Wellderly Definition

Exclusion Criteria:

ICD-9: 149.*172.*, 174.*-198.*, 200.*-239.*, 289.0, 410.*-414.*, 429.2, 453.40, 415.1, 325, 344.5, 362.34, 368.12, 433.00, 433.10, 433.20, 433.80, 433.8, 433.9, 434.00,434.10, 434.90, 434.91, 435.0, 435.1, 435.3, 435.8, 435.9 436, 437.1, 437.6, 437.7, 437.8, 437.9, 438.20, 438.50, 438.50, 438.81, 438.89, 438.9, 784.3, 784.69, V12.51, V12.54,434.91, 250.*, 585.*, V45.11, V56, 39.95, 714.0, 710.0, 710.1, 710.2, 710.3, 710.4, 710.5, 555.*, 556.*, 340, 331.0, 332, 441.*, 437.3

OR

CPT: 566, 4110F, 90935, 90937

OR

Labs: HgbA1C > 6.5 or Gluc >200

OR

Medications: clopidogrel, plavix, prasugrel, effient, ticagrelor, brilinta, cilostazol, pletal, dipyridamole, aggrenox, persantine, ticlopidine, ticlid, donepezil, aricept, rivastigmine, exelon, galantamine, nivalin, razadyne, reminyl, lycoremine, cognex, tacrine

Notes:

- Any Cancer (including polycythemia (289.0) and Melanoma (172.*, V10.82); excluding basal or squamous cell skin cancer). (149.*172.*, 174.*-198.*, 200.*-239.*)
- Coronary Artery Disease (411.*-414.*, 429.*)/Myocardial Infarction (410.*) (CPT 566 – anesthesia for direct CABG w/o pump oxygenator, 4110F – internal mammary artery graft performed for primary, isolated CABG)
- Stroke (325, 344.5, 362.34, 368.12, 433.00, 433.10, 433.20, 433.80, 433.8, 433.9, 434.00,434.10, 434.90, 434.91, 435.0, 435.1, 435.3, 435.8, 435.9 436, 437.1, 437.6, 437.7, 437.8, 437.9, 438.20, 438.50, 438.50, 438.81, 438.89, 438.9, 784.3, 784.69, V12.51, V12.54,434.91) /TIA (435.9)
- Deep Vein Thrombosis (453.40)/Pulmonary Embolus (415.1)
- Chronic Renal Disease (585.*)/Hemodialysis (V45.11, V56, 39.95, cpt: 90935, 90937)
- Significant Auto-immune/Inflammatory conditions such as (Rheumatoid Arthritis (714.0, Lupus & other diffuse diseases of connective tissue (710.0), Crohn's (555.*), Ulcerative colitis (556.*), MS (340) etc.)
- Alzheimer (331.0)/Parkinson (332)
- Diabetes (Hemoglobin A1C > 6.5 % or fasting glucose >126 mg/dL or treated with oral diabetic medication or insulin if known)
- Aortic or Cerebral Aneurysm (441.*, 437.3)
- Anti-platelet agents, not including aspirin (ex.:clopidogrel/plavix, dipyridamole/aggrenox/ persantine, ticlopidine/ticlid)
- Cholinesterase inhibitor for Alzheimer disease (i.e. donepezil/Aricept)

Allowed Basal/Squamous Skin Cancer Definition:

Histology:

80702 - Squamous cell carcinoma in situ, NOS
80703 - Squamous cell carcinoma, NOS
80712 - Sq. cell carcinoma, keratinizing, NOS, in situ
80713 - Squamous cell carcinoma, keratinizing, NOS
80722 - Sq. cell carcinoma, lg cell non-ker., situ
80723 - Squamous cell carcinoma, lg cell, nonkeratinizing, NOS
80733 - Squamous cell carcinoma, sm cell, nonkeratinizing
80743 - Squamous cell carcinoma, spindle cell
80753 - Squamous cell carcinoma, adenoid
80762 - Squamous cell carcinoma in situ, question stromal inv
80763 - Squamous cell carcinoma, microinvasive
80772 - Squamous intraepithelial neoplasia, grade III
80783 - Squamous cell carcinoma with horn formation
80802 - Queyrat erythroplasia
80812 - Bowen disease
80823 - Lymphoepithelial carcinoma
80833 - Basaloid squamous cell carcinoma
80843 - Squamous cell carcinoma, clear cell type
80901 - Basal cell tumor
80903 - Basal cell carcinoma, NOS
80913 - Basal cell carcinoma, multifocal superficial
80923 - Basal cell carcinoma, infiltrating, NOS
80933 - Basal cell carcinoma, fibroepithelial
80943 - Basosquamous carcinoma
80953 - Metatypical carcinoma
80960 - Intraepidermal epithelioma of Jadassohn
80973 - Basal cell carcinoma, nodular
80983 - Adenoid basal carcinoma

AND

Primary Site:
C440 - Skin of lip
C441 - Eyelid
C442 - External ear
C443 - Skin of other/unspecified parts of face, NOS
C444 - Skin of scalp and neck
C445 - Skin of trunk
C446 - Skin of upper limb and shoulder
C447 - Skin of lower limb and hip
C448 - Skin, overlapping lesion
C449 - Skin, NOS

Gene Lists Considered for Pathogenic Variant Burden Analysis

Hereditary Dementia: ALS2, ANG, APP, ATP13A2, ATXN2, C9orf72, CHGB, CHMP2B, DCTN1, DNAJC6, EIF4G1, ERBB4, FBXO7, FIG4, FUS, GIGYF2, GRN, HNRNPA1, HTRA2, LRRK2, MAPT, MATR3, NEFH, OPTN, PARK2, PARK7, PFN1, PINK1, PLA2G6, PRNP, PRPH2, PSEN1, PSEN2, SETX, SIGMAR1, SNCA, SOD1, SORL1, SPG20, SYNJ1, TARDBP, TREM2, UBQLN2, VAPB, VCP, VEGFA, VPS35, VPS54

Hereditary Cancer: AIP, APC, ARID1A, ARID1B, ATM, AXIN2, BAP1, BARD1, BHD, BLM, BMPR1A, BRCA1, BRCA2, BRIP1, BTBD12, BUB1B, C17orf68, CDC73, CDH1, CDKN1A, CDKN1B, CDKN1C, CDKN2A, CDKN2B, CDKN2C, CHEK2, CREBBP, CYLD, DDB2, DICER1, DKC1, DNMT3A, EP300, EPCAM, ERCC1, ERCC2, ERCC3, ERCC4, ERCC5, ERCC6, ERCC8, EXO1, EXT1, EXT2, FANCA, FANCB, FANCC, FANCD2, FANCE, FANCF, FANCG, FANCI, FANCL, FANCM, FH, FLCN, GPC3, HNF1A, MAX, MEN1, MINPP1, MITF, MLH1, MLH3, MRE11A, MSH2, MSH3, MSH6, MUTYH, NBN, NF1, NF2, NHP2, NOP10, PALB2, PAX3, PHOX2B, PMS1, PMS2, POLD1, POLE, POLE1, POLH, PRF1, PRKAR1A, PTCH1, PTCH2, PTEN, PTPN11, RAD50, RAD51, RAD51C, RAD51L3, RB1, RECQL4, SBDS, SDHA, SDHB, SDHC, SDHD, SETBP1, SMAD4, SMARCA4, SMARCB1, SMARCE1, SOS1, SPRED1, STK11, SUFU, TERC, TERT, TET2, TGFBR1, TGFBR2, TINF2, TMEM127, TP53, TRAD, TSC1, TSC2, VHL, WRAP53, WRN, WT1, XPA, XPC

Common Monogenic Disorders: ACTA2, ACTC1, APC, APOB, BRCA1, BRCA2, CACNA1S, COL3A1, DSC2, DSG2, DSP, FBN1, GLA, KCNH2, KCNQ1, LDLR, LMNA, MEN1, MLH1, MSH2, MSH6, MUTYH, MYBPC3, MYH11, MYH7, MYL2, MYL3, MYLK, NF2, NTRK1, PCSK9, PKP2, PMS2, PRKAG2, PTEN, RB1, RET, RYR1, RYR2, SCN5A, SDHAF2, SDHB, SDHC, SDHD, SMAD3, STK11, TGFBR1, TGFBR2, TMEM43, TNNI3, TNNT2, TP53, TPM1, TSC1, TSC2, VHL, WT1

Supplemental Table Legends

Supplemental Table S1. Variant Filtration, Related to Experimental Methods – Variant Filtration: The number of variants removed per applied filter, broken down into rare (<1%), uncommon (1-5%) and common (>5%) variants. The cumulative total number of remaining variants is provided in the last row.

Supplemental Table S2. Variant Characteristics, Related to Experimental Methods – Variant Filtration: The number of variants identified in each cohort, broken down by coding impact, and allele frequency class - rare (<1%), uncommon (1-5%) and common (>5%) variants.

Supplemental Table S7. COL25A1 Variants, Related to Figure 4. The *COL25A1* variants observed in this study is displayed with the cDNA and protein impact, counts per cohort, and allele frequency in the Exome Aggregation Consortium cohort.