 93% of respectively.
27	Hossain D 2011	Differentiation of melanoma and benign nevi by fluorescence in situ hybridization	retrospective comparative case series	63	32		31			MelanoFISH, which uses probes that target chromosomes 6, 7, 11 and 20, had a sensitivity and specificity of 94% and 94% in differentiating melanoma from nevi, with the advantage that FISH hybridization with MelnaoFISH was shorter because of the use of DNA probes instead of artificial chromosome probes from bacteria that was described in prior studies.
28	Moore MW 2011	FISH as an effective diagnostic tool for the management of challenging melanocytic lesions	retrospective comparative case series	500	157	176	167			Examined 500 cases (157 nevi, 167 dysplastic nevi, and 176 melanoma cases) using the melanoma FISH test and showed it was able to identify 83.8% of melanomas, and 98.1% of all benign nevi. In their analysis they also varied cutoff levels for FISH, and found that the levels previously defined by the Melanoma FISH test had a lower sensitivity in ambiguous lesions. They also showed that the RREB1 probe had the highest sensitivity for melanoma in their cases with a sensitivity of 60%.
29	Pouryazdanparast P 2011	Melanocytic nevi with an atypical epithelioid cell component: clinical, histopathologic and fluorescence in situ hybridization findings	case series	28	28					Explored cases of melanocytic leisons wtih large epithelioid component using the Melanoma FISH test. These cases were foud to be negative by FISH. The authors noted however that some of these leisons have tetraploid cells and cautioned not to misintrepret this as melanoma.
30	Vergier B 2011	Fluorescence in situ hybridization, a diagnostic aid in ambiguous melanocytic tumors: European study of 113 cases	comparative case series	113		113				Used the melanoma FISH test in ambigious lesions. Also had blinded pathology review of these leisons. Showed that histologic features are still the mainstay for diagnosis. In comparison of FISH with histology, FISh had a sensitivity and specificity of 34.5% and 91%, respectiely. This incresed to 90% sensitivity and 76% sensitivity in senarios where both histologocal classificationand FISh were used together.
31	Massi D 2011	Atypical Spitzoid melanocytic tumors: a morphological, mutational and FISH analysis		38		38				FISH analysis demonstrated the presence of chromosomal alterations in 6 of 25 cases. Correlation with follow-up data showed that the only case with fatal outcome showed multiple chromosomal alterations by FISH analysis. (38 atypical spitz)
32	Gerami P 2011	Fluorescence in situ hybridization as an ancillary method for the distinction of desmoplastic melanomas from sclerosing melanocytic tumors	comparative case series	30	15		15			Used the Melanoma FISH test to examine 15 sclerosing nevi (composed of cases that were diagnosed as desmoplastic Spitz nevi, conventional nevi with sclerosis and sclerotic blue nevi) to differentiate between cases of known desmoplastic melanoma. None of the nevi were positive by FISH. However, only 7/15 of the desmoplastic melnaomas were positive by FISH (8/15, over half were not posittive by FISH). Thus caution was recommended in negative cases of DMM and suggested a lower sensitivity of the test in this group of melanoma.
33	Gammon B 2011	Fluorescence in situ hybridization for distinguishing cellular blue nevi from blue nevus like melanoma	comparative case series	17	12		5			Looked at FISH for distinguishing cellular blue nevi from blue nevus like melanoma and showed the assay to have 100% sensitivity and 100% specificity. All 5 cases of blue nevus like melanoma met FISH criteria for a diagnosis of melanoma, with three of five cases met the 6p25/Cep6 criteria, all five met the 6p25 gain criteria and three of five met the 6q23/Cep6 loss criteria. None of the cases met criteria for gains in 11q13. There were 12 cellular blue nevi in this cohort. None of the 12 met any FISH criteria for melanoma.
34	Raskin L 2011	Copy number variations and clinical outcome in atypical spitz tumors	comparative case series	27	8	16	3			Chromosomal aberrations were found in 7 of 16 atypical spitzpid tumors, 1 with fatal outcome, 2 spitzoid melanomas, and 1 conventional melanoma. (16 atypical spitz, 8 spitz)
35	Zembowicz A 2012	Correlation between histologic assessment and fluorescence in situ hybridization using MelanoSITE in evaluation of histologically ambiguous melanocytic lesions.	prospective histologic/FISH correlation study	140		140				All lesions considered atypical nevi showed normal FISH signals. Abnormal FISH signals were reported in 30% of lesions considered histologically borderline and in 48% of lesions in which a diagnosis of melanoma was favored
36	Fang Y 2012	Fluorescence in situ hybridization (FISH) analysis of melanocytic nevi and melanomas: sensitivity, specificity and lack of association with sentinal node status	case series	115		50	65			Examined a range of melanocytic lesions by 4 probe FISH. Showed a 94% sensitivity in benign melanocytic lesions. This sensitivity was increased to 98% when correction for tetraploidy was applied. For malignant melanocytic lesion, the sensitivity of FISH was 82% for primary melanoma and 85% for metastatic melanoma.
37	Abasolo A 2012	Application of fluorescence in situ hybridization as a diagnostic tool in melanocytic lesions, using paraffin wax embedded tissues and imprint cytology specimens		50	10	9	31			Showed a sensitivity of 100% and a specificity when FISH is applied to melanocyic lesions
38	Requena C 2012	Fluorescence in situ hybridization for the differential diagnosis between Spitz naevus and spitzoid melanoma	retrospective comparative case series	18	6		12			4 probe FISH had a 87.5% sensitivity and 100% specificity in distinguishing Spitz nevi from spitzoid melanoma. (12 spitzoid melanoma, 6 spitz nevi)
39	Nijhawan RI 2012	Clinical application and limitations of the fluorescence in situ hybridization (FISH) assay in the diagnosis and management of melanocytic lesions: a report of 3 cases	case series	3		3				Report of 3 cases where FISh was used to help clarify a previously abmibious histologic diagnosis.
40	Pennacchia I 2012	Morphological and molecular characteristics of nested melanoma of the elderly (evolved lentiginous melanoma)	comparative case series	13	5		8			Examined leisons classified as lentiginous nevi of the elderly and benign lentiginous nevi. Showed that the former met FISh criteria for melanoma.
41	Kerl K 2012	A proposal for improving multicolor FISH sensitivity in the diagnosis of malignant melanoma using combined criteria	retrospective comparative case series	560	30	367	163			Reported how alteration of FISH criteria varies the sensiitivity and specificity whe applied to melanocytic lesions.

42	Gerami P 2012	A highly specific and discriminatory FISH assay for distinguishing between benign and malignant melanocytic neoplasms	comparative case series	102	51		51			Due to the relative poor performance of the initial FISH panel in the subsets of spitzoid and spindle melanomas a second generation of the probe set was developed that included probes for 9p21 (CDKN2A) and 8q24 (MYC)
43	Nardone B 2012	Integrating clinical/dermatoscopic findings and fluorescence in situ hybridization in diagnosing melanocytic neoplasms with less than definitive histopatholgoic features	case series	9		9				Showed that combining FISH with clinical information increases the detection of early melanoma.
44	Martin V 2012	Presence of cytogenetic abnormalities in Spitz naevi: a diagnostic challenge for fluorescence in situ hybridization	retrospective comparativecase series	76	62		14			Gene copy number changes in Spitz nevi by FISH with probes targeting 6p25, 6q23, CEP6 and 11q13 is frequent and not explained by a polypoid state.
45	Gammon B 2012	Enhanced detection of spitzoid melanomas using fluorescence in situ hybridization with 9p21 as an adjunctive probe	comparative case series	43			43			Established that FISH for 9p21, that targets the CDKN2A (cyclindependent kinase inhibitor 2A) gene locus that encodes the p16 and p14 tumor suppressors, is a useful complementary test to the standard 4-probe FISH assay in spitzoid melanomas, increasing the sensitivity from 70% to 85%.
46	Horst BA 2013	9p21 gene locus in Spitz nevus of older individuals: absence of cytogenetic and immunohistochemical findings associated with malignancy	case series	25	25					Explored Spitz nevi in older individuals that were initially proven to lack aberrations with 4 probe FISH by adding p16 immunohistochemistry and FISH for 9p21. These cases showed retained p16 by immunohistochemistry and also normal cytogenetic findings at Chr9p21.
47	Tetzlaff MT 2013	Ambiguous melanocytic tumors in a tertiary referral center: the contribution of fluorescenc in situ hybridization (FISH) to conventional histopathologic and immunophenotypic analyses	case series	34		34				In ambiguous lesions, the authors emphasized the incorporation of histology in the analysis of FISH reporting a sensitivity of 50%, specificity of 87.5%, positive predictive value of 62.5% and negative predictive value of 80.7% in their cohort.
48	Wang L 2013	A genome wide high resolution array CGH analysis of cutaneous melanoma and comparison of array CGH to FISH in diagnostic evaluation	case series	20			20			Compared FISH and aCGH in the diagnosis of melanoma and found a concordance rate of 90%
49	Gerami P 2013	Risk assessment for atypical spitzoid melanocytic neoplasms using FISH to identify chromosomal copy number aberrations	case controlled series	75	75					Explored a spectrum of Spitzoid tumors by a limited FISH panel using 4-probe FISH assay that targets 6p25, 6q23, 11q13, and Cep6 and a second 4-probe FISH assay targeting 6p25, 9p21, 11q13, and 8q24. They showed that homozygous deletions in 9p21 are associated with the greatest risk of aggressive clinical behavior. Cases with 6p25 or 11q13 gains also have higher risk for aggressive clinical behavior. Atypical Spitz tumors that are FISH-negative or cases with 6q23 deletions have the least likelihood of aggressive clinical behavior. (75 spitz nevi)
50	Ponti G 2013	Fluorescence in-situ hybridization and dermoscopy in the assessment of controversial melanocytic tumors	retrospective case series	20		20				Explored the utility of FISH as an ancillary tool in cases ambiguous melanocytic lesions where there was a dermatoscopic and histological discrepancy.
51	Horst BA 2012	Chromosomal aberrations by 4 color fluorescence in situ hybridization not detected in spitz nevi of older individuals	retrospective case series	25	25					None of the study cases showing histopathological features typical of Spitz nevi had detectable chromosomal abnormalities by FISH. (25 spitz nevi)
52	Magro CM 2014	Deep penetrating nevus-like borderline tumors: a unique subset of ambiguous melanocytic tumors with malignant potential and normal cytogeneteix	retrospective case series	46		40	6			7 of 9 showed normal FISH
53	DeMarchis EH 2014	Fluorescence in situ hybridization analysis of atypical melanocytic proliferations and melanoma in young patients	case series	21	14	2	5		21	5 melanomas and 1 meltump with positive FISH, all Spitz and 1 meltump were normal FISH. 14 spitz nevi
54	North JP 2014	Fluorescence in situ hybridization as an ancillary tool in the diagnosis of ambiguous melanocytic neoplasms: a review of 804 cases	case series	804	659	145				Examined ambigious melanocytic leisons and showed that FISH could help classify these lesion. (378 spitz 281 nevi 145 melanoma)
55	Urso C 2014	Animal type melanoma: report of five cases with sentinel node biopsy and fluorescence in situ hybridization analysis	case series	5			5			Examined 5 Animal-type melanoma (ATM) that were all negative by FISH
56	Dika E 2015	Spitzoid tumors in children and adults: a comparative clinical, pathological and cytogenetic analysis	comparative study	15	9	3	3	8	5	Using the commercially available FISH melanoma kit they explored the assay in Spitz tumors in children and adults and suggested that the assay is more reliable in lesions found in adults than in children. (9 spitz nevi)
57	Yelamos O 2015	A comparative study of proliferative nodules and lethal melanomas in congenital nevi from children	comparative study	24	22		2	24		Examined proliferative nodules versus melanoma in children. Proliferative nodules were found to have mostly whole chromosomal copy number aberrations by FISH whereas melanoma showed highly elevated copy number aberrations involving 6p25 without gains of the long arm of chromosome 6.
58	Amin SM 2015	Combined cutaneous tumors with a melanoma component: a clinical, histologic, and molecular study	case series	14		14				Examined 15 combined cutaneous tumors composed of meschchymal and melanoma components by FISH and revealed 55% had aberrations.
59	Minca EC 2016	Comparison between melanoma gene expression score and fluorescence in situ hybridization for the classification of melanocytic lesions.	case series	117	24	78	15			In a group of unequivocal melanocytic neoplasms, FISH and qRT-PCR showed 97% and 83% agreement with the histopathologic diagnosis, respectively, with 93% and 62% sensitivity, 100% and 95% specificity, and 80% inter-test agreement.
60	Harms PW 2016	Loss of p16 Expression and Copy Number Changes of CDKN2A in a Spectrum of Spitzoid Melanocytic Lesions	case series	70	24	27	19			Analyzed a spectrum of benign (n = 24), borderline (n = 27), and malignant (n = 19) spitzoid lesions. Proposed an algorithm for risk stratification of spitzoid lesions using p16 immunohistochemistry and FISH, where p16 immunohistochemistry is preformed first and then guides the use of FISH to further classify lesions
				5283	1895	1398	1990		26	

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Table S3 qRT-PCR

Reference#	1st Author & Year	Article Title	Study Type	n	nevus	proliferation	melanoma	Results Summary
1	Clarke LE 2015	Clinical validation of a gene expression signature that differentiates benign nevi from malignant melanoma.	validation	437	226		211	90% sensitivity for melanoma, 91% specificity for nevi
2	Minca EC 2016	Comparison between melanoma gene expression score and fluorescence in situ hybridization for the classification of melanocytic lesions.	case series	117	24	78	15	In a group of unequivocal melanocytic neoplasms, FISH and qRT-PCR showed 97% and 83% agreement with the histopathologic diagnosis, respectively, with 93% and 62% sensitivity, 100% and 95% specificity, and 80% inter-test agreement.
3	Clarke LE 2017	An Independent validation of a gene expression signature to differentiate malignant melanoma from nenign melanocytic nevi	validation with a prospective cohort	1400	823	228	349	The gene expression signature differentiated benign nevi from malignant melanoma with a sensitivity of 91.5% and a specificity of 92.5%. The reference standard used in this validation study was a triple concordant histopathologic
4	Cockerell CJ 2016	The influence of a gene expression signature on the diagnosis and recommended treatment of melanocytis tumors by dermatopathologists	prospective cohort	1695	928	175	592	In diagnostically challenging cases initially diagnosed as indeterminate by histomorphology and IHC, definitive diagnoses increased by 56.6% following qRT-PCR testing
				3649	2001	481	1167	

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