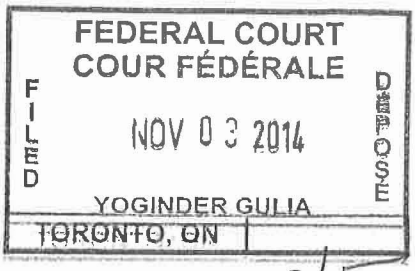
Court File No. T-2249-14



FEDERAL COURT

B E T W E E N:

CHILDREN'S HOSPITAL OF EASTERN ONTARIO

Plaintiff

-and-

UNIVERSITY OF UTAH RESEARCH FOUNDATION, GENZYME GENETICS and YALE UNIVERSITY

Defendants

STATEMENT OF CLAIM

TO THE DEFENDANTS:

A LEGAL PROCEEDING HAS BEEN COMMENCED AGAINST YOU by the Plaintiff. The claim made against you is set out in the following pages.

IF YOU WISH TO DEFEND THIS PROCEEDING, you or a solicitor acting for you are required to prepare a statement of defence in Form 171B prescribed by the Federal Court Rules, serve it on the plaintiff's solicitor or, where the plaintiff do not have a solicitor, serve it on the plaintiff, and file it, with proof of service, at a local office of this Court, WITHIN 30 DAYS after this statement of claim is served on you, if you are served within Canada.

If you are served in the United States of America, the period for serving and filing your statement of defence is forty days. If you are served outside Canada and the United States of America, the period for serving and filing your statement of defence is sixty days.

Copies of the Federal Court Rules, information concerning the local offices of the Court and other necessary information may be obtained on request to the Administrator of this Court at Ottawa (telephone 613-992-4238) or at any local office.

IF YOU FAIL TO DEFEND THIS PROCEEDING, judgment may be given against you in your absence and without further notice to you.

November 3, 2014

Issued by: _____

Address of
local office: _____

TO: The Administrator
Federal Court

AND TO: University of Utah Research Foundation
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Representative for service per *Patent Act*, s. 29(2)
(Agent of record for Canadian Patents Nos. 2,240,737; 2,336,236; 2,337,491; 2,369,812; and 2,416,545)

CLAIM

1. The Plaintiffs claim:

   (a) a declaration under section 60(2) of the *Patent Act* that the processes proposed to be used by the Plaintiffs to diagnose and/or assess the risk of Long QT syndromes in human patients (the "Proposed Tests"), as described herein, do not and would not constitute an infringement of any of the claims in Canadian Patents Nos. 2,240,737 (the "737 Patent"), 2,336,236 (the "236 Patent"), 2,337,491 (the "491 Patent"), 2,369,812 (the "812 Patent") or 2,416,545 (the "545 Patent") (collectively, the "Long QT Patents");

   (b) a declaration under section 60(1) of the *Patent Act* R.S.C. 1985, c.P-4 (the "*Patent Act*") that each and every one of the Isolated Nucleic Acid Claims and Testing Method Claims, as defined herein, in the Long QT Patents is invalid, void and of no force and effect;

   (c) a direction under section 62 of the *Patent Act* to the Commissioner of Patents that the certificate of judgment voiding the Isolated Nucleic Acid Claims and Testing Method Claims of the Long QT Patents be made a record in the Patent Office and be entered on the margin of the enrolment of their respective patents in the Patent Office, so that these claims shall thereupon be and be held to have been void and of no effect;

   (d) in the alternative, a declaration under section 19.1(2) of the *Patent Act* that the Proposed Tests constitute a public non-commercial use of the Long QT Patents;

   (e) costs of and incidental to this action, plus HST, and including all disbursements; and

   (f) such further and other relief as this Honourable Court may deem just.

THE PARTIES

2. The plaintiff, Children's Hospital of Eastern Ontario ("Children's Hospital"), is a pediatric health and research center in Ottawa, Ontario providing patient care, research and training of healthcare professionals. Children's Hospital wishes to conduct genetic testing for Long QT syndrome among its patient population for public, non-commercial purposes.

3. The defendant University of Utah Research Foundation ("UURF") is a recorded owner of all of the Long QT Patents. UURF is a subsidiary of the University of Utah, a public research university in Salt Lake City, Utah, that collects royalties from patents arising from university activities.

4. The defendant Genzyme Genetics is a recorded owner of the 737 Patent. Genzyme Genetics has been succeeded by Laboratory Corporation of America Holdings ("LabCorp"), a North Carolina-based company providing laboratory testing services.

5. The defendant Yale University is a recorded owner of the 812 Patent. Yale University is a private research university located in New Haven, Connecticut.

LONG QT SYNDROME

6. Long QT syndrome ("Long QT") is an inherited cardiac disorder affecting about 1 in 3000 to 1 in 5000 people, in which the heart takes too long to recharge after each beat. Patients with Long QT may experience seizures, cardiac arrest or sudden death.

7. Symptoms of Long QT can present at any time from infancy to middle age. Sudden death is the first sign of the disease in 10 to 15 percent of affected individuals.

8. Treatment is available to prevent fainting, cardiac arrest and sudden death. Therefore, diagnosis of Long QT is extremely important.

9. Long QT is known to be associated with mutations in 13 human genes, five of which are the subject matter of unexpired Canadian patents. These five genes are KCNQ1, KCNH2, KCNE1, KCNE2 and SCN5A (the "Patented Long QT Genes").

10. The Patented Long QT Genes encode for human proteins involved in cardiac ion channel function. Certain mutations in these genes can disrupt the normal function of cardiac ion channels, resulting in the symptoms of Long QT.

11. Presently, no laboratory in Ontario has obtained approval from the Ontario Government to conduct on-site genetic screening for Long QT. The Long QT Patents are currently preventing such testing from being approved and conducted for the benefit of Ontario patients.

12. Ontario hospitals and physicians that wish to screen patients for Long QT must obtain Ontario government funding to purchase testing services from genetic testing laboratories located outside Canada. Ontario hospitals and laboratories are therefore prevented from developing the institutional capability to properly diagnose Long QT genetic mutations in Ontario patients.

CHILDREN'S HOSPITAL'S PROPOSED LONG QT SCREENING TESTS

13. Children's Hospital currently provides genetic testing services to determine hereditary predisposition for more than 20 genetic disorders. However, the Long QT Patents are preventing Children's Hospital from offering genetic screening for Long QT.

14. Children's Hospital now desires to implement next-generation sequencing technology that will permit the simultaneous sequencing of all 13 genes relating to Long QT from multiple patients at once for Children's Hospital's patients. This technology will allow Children's Hospital to screen all desired genes for patients to assist in determining predisposition to Long QT (the "Proposed Tests").

15. The Proposed Tests would involve sequencing multiple genes known to be associated with Long QT, and determining whether patients' genes have mutations and whether any such mutations are indicative or increase the risk of Long QT.

16. Genes contain intron and exon segments. Each exon segment encodes a corresponding messenger RNA (mRNA) sequence which itself encodes 1 of 22 amino acids. Collectively the exons of a gene provide a template for all the amino acids

making up a given protein. Introns do not encode mRNA sequences but rather contain important sequences that regulate the production of mRNA.

17. The Proposed Tests would involve the simultaneous sequencing of patient exons of all 13 Long QT genes at the same time. Large numbers of exon fragments from many different genetic samples (including from different patients) would be sequenced in a massively parallel manner in a single experiment.

18. The resultant patient exon sequences would be electronically compared with known reference exon sequences for the genes of interest. Variants from the reference sequence would be identified electronically, and the risk associated with any identified variant would be assessed by a clinical professional, e.g. a molecular geneticist, a clinical geneticist and/or a cardiologist.

19. Implementation of the Proposed Tests would enable Children's Hospital to build the first repository of Long QT patient genetic information in Canada, which would permit additional non-commercial genetic research to be conducted on the disease to improve its diagnosis and treatment.

20. Children's Hospital requires the approval of Ontario's Ministry of Health and Long-Term Care to conduct the Proposed Tests. However, currently, Children's Hospital cannot obtain such approval due to the Long QT Patents.

21. The inclusion of the Patented Long QT Genes in the Proposed Tests is ethically necessary to enable the diagnosis of Long QT in Ontario patients. If the Patented Long QT Genes are omitted from the Proposed Tests, then Children's Hospital will be forced to willfully ignore patient predisposition to Long QT associated with the Patented Long QT Genes when screening for Long QT.

22. Children's Hospital intends the Proposed Tests to eventually involve sequencing of additional genes, including unpatented genes associated with other hereditary disorders, and eventually including patients' entire exomes (i.e., all of a patient's exons) and/or genomes (i.e., all of a patient's genes). It will be impractical and unethical for Children's Hospital to selectively omit the Patented Long QT Genes from the Proposed Tests.

23. Accordingly, Children's Hospital is an interested person within the meaning of section 60 of the *Patent Act*.

THE LONG QT PATENTS

24. The Long QT Patents relate to the identification of the molecular basis for Long QT, including the identification of genetic mutations that cause Long QT in the Patented Long QT Genes: KCNQ1, KCNH2, KCNE1, KCNE2 and SCN5A.

Canadian Patent No. 2,240,737

25. The 737 Patent, titled "A Long QT Syndrome Gene Which Encodes KVLQT1 and its Association with MINK", was filed as a PCT application on December 20, 1996. The application was published on July 3, 1997 and issued to patent on September 29, 2009. The 737 Patent will expire on December 20, 2016 if all maintenance fees are paid in a timely manner.

26. The 737 Patent relates the nucleic acid sequence of the KVLQT1 gene (also called KCNQ1) and various alleged applications of the discovery of this gene sequence.

27. The 737 Patent contains 22 claims, including claims of the following types: nucleic acid, vector, host cell, polypeptide synthesis, polypeptide, testing method and transfected cell. A copy of the 737 Patent is marked as Schedule "A" to this Statement of Claim.

Canadian Patent No. 2,336,236

28. The 236 Patent, titled "Mutations in and Genomic Structure of HERG – A Long QT Syndrome Gene", was filed as a PCT application on July 20, 1999. The application was published on February 10, 2000 and issued to patent on September 25, 2012. The 236 Patent will expire on July 20, 2019 if all maintenance fees are paid in a timely manner.

29. The 236 Patent relates to the genomic structure of HERG, (also called KCNH2) including the sequences of the 15 intron/exon junctions, and various alleged applications of the discovery of this genomic information.

30. The 236 Patent contains 11 claims, all of which are directed to testing methods. A copy of the 236 Patent is marked as Schedule "B" to this Statement of Claim.

Canadian Patent No. 2,337,491

31. The 491 Patent, titled "Human MINK Gene Mutations Associated with Arrhythmia", was filed as a PCT application on October 6, 1998. The application was published on February 10, 2000 and issued to patent on June 22, 2010. The 491 Patent will expire on October 6, 2018 if all maintenance fees are paid in a timely manner.

32. The 491 Patent relates to the intron/exon junction sequences of the KVLQT1 (i.e., KCNQ1) and KCNE1 genes and various alleged applications of the discovery of this genomic information.

33. The 491 Patent contains 17 claims, including claims of the following types: nucleic acid, testing method, polypeptide, vector, transfected cell, and drug screening method. A copy of the 491 Patent is marked as Schedule "C" to this Statement of Claim.

Canadian Patent No. 2,369,812

34. The 812 Patent, titled "MINK-Related Genes, Formation of Potassium Channels and Association with Cardiac Arrhythmia", was filed as a PCT application on April 14, 2000. The application was published on October 26, 2000 and issued to patent on September 18, 2012. The 812 Patent will expire on April 14, 2020 if all maintenance fees are paid in a timely manner.

35. The 812 Patent relates to various genetic information, including the DNA sequence for KCNE2, the coassembly of HERG (KCNH2) and KCNE2 to form a cardiac IKr potassium channel, and various alleged applications of the discovery of this genetic and protein information.

36. The 812 Patent contains 21 claims, including claims of the following types: nucleic acid, polypeptide, vector, transfected cell, exon amplification method, testing method, and drug screening method. A copy of the 812 Patent is marked as Schedule "D" to this Statement of Claim.

Canadian Patent No. 2,416,545

37. The 545 Patent, titled "Common Polymorphism in SCN5A Implicated in Drug-Induced Cardiac Arrhythmia", was filed as a PCT application on July 19, 2001. The application was published on January 31, 2002 and issued to patent on November 27, 2012. The 545 Patent will expire on July 19, 2021 if all maintenance fees are paid in a timely manner.

38. The 545 Patent relates to a specific mutation in SCN5A which is said to cause drug-induced *Torsade de Pointes* or ventricular fibrillation in patients when administered certain drugs, as well as various alleged applications of the discovery of this mutation information.

39. The 545 Patent contains 13 claims, including claims of the following types: nucleic acid, testing method, polypeptide, transfected cell and vector. A copy of the 545 Patent is marked as Schedule "E" to this Statement of Claim.

Claims of the Long QT Patents

40. All of the claims of the Long QT Patents pertain to the nucleotide and amino acid sequences of genes and proteins related to Long QT. The types of claims in the Long QT Patents are defined as follows for the purposes of this Statement of Claim:

Claim Type	**Long QT Patent Claims**
Isolated Nucleic Acid Claims	737 Patent: Claims 1, 2, 3, 4, 5 491 Patent: Claims 1, 2 812 Patent: Claims 1, 2, 6, 7 545 Patent: Claim 1
Testing Method Claims	**Not Mutation-Specific:** 236 Patent: Claims 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 812 Patent: Claims 11, 12 **Mutation-Specific:** 737 Patent: Claims 14, 15, 16, 17, 18 491 Patent: Claims 7, 8, 9, 10, 11, 12 545 Patent: Claims 6, 7 **Hybridization Probe:**

Claim Type	Long QT Patent Claims
	491 Patent: Claims 4, 5, 6 545 Patent: Claims 3, 4, 5
Hybridization Probe Claims	737 Patent: Claims 6, 7 491 Patent: Claim 3 545 Patent: Claim 2
Irrelevant Claims (i.e., no relation to genetic testing)	737 Patent: Claims 8, 9, 10, 11, 12, 13, 19, 20, 21, 22 491 Patent: Claims 13, 14, 15, 16, 17 812 Patent: Claims 3, 4, 5, 8, 9, 10, 13, 14, 15, 16, 17, 18, 19, 20, 21 545 Patent: Claims 8, 9, 10, 11, 12, 13

NON-INFRINGEMENT OF CHILDREN'S HOSPITAL'S PROPOSED TESTS

41. Children's Hospital's Proposed Tests will not infringe any claim of the Long QT Patents.

42. The Proposed Tests will not infringe the Isolated Nucleic Acid Claims, because extraction of genetic material from human patients under the Proposed Tests will not be carried out in a manner that isolates or amplifies the particular nucleotide or amino acid sequences claimed in any of the Isolated Nucleic Acid Claims.

43. The Proposed Tests will isolate only fragments of patient exons from the genes tested. Such isolation will not be directed toward amplification of any particular claimed mutation. The Proposed Tests will not involve the isolation of cDNA or RNA fragments.

44. The Proposed Tests will not infringe the Testing Method Claims because diagnosis and/or assessment of risk of Long QT under the Proposed Tests will require the clinical judgment of a clinical professional and will not be possible based on identification of mutations alone.

45. The Proposed Tests will not perform the step of "screening" for the specified breadth of mutations in the Testing Method Claims, according to the understanding of the person skilled in the art of the term "screening" on the relevant publication date for each of the Testing Method Claims.

46. Additionally:

(a) The Proposed Tests will not involve the specific procedures specified in claims 15 and 16 of the 737 Patent;

(b) The Proposed Tests will not amplify the entirety of the exon or the specific number of exons required in each of claims 1 to 11 of the 236 Patent, and other exons will be amplified simultaneously with the exons that are the subject matter of these claims;

(c) The Proposed Tests will not involve the use of the single-stranded confirmation polymorphism technique claimed in claims 2, 3, 5, 6, 8, 9 and 11 of the 236 Patent and claim 9 of the 491 Patent;

(d) The Proposed Tests will not involve sequencing of human KCNE1 as claimed in claim 10 of the 491 Patent;

(e) The Proposed Tests will not involve a RNAse assay as claimed in claim 11 of the 491 Patent;

(f) The Proposed Tests will not involve hybridization probes or the specific hybridization procedures claimed in the Testing Method Claims that involve hybridization in a manner that detects mutated human DNA to the exclusion of unmutated human DNA;

(g) The Proposed Tests will not amplify the entirety of the exon in claim 11 of the 812 Patent, nor will amplification be limited to a pair of primers; and

(h) The Proposed Tests will not involve each and every method step claimed in claim 7 of the 545 Patent.

47. The Proposed Tests will not infringe the Hybridization Probe Claims, because the Proposed Tests will not employ hybridization probes that hybridize specifically to the mutations set out in the Hybridization Probe Claims.

48. The Proposed Tests will not infringe the Irrelevant Claims because the Proposed Tests use next-generation sequencing technology and will not utilize or involve vectors, host cells, polypeptides or their synthesis, transfected cells or drug screening methods.

49. Additionally, the Proposed Tests will not infringe any of the claims of the Long QT Patents because the Proposed Tests will be used on a non-commercial scale and for a non-commercial purpose, supported by public funding.

INVALIDITY OF THE LONG QT PATENT CLAIMS

50. As set out herein, each of the Isolated Nucleic Acid Claims and Testing Method Claims in the Long QT Patents is invalid and unenforceable.

Isolated Nucleic Acid Claims

Unpatentable Subject Matter & Lack of Novelty

51. Contrary to section 2 of the *Patent Act*, as amended, the subject matter defined by each of the Isolated Nucleic Acid Claims is directed to unpatentable subject matter.

52. The nucleic acids claimed in the Isolated Nucleic Acid Claims encode naturally-occurring genetic sequences that encode for naturally-occurring human genes. The genetic sequences were discovered by extracting genetic material from human beings. Thus, the subject matter of the claims is not directed to a new and useful art, process, manufacture or composition of matter nor any improvement in any art, process, machine manufacture or composition of matter.

53. Naturally-occurring phenomena and discoveries thereof are not patentable. The isolation of the claimed nucleic acids from their natural environment requires trivial effort and does not constitute a sufficiently marked departure from the naturally-occurring unpatentable nucleic acids to warrant patentability under section 2. Isolated naturally-occurring nucleic acids are neither new compositions of matter nor improvements of compositions of matter.

54. For the foregoing reasons, the Isolated Nucleic Acid Claims also lack novelty. Before the claim date, the subject matter defined by each of the Isolated Nucleic Acid Claims was disclosed in such a manner that the subject matter became available to the public in Canada and elsewhere, contrary to section 28.2(1) of the *Patent Act*.

Obviousness

55. The subject matter defined in the Isolated Nucleic Acid Claims would have been obvious on the claims' respective claim dates to a person skilled in the art, having regard to the prior art disclosed within the Long QT Patents and the common general knowledge.

56. For claims 1, 2, 6 and 7 of the 812 Patent, Children's Hospital additionally relies on the following prior art publication in support of its obviousness allegation:

> Abbott et al., "A superfamily of small potassium channel subunits: form and function of the MinK-related peptides (MiRPs)", *Quarterly Reviews of Biophysics* 31, 4 (1998), pp. 357-398

57. Methods of isolation of nucleic acids was well-known on the claim dates for each of the Isolated Nucleic Acid Claims, and the genes encoding for cardiac ion-channel proteins playing a role in Long QT were also well-known. The only new information disclosed by the patentee in each of the Long QT Patents was the discovery of specific gene sequences and/or mutations, and related genomic information.

58. In the 737 Patent, having the earliest claim date of the Long QT Patents, the patentee has admitted *inter alia* that:

(a) Methods for purifying (i.e., isolating) nucleic acids in accordance with the methods of the Long QT Patents were described in the prior art, e.g., in Sambrook et al., 1989 or Ausubel et al., 1992. (page 18 lines 11 to 19)

(b) The polynucleotides (i.e., nucleic acids) of the Long QT Patents could be produced by chemical synthesis using methods well-known in the art, e.g. by the phosphoramidite method described by Beaucage &

> Carruthers, 1981 or the trimester method according to Matteucci and Caruthers, 1981. Such methods could be performed on commercial, automated oligonucleotide synthesizers. (page 18 lines 20 to 26)

59. The discovery of naturally-occurring gene sequences for genes known or expected to be affiliated with Long QT was obvious at the claim dates. Such discovery cannot constitute the inventive concept of a claimed invention, and there is no additionally inventive contribution made by the patentees in any of the Isolated Nucleic Acid Claims, nor any inventive step.

Claims Broader than Invention Made or Disclosed

60. Contrary to section 27(4) the *Patent Act*, the Isolated Nucleic Acid Claims do not claim distinctly and in explicit terms the subject-matter of the invention for which an exclusive privilege or property is claimed. Further the claims are not fully supported by their respective disclosures. To avoid failing for being unpatentable subject matter, the Isolated Nucleic Acid Claims must include, as an essential element, the practical application of the nucleic acids claimed. They do not. The Isolated Nucleic Acid Claims are therefore invalid for exceeding the invention made or disclosed.

Testing Method Claims

Unpatentable Subject Matter – Abstract Mathematical Comparison

61. Each of the Testing Method Claims, purposively construed, describes subject matter that is outside the enumerated categories in the statutory definition of "invention" under section 2 of the *Patent Act*.

62. Each of the Testing Method Claims is directed to an abstract mathematical comparison between a human patient genetic sequence and a reference genetic sequence. Such subject matter is a "mere scientific principle or abstract theorem", and is prohibited from patentability under section 27(8) of the *Patent Act*.

63. The subject matter of the Testing Method Claims is not concrete or tangible. The claimed subject matter does not have a physical existence, nor does the subject matter manifest a discernible effect or change, as required under section 2 of the *Patent Act*.

64. The elements of the Testing Method Claims are highly general in nature, cover substantially all practical applications of naturally-occurring phenomena and abstract mathematical comparisons based on such phenomena, and relate to insignificant, well-understood, purely conventional and routine subject matter.

65. Accordingly, each of the Testing Method Claims fails for want of patentable subject matter.

Unpatentable Subject Matter – Professional Skills Defence & Lack of Utility

66. Each of the Testing Method Claims is directed to the comparison of a human patient genetic sequence and a reference genetic sequence. Such information can only be compared in a useful manner through application of skill and judgment by a skilled professional having access to reliable and valid information about past clinical assessment of the mutation of interest.

67. Subject matter which interferes with the skill and judgment required of a skilled professional is not patentable under section 2 of the *Patent Act*. Accordingly, the Testing Method Claims claim unpatentable subject matter.

68. In the alternative to paragraphs 66 and 67, since the Testing Method Claims do not contain any step requiring the interpretation of the genetic sequence comparison by a skilled professional, and such a step is necessary to achieve a useful result, these claims fail for lack of utility under section 2 of the *Patent Act*.

Obviousness

69. The subject matter defined in the Testing Method Claims would have been obvious on the claims' respective claim dates to a person skilled in the art, having regard to the prior art disclosed within the Long QT Patents and the common general knowledge.

70. For claims 11 and 12 of the 812 Patent, Children's Hospital additionally relies on the following prior art publication in support of its obviousness allegation:

> Abbott et al., "A superfamily of small potassium channel subunits: form and function of the MinK-related peptides (MiRPs)", *Quarterly Reviews of Biophysics* 31, 4 (1998), pp. 357-398

71. Numerous methods for genetic sequencing and detection of genetic mutations were well-known on the claim dates for each of the Testing Method Claims, and genes encoding for cardiac ion-channel proteins playing a role in Long QT were also known. The only new information disclosed by the patentee in each of the Long QT Patents was the discovery of specific human gene sequences and/or mutations, and related genomic information.

72. In the 737 Patent, having the earliest claim date of the Long QT Patents, the patentees have admitted (in addition to its admissions set out in paragraph 58, above) *inter alia* that:

(a) Several methods to detect DNA sequence variation were known to a person skilled in the art, including manual sequencing, automated fluorescent sequencing, single-stranded conformation polymorphism assay, clamped denaturing gel electrophoresis, heteroduplex analysis, chemical mismatch cleavage, protein truncation assay, asymmetric assay, and (for a rapid preliminary analysis) Southern blots of DNA cut with one or more restriction enzymes. (page 11 lines 3 to 29)

(b) Methods for detecting DNA sequence variation had been described in a review by Grompe (1993). (page 11 lines 19 to 20)

(c) Detection of point mutations in a genetic sequence could be accomplished by molecular cloning of the relevant allele and sequencing the allele using techniques well known in the art. (page 11 lines 30-31)

(d) Six well-known methods existed for a complete test for confirming the presence of a susceptibility allele, all of which had been described in the literature: (page 11 line 32 to page 12 line 14)

i. Single-stranded conformation analysis

ii. Denaturing gradient gel electrophoresis

iii. RNase protection assays

iv. Allele-specific oligonucleotides

v. Use of proteins which recognize nucleotide mismatches, such as the *E. coli* mutS protein

vi. Allele-specific PCR

(e) Restriction enzymes and binding sites were well known in the art. (page 15 line 1)

(f) Primers could be synthesized using techniques well-known in the art, including by using oligonucleotide commercially-available synthesizing machines. Given the relevant sequence, design of particular primers is well within the skill of the art. (page 15 lines 1 to 5)

73. The claimed testing methods based on naturally-occurring gene sequences and mutations for genes known to be affiliated with Long QT were obvious at the claim dates. Discovery of naturally-occurring human gene sequences and mutations cannot constitute the inventive concept of a claimed invention, and there is no additionally inventive contribution made by the patentees in any of the Testing Method Claims, nor any inventive step beyond the discovery of naturally-occurring information.

Insufficient Disclosure

74. None of the Long QT Patents disclose any method for sequencing multiple patients' exons in parallel, electronically comparing the patient exon sequences to reference sequences, identifying genetic variants, and applying professional skill and judgment to interpret the significance of the variants, alone and in combination, to assess a patient's risk of Long QT.

75. If the Testing Method Claims are construed to encompass such a method, then the claims are invalid for being broader than the invention made or disclosed, in violation of section 27(3) of the *Patent Act*.

76. Additionally, in respect of the non-mutation-specific Testing Method Claims, neither the disclosure nor the claims of the 236 or 812 Patents specify which mutations will increase a patient's risk of Long QT. Ascertaining the significance of any specific

mutation requires the application of skill and judgment by a professional and is not part of the common general knowledge. Accordingly, the subject matter of the claims is insufficiently disclosed and not enabled by the disclosure of the 236 and 812 Patents and these claims are broader than the invention made or disclosed, all in violation of section 27(3) of the *Patent Act*.

77. Additionally, claim 16 of the 737 Patent and claim 12 of the 491 Patent contain dependent claim elements that are broader than the claims upon which they depend and their respective specifications, in that they involve screening for mutations not contemplated in their parent claims or associated disclosures. Accordingly, claim 16 of the 737 Patent and claim 12 of the 491 Patent are insufficiently disclosed and not enabled by their respective disclosures, and are broader than the respective inventions made or disclosed in their respective patents, all in violation of section 27(3) of the *Patent Act*. These claims also contain improper dependencies, resulting in indefiniteness in violation of section 27(4) of the *Patent Act* and section 87 of the *Patent Rules*. These claims are additionally invalid for lacking utility, because screening for the uncontemplated mutations was not soundly predicted and is inoperable.

78. Additionally, in respect of claim 11 of the 812 Patent, neither the disclosure nor the claims of the 812 Patent specify which primers or which exons are to be used to achieve a useful result. Nor does the 812 Patent explain how to carry out the claim for any exon but the lone naturally-occurring exon encoding for KCNE2. Selecting primers and applying those primers to particular exons requires the application of skill and judgment by a professional. Accordingly, the subject matter of claim 11 of the 812 Patent is insufficiently disclosed and not enabled by the disclosure of the 812 Patent and the claim is broader than the invention made or disclosed, all in violation of section 27(3) of the *Patent Act*. This claim is additionally invalid because the subject matter of the claim, in and of itself, lacks utility.

79. Additionally, in respect of the mutation-specific Testing Method Claims in the 491 Patent (claims 7 to 12), the claimed mutations are of uncertain clinical significance and have not been demonstrated to cause Long QT. Therefore, these claims are additionally invalid for lacking utility.

CONCLUSION

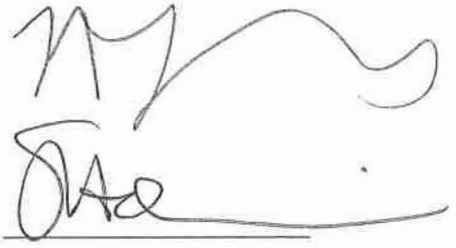
80. In view of the foregoing, no claim of the Long QT Patents will be infringed by Children's Hospital's implementation of the Proposed Tests for the benefit of patients requiring genetic testing for heart conditions.

81. In addition, the Isolated Nucleic Acid Claims, Testing Method Claims and Hybridization Probe Claims, as defined herein, are invalid and void.

82. In the alternative, the Proposed Tests constitute public, non-commercial uses of the subject matter claimed by the Long QT Patents. Pursuant to s. 19.1(2) of the *Patent Act*, as public, non-commercial uses, the Proposed Tests are eligible for authorization to be used without seeking licenses from the defendants.

83. The plaintiffs propose that this action to be tried at Toronto, Ontario or Ottawa, Ontario.

November 3, 2014



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