Participant Choices for Return of Genomic Results in the eMERGE Network – Supplemental Materials

Figure S1 – Site Specific Tools for Participant Choices

Cincinnati Children's Hospital Medical Center – Retrospective Biobank Cohort

If you do not want to learn about any gene results, please initial here_____. Sign below and return the form so we know not to contact you again about learning these gene results.

Please indicate your choices by placing an X in the YES or NO column for each row.

***Risk* for diseases that may occur during childhood**	**YES, I want to learn about my child's gene change for this disease risk.**	**NO, I do NOT want to learn about my child's gene change for this disease risk.**
Some cancers		
Some conditions that can cause fragile blood vessels		
Some conditions that can cause liver or kidney failure		
Some heart diseases		
Risk for serious side effects from some medicines		

The study coordinator will contact you to set up a telephone appointment if a gene change is found that matches your choices. A licensed genetic counselor will explain the results to you during the telephone appointment.

Cincinnati Children's Hospital Medical Center – Adolescent/Parent Dyad Cohort

The decision tool for the CCHMC adolescent/parent dyads can be viewed in the supplement to Myers et. al (2019)[1].

Children's Hospital of Philadelphia

1. Results that are immediately actionable (Yes/No)
2. Results related to disease that could be medically actionable (Yes/No)
3. Results related to pharmacogenetics (drug processing) (Yes/No)

   Results related to an adult onset disorder that are medically actionable and cause symptoms, or require intervention, after the age of 18 (adulthood) will be returned to participants who consent as an adult to receive those results. These results will not be returned automatically to children that age into adulthood during the study.

Columbia University

Genetic mutation: a change in a gene that affects the gene's normal function and increases a person's risk of developing a genetic condition or having a child affected with a genetic condition

Recessive genetic condition: a genetic condition in which a person must have a mutation in both copies of the gene of the gene in order to be affected

Carrier of a recessive condition : a person who has a genetic mutation in one of their two copies of a gene for a recessive condition and therefore is not at risk to develop the condition but could have a child with the condition.

In the next sections, we review the possible genomic results available through this genomic screening. Please indicate which types of results you would like to receive.

❑ I would like to learn whether I have genetic mutation(s) that increase my risk of developing conditions for which there is effective prevention to reduce the risk of developing the condition or good treatment if a person is diagnosed with the condition.

Health care providers consider the following conditions to be included in this category (conditions for which there is effective prevention to reduce the risk of developing the condition or good treatment). You will be provided with results for the following conditions, unless you indicate otherwise.

CHECK THE CONDITIONS FOR WHICH YOU DO NOT WANT TO BE PROVIDED RESULTS. IF YOU DO NOT CHECK ANY, YOU WILL BE PROVIDED WITH ALL RESULTS.

- ☐ Breast and ovarian cancer in females or breast and prostate cancer in males
- ☐ Colon cancer and other genetically related cancers, including cancers of the uterus, ovaries, stomach
- ☐ Leukemia – cancer of the blood
- ☐ Thyroid cancer and other genetically related cancers including cancers of the adrenal gland, parathyroid gland and pituitary gland.
- ☐ Hypercholesterolemia (high cholesterol)
- ☐ Cardiac arrhythmias (heart rhythm problems)
- ☐ Gaucher's disease – a metabolic condition that can affect the liver, spleen and bones that most often occurs in people with Jewish ancestry
- ☐ Bleeding disorders such as hemophilia and thrombophilia
- ☐ Type 2 Diabetes, a condition usually diagnosed in adulthood
- ☐ Adverse reaction to some anesthesia medications

❑ I would like to learn whether I have genetic mutation(s) that increase my risk of developing genetic conditions for which there are currently some available treatment options, though treatment may not be effective or treat all of the symptoms.

Health care providers consider the following conditions to be included in this category (conditions for which there are some available treatment options though treatment may not be effective or treat all of the symptoms). You will be provided with results for the following conditions, unless you indicate otherwise.

CHECK THE CONDITIONS FOR WHICH YOU DO NOT WANT TO BE PROVIDED WITH RESULTS. IF YOU DO NOT CHECK ANY, YOU WILL BE PROVIDED WITH ALL RESULTS.

- ☐ Female infertility related to hormone abnormalities
- ☐ Kidney disease that may go on to kidney failure
- ☐ Heart disease that may go on to heart failure
- ☐ Aortic Aneurysm – risk that the aorta, the large vessel that carries blood out of your heart, will rupture
- ☐ Parkinson's disease
- ☐ Liver disease that may go on to liver failure
- ☐ Chronic lung disease
- ☐ Tumors of the nerve cells called ganglia usually in the head neck and spine that may cause nerve damage or progress on to cancer

❑ I would like to have carrier screening to learn if I'm a carrier of certain recessive conditions that increase my risk of having a child with a serious medical condition for which there is no treatment available. *Rarely, these types of results may indicate that you have a mild form of the condition yourself. If this is identified through this screening, these results will be shared with you.*

❑ I would like to have carrier screening to learn if I'm a carrier of certain recessive conditions that increase my risk of having a child with a medical condition for which there is treatment available. *Rarely, these types of results may indicate that you have a mild form of the condition yourself. If this is identified through this screening, these results will be shared with you.*

Mayo Clinic

Please check one of the boxes below to indicate your choice about receiving the information for the optional results.

- ☐ I want to receive optional results only if they may be medically actionable. If you choose to learn these results, they will be put into your medical record and given to your healthcare provider.

- ☐ I want to receive all available optional results—either actionable or not actionable. If you choose to learn these optional results, they will be put into your medical record and given to your healthcare provider.

- ☐ I do NOT want to receive any optional results.

Northwestern University

Every participant will receive results on genes we are testing that have been recommended to be returned by a professional organization. You have been randomized to the group that can choose which types of additional results you would like to receive. Please write your initials in the "yes" or "no" column, indicating your choice about which type of results you would like to receive.

Yes	**No**	
_____	_____	Information related to conditions or risk to develop conditions where treatment **is** available for symptoms (This does not mean curable).
_____	_____	Information related to conditions or risk to develop conditions where treatment **is not** available for symptoms.
_____	_____	Information related to dementia or my risk to develop dementia.
_____	_____	Information related to cancer or my risk to develop cancer.
_____	_____	Information related to behavior and learning conditions.
_____	_____	Information about being a carrier of a condition (can pass it on to children, but not at risk to develop the condition).
_____	_____	Information about genetic differences where we are still learning if there is a link between the gene and disease. We may not know if this information will affect you or your healthcare at this time.

Table S1: Site Categorization for Other eMERGEseq Panel Genes and SNVs

Other eMERGEseq Panel		Site Categorization					
Diseases	**Gene(s)/ SNV**[b]	**CCHMC**[c]	**CCHMC**[d]	**CHOP**	**CU**	**MC**	**NU**
Neonatal diabetes/congenital hyperinsulinism	*ABCC8*[b]	-	-	-	-	-	T
Long QT syndrome	*ANK2, CACNA1C, KCNE2*[b]	-	-	-	G	-	T
Ataxia telangiectasia	*ATM*	-	-	-	G	-	T, Ca
Hemiplegic migraine	*ATP1A2*	-	-	-	-	-	T
Wilson disease	*ATP7B*[a,b]	-	-	-	-	-	NC
Pulmonary arterial hypertension	*BMPR2*	T	-	-	-	-	-
Episodic ataxia	*CACNA1A*	T	-	IA	OK	-	NT
Atypical hemolytic-uremic syndrome	*CFH*	-	-	-	OK	-	T
Macular degeneration allele	*CFH*[b]	-	-	-	OK	-	NT
Cystic fibrosis	*CFTR*	T, C	-	-	-	-	T
Breast cancer susceptibility	*CHEK2*	P, T, AO	-	-	G	-	T, Ca
Usher syndrome	*CLRN1*[b]	-	-	-	-	-	NT
Ehlers Danlos syndrome, classic type	*COL5A2*[b]	-	-	-	-	-	T
Retinitis pigmentosa	*DHDDS*[b]	-	-	-	-	-	NT
Dihydrolipoamide dehydrogenase deficiency	*DLD*[b]	-	-	-	-	-	T
Fanconi anemia	*FANCC*[a]	-	-	-	-	-	T, Ca, B
Factor XI deficiency	*F11*[b]	-	-	-	-	-	T
Atopic dermatitis	*FLG*	-	-	-	-	-	U
Hermansky-Pudlak syndrome	*HPS3*[b]	-	-	-	-	-	T
Obesity susceptibility	*MC4R*	-	-	-	G	-	NT
Congenital insensitivity to pain with anhidrosis	*NTRK1*	-	-	-	-	-	NT, B
Seizure disorders	*SCN1A*	-	-	-	-	-	T
Congenital insensitivity to pain	*SCN9A*	-	-	-	-	-	NT
Alpha-1-antitrypsin deficiency	*SERPINA1*	P, T, C	-	-	-	-	T
Arterial tortuosity	*SLC2A10*	-	-	-	-	-	T
Spastic paraplegia	*SPG7*[b]	-	-	-	-	-	NT
Pitt Hopkins syndrome	*TCF4*	-	-	-	-	-	NT

Osteopetrosis	*TCIRG1*	T, C	-	-	-	-	T
Early-onset primary dystonia	*TOR1A*[b]	-	-	-	-	-	T
Transthyretin amyloidosis	*TTR*	-	-	-	OK	-	T, D
Tyrosine kinase 2 deficiency	*TYK2*	T, C	-	-	-	-	NT
Uromodulin-associated kidney disease	*UMOD*	-	-	-	OK	-	T
Vitamin-D dependent rickets	*VDR*	-	-	-	-	-	T

Footnotes: -, Not returned. [a], Gene considered medically actionable by the American College of Medical Genetics and Genomics. [b], SNV only. CHOP, Children's Hospital of Philadelphia categories: IA, Immediately actionable. CCHMC, Cincinnati Children's Hospital Medical Center ([c], adolescent and [d], biobank) categories: P, Preventable; T, Treatable, AO, Adult Onset. CU, Columbia University categories: G, Good treatment or prevention; OK, treatment options partially effective. MC, Mayo Clinic. NU, Northwestern University categories: NC, no choice; Ca, cancer risk; T, treatment available; NT, no treatment available; D, dementia risk; B, behavior and learning problems; U, uncertain effect.

Table S2: Participant Selections for Exclusions of Other eMERGEseq Panel Results

Other eMERGEseq Panel	**Number (%) of Participants who Chose to Exclude Other Panel Genes**					
Diseases	**CCHMC**[a,b] **N=163**	**CCHMC**[c] **N=19**	**CHOP N=72**	**CU**[a] **N=325**	**MC N=2535**	**NU N=772**
Neonatal diabetes/congenital hyperinsulinism						3 (0.4%)
Long QT syndrome				29 (8.9%)		3 (0.4%)
Ataxia telangiectasia				29 (8.9%)		7 (0.9%)
Hemiplegic migraine						3 (0.4%)
Wilson disease						
Pulmonary arterial hypertension	22 (13.5%)					
Episodic ataxia	22 (13.5%)		0 (NA)	29 (8.9%)		28 (3.6%)
Atypical hemolytic-uremic syndrome				32 (9.8%)		3 (0.4%)
Macular degeneration allele						28 (3.6%)
Cystic fibrosis	22 (13.5%)					3 (0.4%)
Breast cancer susceptibility	15 (9.2%)			29 (8.9%)		7 (0.9%)
Usher syndrome						28 (3.6%)
Ehlers Danlos syndrome, classic type						3 (0.4%)
Retinitis pigmentosa						28 (3.6%)
Dihydrolipoamide dehydrogenase deficiency						3 (0.4%)
Fanconi anemia						27 (3.5%)
Factor XI deficiency						3 (0.4%)
Atopic dermatitis						16 (2.1%)
Hermansky-Pudlak syndrome						3 (0.4%)
Obesity susceptibility				11 (3.4%)		28 (3.6%)
Congenital insensitivity to pain with anhidrosis						43 (5.6%)
Seizure disorders						3 (0.4%)

Congenital insensitivity to pain			28 (3.6%)
Alpha-1-antitrypsin deficiency	2 (1.2%)		3 (0.4%)
Arterial tortuosity			3 (0.4%)
Spastic paraplegia			28 (3.6%)
Pitt Hopkins syndrome			28 (3.6%)
Osteopetrosis	22 (13.5%)		3 (0.4%)
Early-onset primary dystonia			3 (0.4%)
Transthyretin amyloidosis		29 (8.9%)	30 (3.9%)
Tyrosine kinase 2 deficiency	22 (13.5%)		28 (3.6%)
Uromodulin-associated kidney disease		32 (9.8%)	3 (0.4%)
Vitamin-D dependent rickets			3 (0.4%)

Footnotes: Blackened cells indicate genes not returned or choices not offered. [a], participants were allowed to make selections for individual diseases. CHOP, Children's Hospital of Philadelphia: Adult onset disorders, while selected, only returned to participants after consenting as an adult. CCHMC, Cincinnati Children's Hospital Medical Center: [b], Adolescent cohort - choices reflect dyad categorical joint decision and any changes made within 2 week period when choices could be changed. [c], Biobank cohort - choices made by parents. CU, Columbia University. MC, Mayo Clinic. NU, Northwestern University.

REFERENCES

1. Myers MF, Martin LJ, Prows CA. Adolescents' and Parents' Genomic Testing Decisions: Associations With Age, Race, and Sex. *J Adolesc Health.* 2019.