Initiative in Wisconsin: Update

Genomic Medicine and the Plain Populations of North America

July 17-18, 2013

Clinic *for* Special Children

Christine Seroogy, MD
Associate Professor
University of Wisconsin
Department of Pediatrics
Division of Allergy, Immunology & Rheumatology

Table 2:
Inherited Diseases Among the Amish and Mennonite Populations by Geographic Location

	Disease	Patients PA (CSC)	Patients OH (DDC)	Patients IN (CHC) & Midwest	Patients OH (Holmes Co)	Patients WI (AFCH)	Gene symbol
1	11-beta-hydroxylase deficiency	x					CYP11B1
2	21 hydroxylase deficiency				x		CYP21A2
3	3-methylcrotonylglycinuria	x					MCCC2
4	3-β-OH-steroid dehydrogenase deficiency	x					HSD3B2
5	Achromotopsia	x					CNGA3
6	Adenylosuccinase (adenylosuccinate lyase, ADSL) deficency		x				ADSL
7	Alagille syndrome		x				JAG1
8	Aldosterone deficiency	x				x	CYP11B2
9	Alpha-1 antitrypsin deficiency	x					SERPINA1
10	Amish albinism		x			x	TYR
11	Amish brittlehair syndrome		x		x		MPLKIP
12	Amish microcephaly	x					SLC25A19
13	Aplastic anemia and pulmonary fibrosis	x					TERT
14	Bardet-Biedl syndrome	x					BBS1
15	Bartter syndrome	x					CLCNKB
16	Beal's syndrome		x				FBN2
17	Biotinidase deficiency	x					BTD
18	Byler disease	x	x	x			ATP8B1
19	Cartilage-hair hypoplasia	x	x	x	x	x	RMRP
20	Cerebral cavernous malformations	x					KRIT1
21	CHARGE syndrome			x			CHD7
22	Charcot-Marie-Tooth disease		x	x			GDAP1
23	Chronic granulomatous disease	x					CYBB
24	Cockayne syndrome	x	x				ERCC6
25	Cohen syndrome		x				COH1
26	Congenital insensitivity to pain with anhidrosis	x					NTRK1
27	Congenital nephrotic syndrome	x					NPHS1
28	Cortical dysplasia and focal epilepsy	x	x				CNTNAP2
29	Crigler-Najjar syndrome	x	x	x			UGT1A1
30	Cystic fibrosis			x			CFTR
31	Deafness, non-syndromic	x					GJA2
32	Cystinuria	x					SLC3A1
33	DiGeorge syndrome			x			TBX
34	Dilated cardiomyopathy with AV block	x		x			LMNA
35	Duchenne muscular distrophy		x	x			DMD
36	Ellis-van Creveld syndrome	x		x			EVC
37	Factor 11 deficiency	x					F11
38	Factor V Leiden Mutation						F5
39	Familial hypercholanemia	x					TJP2
40	familial hypercholanemia	x					BAAT
41	Familial periodic fever	x					TNFRSF1A
42	Fragile X syndrome	x				x	FMR1
43	Fructose intolerance		x				ALDOB
44	Galactosemia	x		x		x	GALT
45	Gaucher disease		x				GBA
46	Gitelman syndrome	x					SLC12A3
47	Glutaric aciduria, type 1	x	x	x		x	GCDH
48	Glutaric aciduria, type 3	x					C7orf10
49	Glycogen storage disease, type 6	x					PYGL
50	GM1-gangliosidosis	x					GLB1
51	GM3 synthase deficiency	x	x				ST3GAL5
52	Grey platelet syndrome	x					NBEAL2
53	Hemophilia B - Factor IX deficiency		x	x		x	F9
54	Hereditary hemochromatosis	x					HFE
55	Hershberger syndrome				x		SCN5A
56	Hirschsprung disease	x		x		x	EDNRB
57	Homocystinuria	x					MTHFR
58	Hypertrophic cardiomyopathy	x	x				SLC25A4
59	Hypomyelinating leukodystrophy	x					GJC2
60	Infantile lethal cardiomyoapthy		x				MYBPC3
61	Infantile parkinsonism-dystonia syndrome	x					SLC6A3
62	Infantile parkinsonism-dystonia syndrome	x					SLC6A3
63	ITCH deficiency	x		x			ITCH
64	Lamellar ichthyosis				x		TGM1
65	Leigh syndrome		x				Multiple

	Disease	Patients PA (CSC)	Patients OH (DDC)	Patients IN (CHC) & Midwest	Patients OH (Holmes Co)	Patients WI (AFCH)	Gene symbol
66	Leri-Weill syndrome		x				SHOXY
67	Lethal neonatal rigidity and multifocal epilepsy	x					C7orf27
68	Limb-girdle muscular dystrophy	x		x			SGCB
69	Limb-girdle muscular dystrophy, type 2A	x					CAPN3
70	Long QT			x	x		LQT2
71	Maple syrup urine disease	x	x	x		x	BCKDHA
72	McKusick-Kauffman syndrome	x	x				MKKS
73	Meckel-Gruber syndrome			x			MKS1
74	Medium-chain acyl-CoA dehydrogenase deficiency	x		x			ACADM
75	Metachromatic leukodystrophy		x				ARSA
76	Methylmalonic acidemia			x			MUT
77	Mevalonate kinase deficiency	x					MVK
78	Microcephalic osteodysplastic primordial dwarfism, Type 1		x				RNU4ATAC
79	Microcephaly with chorioretinopathy	x					TUBGCP6
80	Nemaline rod myopathy (chicken breast disease)	x		x		x	TNNT1
81	Nephrotic syndrome	x					NPHS2
82	Non-syndromic deafness	x					GJB2
83	Non-syndromic mental retardation	x					CRADD
84	Nonketotic hyperglycinemia			x			GLDC
85	Osteogenesis imperfecta	x					COL1A2
86	Osteoporosis-pseudoglioma syndrome	x					LRP5
87	Phenylketonuria	x	x	x		x	PAH
88	Pierson syndrome	x					LAMB2
89	Posterior column ataxia and retinitis pigmentosa	x					FLVCR1
90	Primary ciliary dyskinesia	x				x	DNAH5
91	Prolidase deficiency		x				PEPD
92	Properdin deficiency	x					CFP
93	Propionic acidemia	x	x	x		x	PCCB
94	Pyruvate kinase deficiency	x	x				PKLR
95	Restrictive dermopathy	x					ZMPSTE24
96	Retinitis pigmentosa			x			RPGR
97	Rett syndrome	x	x			x	MECP2
98	Rubinstein-Taybi syndrome		x				CREBBP
99	Salla disease	x					SLC17A5
100	Seckel syndrome			x			ATR
101	Severe combined immune deficiency (IL7Rα)	x				x	IL7Rα
102	Severe combined immune deficiency (RAG1)	x		x		x	RAG1
103	Severe Combined Immunodeficiency (ADA)	x		x			ADA
104	Sitosterolemia	x					ABCG8
105	Spinal muscular atrophy	x		x			SMN1
106	Spondyloepiphyseal dysplasia, humerospinal dysostos	x					CHST3
107	STRADA deficiency	x					STRADA
108	Sudden infant death with dysgenesis of the testes	x		x			TSPYL1
109	Symptomatic epilepsy and skull dysplasia	x					SNIP1
110	Tarsal syndrome		x				TCC
111	Thanotophoric Dysplasia	x					FGFR3
112	Torkelson Syndrome	x					APOA4
113	TMCO1 defect syndrome	x					TMCO1
114	Torsion dystonia	x					TOR1A
115	Troyer syndrome	x	x		x		SPG20
116	Tyrosine hydroxylase deficiency	x					TH
117	Tyrosinemia, type 3	x					HPD
118	Usher syndrome, type II		x				USH2A
119	Usher-like syndrome	x					HARS
120	VLCAD Deficiency	x					ACDVL
121	Vitamin B12 deficiency	x					AMN
122	Von Willebrand disease, type 2B			x			VWF
123	Von Willebrand disease, type 2M			x		x	VWF
124	Von Willebrand disease, type I			x	x		VWF
125	Weil-Marchesani syndrome	x					ADAMTS10
126	Wolf-Hirschhorn syndrome (4p minus)			x			WHSC1L1
127	Yoder dystonia	x	x			x	WDR-73
128	Zellweger syndrome			x			PEX1

= Part of Newborn Screening

= Disease presented to AFCH or anecdotal awareness of detection in Wisconsin Amish and Mennonite

= Genetic assay will be developed and/or validated or is readily available in this proposal

Abbreviations: CSC: Clinic for Special Children; DDC: Das Deutch Clinic; CHC: Community Health Clinic; AFCH: American Family Children's Hospital

Differences in Immunologic & Hematologic Conditions Between Plain Communities

Table: Immunologic and Hematologic Diseases	CSC (Lancaster Co, PA)	DDC (Northeast OH)	WI	Plain Community
RAG1 SCID	X		X	Amish
ADA SCID	X		?	Amish
IL7Ra SCID	X		X	Mennonite
Cartilage Hair Hypoplasia	X	X	X	Amish
Primary Ciliary Dyskinesia	X		X	Amish
ITCH	X		?	Amish
Chronic Granulomatous Disease	X		?	Amish
Biotinidase Deficiency	X		?	Amish
Properidin Deficiency	X		?	Mennonite
Aplastic Anemia and Pulmonary Fibrosis	X		?	Mennonite
TRAPS (familial periodic fever)	X		?	Mennonite
Mevalonate Kinase Deficiency (familial periodic fever)	X		?	Mennonite
Factor 5 Leiden	X	X	?	Amish/Mennonite
von Willebrand Disease 2M	X		X	Amish
Hemophilia B (Factor IX deficiency)		X	X	Amish
Gray Platelet Syndrome	X		?	Mennonite
Pyruvate Kinase Deficiency	X	X	?	Amish