Current Status of Diseases/Genes discovered through the AMGGI project to be studied in the IGNITE Project

DISEASE	COMMENTS	ESTIMATED DISEASE PREVALENCE	PHENOTYPICALLY RELATED CONDITIONS
Gene Identified (projects entering Phase 3 and Phase 4 directly)			
Schnyder Corneal Dystrophy (SCD) **gene: UBIAD1**	UBIAD1 is a prenyltransferase thought to be involved in cholesterol and phospholipid metabolism	Extremely rare: until recently < 200 known cases	Possibly related to systemic dyslipidemia and thus to heart attack and stroke risk.
Sideroblastic Anemia **gene: SLC25A38**	Solute carrier 25, member 38 Mitochondrial solute carrier	Rare: Estimated 1:100,000	Myelodysplastic syndrome: Refractory anemia with ringed sideroblasts (RARS). Predominantly adult disease with significant clinical burden. No cure except bone marrow transplant. Incidence 1:19,000 with MDS. In US – 14,000 people per year; 87,000 world wide. Approx 20% are RARS.
Cutis Laxa Type 2 **gene: PYCR1**	PYCR1 plays a critical role in proline biosynthesis, supporting a significant role for proline in normal development.	Extremely rare: Estimated <1:1,000,000	Other neurocutaneous syndromes and possible a model for skin development
Charcot-Marie-Tooth (CMT) **gene: LRSAM1**	LRSAM1 is an e3 ligase which like the ubiquitin ligases, may play a role in neurodegenerative diseases.	Rare: Estimated <1:100,000	Other forms of CMT disease and perhaps other motor/sensory neuropathies. May shed light of none genetic causes of neuropathy, such as diabetic neuropathy
Bardet-Biedl Syndrome (BBS) **gene: BBS1**	BBS1 localizes to ciliated cells. Little is known about the function of the gene. BBS is characterized with obesity, retinitis pigmentosa, mental retardation, renal failure, a variety of cardiac anomalies and other phenotypes.	In Northern Europeans: 1:100,000 to 1:160,000. In Newfoundland: 1:13,500 BBS1 represents ~23% all BBS cases	Alstrom (prevalent in Acadians from Nova Scotia), truncal obesity, renal dysplasia/ nephronopthisis, some forms of retinal degeneration, congenital heart anomalies, and ciliopathies such as forms of Joubert, Leber congenital amaurosis, autosomal recessive Polycystic kidney disease and Senior-Loken syndrome.
Fabry Disease **gene: GLA**	galactosidase alpha hydrolyses the terminal alpha-galactosyl moieties from glycolipids and glycoproteins. This is an expensive orphan disease prevalent in the Maritimes, in particular Nova Scotia.	1: 50,000 but varies by population. As high as 1:1600 to 1:4600 including those with late onset phenotype. Significant morbidity/ mortality related to cardiac, renal and ocular injury.	May explain a number of patients with idiopathic cardiomyopathy: 3/10,000. Has been used by the NIH as a model of premature aging, including early onset CNS vascular disease

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Familial Exudative Vitreoretinopathy (FEVR) **gene: FZD4**	FZD4, frizzled 4, is part of the beta-catenin pathway. We have reported that mutations in FZD4 are associated with severe retinopathy of prematurity (ROP) and with persistent fetal vasculature.	1:10,000, ~20% cases due to FZD4 mutations.	In 2007 in Canada, 106 infants were reported by the Canadian Neonatal Network with severe ROP requiring treatment. 25% will become blind and only 35% will develop driving vision according to a recent study.
DNA Collected and/or Locus Identified (projects completing Phase 2)			
A distinct, heritable form of renal failure **Cape Breton Renal Failure (CBRF)** **locus identified**	Nonspecific kidney failure eventually requiring dialysis or transplant .	Very rare: estimated <1:100,000	May well be related to renal failure from other causes
Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC) **locus identified**	A lethal disorder of young adults manifested by sudden cardiac death.	Estimated 1:10,000	Possibly related to cardiac dysrhythmias in non-inherited circumstances, e.g. following heart attack.
Limb girdle muscular dystrophy **locus identified**	Sequencing candidate genes. No known causative genes in our region.	Very rare: estimated <1:100,000	Many other limb girdle muscular dystrophies result from mutations in genes that involved in attaching the cytoskeleton to the cell membrane. Understanding this form of limb girdle may improve our understanding of other muscular dystrophy including the more common Duchene Muscular dystrophy.
Familial Wilm's tumor **mapping underway**	Known causative genes have been excluded. Putative region identified at 17q.	Familial Wilm's is very rare: estimated 1:1,000,000	Better understanding of inherited predisposition genes may improve our understanding of sporadic Wilms's tumours and renal development
Patients Identified (projects completing Phase 1)			
Familial form of Epilepsy found in local population	Families segregating temporal lobe epilepsy are in ascertainment, amongst other various forms of epilepsy	In general, common	Common seizure disorder
Transient ischemic attacks (TIAs) **preliminary linkage completed**	A familial form of transient ischemic attack Recurrent, non-sustained episodes of stroke-like symptoms	Familial forms: very rare, estimated <1:100,000. Non-familial: a common, high-cost, high-burden disorder.	Other forms of cardiovascular disease