Genetics inMedicine

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CORRECTION

Correction to: ACMG SF v3.0 list for reporting of secondary findings in clinical exome and genome sequencing: a policy statement of the American College of Medical Genetics and Genomics (ACMG)

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Correction to: *Genetics in Medicine* 2021; https://doi.org/10.1038/s41436-021-01172-3; published online 20 May 2021

Unfortunately an error occurred in Table 2 and 3. The correct Table 2 and 3 are given below.

In addition, on page 2 of the article (right column, fifth paragraph, third sentence), the phrase "deletions of" has been added. The correct sentence is given below. Other technical difficulties were noted for genes such as *EPCAM* associated with Lynch syndrome and *GREM1*-associated polyposis, where routine detection of common deletions or duplications could be difficult at this time by ES/GS in many laboratories. On page 7 of the article (right column, third paragraph, fifth sentence), the word "high" should be replaced by "low". The correct sentence is given below. MODY3 does not require insulin treatment and responds well to low dose oral sulfonylureas, typically lower doses than are customary for most type 2 diabetics. On page 8 of the article (left column, third paragraph, second sentence), the word "*SERPINC1*" should be replaced by "*SERPINA1*". The correct sentence is given below. The SFWG decided that including gene phenotypes such as *HMBS*-associated acute intermittent porphyria and *SERPINA1*/alpha-1-antitrypsin deficiency with interventions involving environmental exposures or behavior modification was beyond the scope of this list.

The original article has been corrected.

ADDITIONAL INFORMATION

Supplementary information The online version contains supplementary material available at https://doi.org/10.1038/s41436-021-01278-8.

Correspondence and requests for materials should be addressed to ACMG

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Table 2. New gene–phenotype pairs for secondary findings (SF) list.

Gene–phenotype	Key considerations
Genes related to cancer phenotypes	
MAX/hereditary paraganglioma/pheochromocytoma	Penetrance met threshold to include with other PGL/PCC genes
PALB2/hereditary breast cancer	Risk of breast cancer risk meets penetrance threshold
TMEM127/hereditary paraganglioma/pheochromocytoma	Penetrance met threshold to include with other PGL/PCC genes
Genes related to cardiovascular phenotypes	
CASQ2/catecholaminergic polymorphic ventricular tachycardia (CPVT)	Risk of sudden death with preventive interventions available
FLNC/cardiomyopathy	Risk of sudden death with preventive interventions available
TRDN/catecholaminergic polymorphic ventricular tachycardia (CPVT) & long QT syndrome	Risk of sudden death with preventive interventions available
TTN/cardiomyopathy	Risk of sudden death with preventive interventions available
Genes related to inborn errors of metabolism phenotypes	
BTD/biotinidase deficiency	Features can be nonspecific; highly effective treatment in children and adults
GAA/Pompe disease	Availability of effective enzyme replacement therapy in infantile and later-onset cases
Genes related to miscellaneous phenotypes	
ACVRL1/hereditary hemorrhagic telangiectasia	Potential morbidity meets penetrance threshold and has efficacious intervention
ENG/hereditary hemorrhagic telangiectasia	Potential morbidity meets penetrance threshold and has efficacious intervention
HFE/hereditary hemochromatosis (*HFE* p.C282Y homozygotes only)	Potential morbidity meets penetrance threshold and has efficacious intervention
HNF1A/maturity-onset diabetes of the young (MODY3)	Accounts for 30–50% of known MODY cases likely to respond to low dose sulfonylureas; early treatment may prevent complications
RPE65/*RPE65*-related retinopathy	Availability of gene therapy treatment that may be more efficacious earlier in disease progression

PGL/PCC paraganglioma/pheochromocytoma.

Table 3. Genes not selected for secondary findings (SF) list v3.0 and reasoning.

Gene–phenotype	Category	Additional comments
Technical concerns		
EPCAM-associated Lynch syndrome	Cancer	Concern that deletions or duplications would be difficult to detect by NGS
GREM1-related polyposis	Cancer	Concern that duplication would be difficult to detect with NGS and overall limited information about this gene
HNF1B-related maturity-onset diabetes of the young (MODY5)	Miscellaneous	Accounts for ~5% of known MODY with ~50% of cases associated with deletions difficult to detect on exome sequencing
SDHA/hereditary paraganglioma/ pheochromocytoma	Cancer	Concerns about presence of many pseudogenes that could lead to false positive results that would require labs to perform extensive validation work
Penetrance concerns		
BRIP1/RAD51C/RAD51D-related ovarian cancer	Cancer	Lack of effective surveillance modalities for ovarian cancer also a consideration
DICER1-associated tumors	Cancer	Challenges in *DICER1* missense variant interpretation
HFE-related hemochromatosis (except for *HFE* p. C282Y homozygotes)	Miscellaneous	Penetrance is driven by the p.Cys282Tyr variant, and not other variants in HFE
TTR-amyloidosis	Miscellaneous	Also considered that sudden death was rare, thus allowing time for clinical diagnosis
Clinical management concerns		
ABCD1 X-linked adrenoleukodystrophy	IEM	Severe cases have early onset and would be diagnosed by newborn screening; no specific treatment in adulthood
BAP1-related tumors	Cancer	Small number of families reported to date and no established consensus management recommendations as of time reviewed
COL5A1-associated Ehlers–Danlos syndrome	Miscellaneous	Not considered highly actionable
GCH1-related dopa-responsive dystonia	Miscellaneous	Concern that diagnosis of the classic phenotype is relatively straightforward and that the treatment efficacy was not dependent on the timing of initiation
HMBS-associated acute intermittent porphyria	Miscellaneous	Concern that avoidance of exposures and delays in diagnosis could be out of scope for the ACMG SF list
MEFV-associated familial Mediterranean fever	Miscellaneous	Concern about clinical management of acute episodes being primarily supportive, and diagnosis could then be made through diagnostic testing
NOTCH3/CADASIL	Miscellaneous	Not considered highly actionable
POLD1/POLE-related polyposis	Cancer	Rarity of known pathogenic variants that could be reported and uncertain risks of extracolonic cancers
PRKAR1A/Carney complex	Miscellaneous	Concerns about penetrance and questions about actionability
SERPINA1-related alpha-1-antitrypsin deficiency	Miscellaneous	Concern that avoidance of exposures could be out of scope for the ACMG SF list

ACMG American College of Medical Genetics and Genomics, *IEM* inborn errors of metabolism, *NGS* next-generation sequencing.