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Genoderms with skin cancer associations

By Suchita Sampath, DO, and Kelly Kimball, MD

BCC		
Condition	**Gene**	**High-yield associations**
Basal cell nevus syndrome (Gorlin-Goltz syndrome)	AD, *PTCH1/2, SUFU*	- 2+ palmoplantar pits - Odontogenic keratocysts of the jaw - Calcification of falx cerebri - Bifid ribs - Medulloblastoma - Ovarian/cardiac fibroma
Bazex-Dupré-Christol syndrome	XD, *ACTRT1*	- Pili torti - Milia - Follicular atrophoderma (dorsal hands/feet, face, elbows, knees) - Hypohidrosis - Hypotrichosis (+/– pili torti)
Rombo syndrome	AD, *unknown gene*	- Atrophoderma vermiculatum - Milia - Telangiectasia - Acro-facial vasodilation and cyanosis - Trichoepithelioma
Brooke-Spiegler syndrome	AD, *CYLD*	- Cylindroma - Trichoepithelioma - Spiradenoma - Salivary and parotid gland tumors
Xeroderma pigmentosum (DeSanctis-Cacchione syndrome)	AR, *XPA- XPG XPV*	- XPB, XPD and XPG - XP-Cockayne overlap (skin of XP+ retinal degeneration and basal ganglia calcification - XPB, XPD - trichothiodystrophy - Neurodevelopmental delay, sensorineural hearing loss, hyperreflexia EXCEPT in XPV - 10,000-fold increased risk for BCC
Schöpf-Schulz-Passarge syndrome	AR, *WNT10A*	- Ectodermal dysplasia - Multiple hidrocystomas - Hypodontia - Hypotrichosis - PPK - Nail dystrophy

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Oculocutaneous albinism	All variants AR OCA1a- *TYR* absent OCA1b- decreased *TYR* OCA2- *P gene* (most common) OCA3- *TRYP1* OCA4- *SLC45A2* formerly *MATP*	- Photophobia - Nystagmus - Reduced visual acuity - Increased risk of BCC but SCC is the most common type of skin cancer - Variable pigment dilution in skin hairs and eyes (except OCA1a) - OCA2-like hypopigmentation can occur in patients with Prader-Willi syndrome and Angelman syndrome
Xeroderma pigmentosum	AR, *XPA-XPG* *XPV*	- Defective nucleotide excision repair of UV-induced pyrimidine dimers - Extreme photosensitivity - Eyes: photophobia, keratitis, conjunctivitis, pingueculae/pterygia - *XPB*, *XPD* and *XPG*: XP-Cockayne overlap (retinal degeneration and basal ganglia calcification) - *XPB*, *XPD*: trichothiodystrophy - All except *XPV*: neurodevelopmental delay, sensorineural hearing loss, hyperreflexia - 10,000-fold increased risk for SCC - DeSanctis-Cacchione syndrome: XP with severe neurologic deficits and intellectual disability
Dystrophic epidermolysis bullosa	AR, *COL7A1* premature termination with loss of anchoring fibrils AD, *COL7A1* variants with milder disease (similar to EBS)	- Mucocutaneous blisters that heal with atrophic scarring and milia - Pseudosyndactyly due to repeated scarring - Renal failure - SCC are aggressive and #1 cause of death
Epidermodysplasia verruciformis	AR, *TMC6* (EVER1) and *TMC8* (EVER2)	- Secondary to HPV 3, 5, 8 - Lesions can resemble flat warts or pink, scaly hypopigmented guttae macules

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Dyskeratosis congenita	XLR, *DKC1* (most common) AD, *TERC, TERT, TINF2* AR, *TINF2, NOP10, NHP2*	- Bone marrow failure - Reticulated hyperpigmentation on face/neck/upper torso - Premalignant oral leukoplakia - Onychodystrophy
Porokeratosis, linear type	Somatic mosaicism in mevalonate metabolism: *MVK, PMVK, MVD*	- Onset in newborns - Linear lesion on extremities following lines of Blaschko
Keratitis, ichthyosis, deafness (KID) syndrome	AD, sporadic *GJB2* (Connexin 26)	- Transient neonatal erythroderma - Well-demarcated erythematous, hyperkeratotic plaques on face and extremities - Stippled palmoplantar keratoderma - Congenital sensorineural hearing impairment - Progressive keratitis with consequent blindness and conjunctivitis - Recurrent mucocutaneous *candida* infections
Rothmund-Thomson syndrome (poikiloderma congenitale)	AR, *RECQL4*	- Poikiloderma typically begins in infancy on the face, then spreads to the extremities and buttocks - Radial ray defects (absent or hypoplastic thumbs, radius, and ulna) - Acral verrucous keratoses with malignant transformational potential - Hypogonadism - Juvenile cataracts - Increased risk of osteosarcoma (30%) (common cause of premature death)
Werner syndrome	AR, *WRN/RECQL2*	- Accelerated aging - Sclerodermatous/atrophic change acral/facial - Increased risk of fibrosarcoma and osteogenic sarcoma - Malignancy and CVA are main causes of mortality

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Condition	**Gene**	**High-yield associations**
Chronic mucocutaneous candidiasis	AD, *STAT1*, *IL-17F* AR, *AIRE* (Autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy [APECED] syndrome) AR, *CARD9*	- Impaired response of Th17 cells - Recurrent, treatment-resistant thrush, angular cheilitis, and vaginal candidiasis - Persistent scaly, erythematous plaques in intertriginous areas and nails - Mucocutaneous SCC
Bloom syndrome (congenital telangiectatic erythema)	AR, *BLM/RECQL3*	- Short stature - Photosensitivity - Malar telangiectatic erythema - Beaked nose - High-pitched cry - Primary hypogonadism - Low IgA/IgM with increased risk of respiratory and GI infections - Malignancy, especially leukemia, is most common cause of mortality

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