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Mutations in select cutaneous and soft tissue neoplasms

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Neoplasms	Mutations/translocation	Notes
Melanocytic		
Lentigo simplex	KRT10	
Nevus spilus	NRAS	
Nevocellular nevi	BRAF V600E (80%), NRAS (5%)	
Melanoma	BRAF V600E (40-50%), CDKN2A (25-35%), NF1 (10-15%) TP53 (15%), PTEN, NRAS (15-20%), GNAQ/ GNA11 (80-90% uveal), TERT promoter (40-50%)	
Congenital nevi	NRAS	Especially giant congenital nevi
Blue nevus	GNAQ, GNA11	Also, nevus of Ota
Spitz nevus	GNA11, ALK and other kinase fusions (50%), HRAS (10-20%)	
BAP-1 Inactivated spitzoid nevus	BRAF V600E and BAP-1	
Deep penetrating nevus	BRAF V600E and CTNNB1 (2 hits)	CTNNB1 encodes beta-catenin
Epidermal		
Seborrheic keratosis	FGFR3 (25-90%), PIK3CA	
Lichenoid keratosis	FGFR3, PIK3CA, RAS	
Disseminated superficial actinic porokeratosis	MVK	
Epidermal nevi	KRT1/KRT10, FGFR3, HRAS>NRAS>KRAS PIK3CA, AKT1, PTEN	KRT mosaicism associated with epidermolytic ichthyosis
Inflammatory linear verrucous epidermal nevus	GJA1	
Becker nevus	ACTB	ACTB encodes for β-actin
Nevus comedonicus	NEK9	
BCC	PTCH1 > TP53	85% of BCCs have a mutation in the sonic hedgehog (SHH) pathway. PTCH1 is a receptor for SHH ligand
SCC	TP53	
Nevus sebaceus	HRAS (95%) KRAS (5%)	
Actinic keratosis	TP53	

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Adnexal		
Trichoepitheliomas	CYLD	Associated with Brooke-Spiegler and Rombo Syndromes
Pilomatricoma	CTNNB1	CTNNB1 encodes beta-catenin
Trichilemmoma	PTEN	Associated with Cowden Syndrome
Sebaceous adenoma/ sebaceoma/sebaceous carcinoma	MLH1, MSH2, MSH6, PMS2	Associated with Muir-Torre Syndrome
Hidradenoma	t(11;19) CRTC1/MAML2	
Syringocystadenoma papilliferum	BRAF V600E > HRAS > KRAS	HRAS if associated with nevus sebaceous
Spiradenoma	CYLD	Associated with Brooke-Spiegler
Cylindroma	CYLD	Associated with Brooke-Spiegler
Porokeratotic adnexal ostial nevus	GJB2	
Fibrofolliculoma	FLCN	Associated with Birt-Hogg-Dube Syndrome
Trichodiscoma	FLCN	Associated with Birt-Hogg-Dube Syndrome
Soft Tissue		
Lipoma	HMGA2	
Multiple lipomas	PTEN	Associated with Frohlich, Bannayan-Riley-Ruvalcaba, Cowden, and Proteus syndromes
Liposarcoma	Ring chromosomes derived from chromosome 12 with MDM2 amplifications	
Angiolipoma	Low-level mutations of protein kinase D2 (80%)	
Epithelioid sarcoma	SMARCB1/INI1 gene inactivation	
Spindle-cell lipoma and pleiomorphic lipoma	Loss of 16q or monosomy of chromosome 16	
Hibernoma	Loss of MEN1	
Cutaneous and uterine leiomyomas	FH (fumarate hydratase)	Associated with Reed's syndrome
Multiple mucosal neuromas	RET proto-oncogene	Associated with MEN 2B
Neurofibromas	NF1, NF2	
Sclerotic fibroma	PTEN	Associated with Cowden syndrome
Juvenile hyaline fibromatosis	CMG2	

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Neoplasms	Mutations/translocation	Notes
Soft tissue (cont.)		
Giant cell fibroblastoma	t(17;22)(q22;q13) translocation	Results in COL1A1-PDGFB fusion
Dermatofibrosarcoma protuberans	t(17;22)(q22;q13) translocation	Results in COL1A1-PDGFB fusion
Synovial sarcoma	t(X;18)(p11;q11) translocation	
Extraskeletal Ewing sarcoma	t(11;22)(q24;q12) translocation	On the spectrum with malignant peripheral neuroectodermal tumor (MPNET)

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