HL7 Clinical Genomics and Structured Documents Work Groups

CDA Implementation Guide:
Genetic Testing Report (GTR)

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CDA R2 Co-editor
CCD Implementation Guide Co-editor

HL7 Clinical Genomics Activities

Three Tracks:

v3:

- Family History (Pedigree) Topic
- Genetic Variations Topic
- Gene Expression Topic
- CMETs defined by the Domain

v2:

v2 Implementation Guides

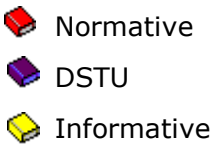
* The IG "Genetic Test Result Reporting to EHR" is modeled after the HL7 Version 2.5.1 Implementation Guide: Orders And Observations; Interoperable Laboratory Result Reporting To EHR (US Realm), Release 1

CDA:

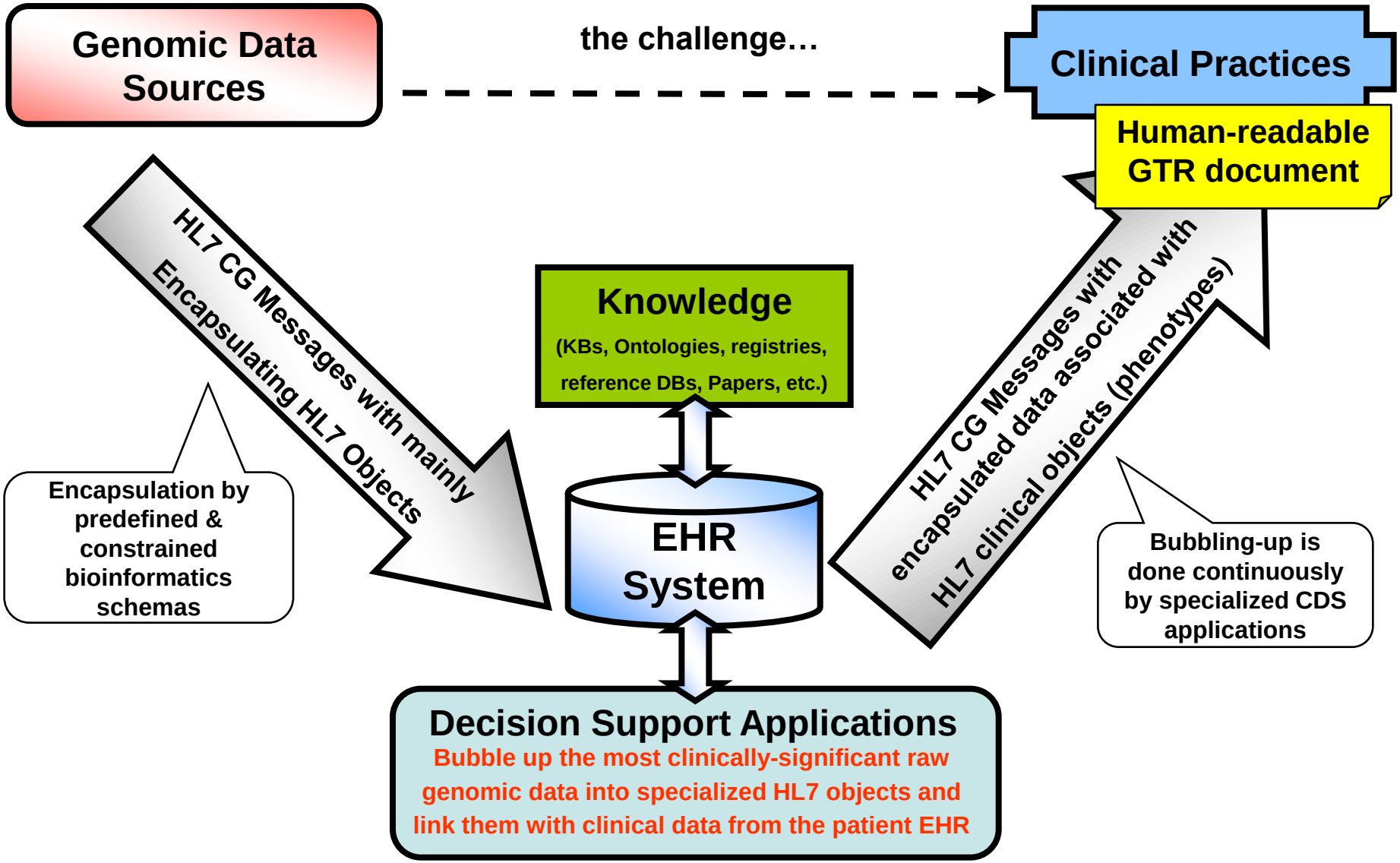
- A CDA Implementation Guide for Genetic Testing Reports

Common:

- Domain Analysis Models for the various topics
- A Domain Information Model (v3) describing the common semantics
- Semantic a*lignment among the various specs*



The Underlying Paradigm: Encapsulate & Bubble-up



CDA IG: Genetic Testing Report (GTR)

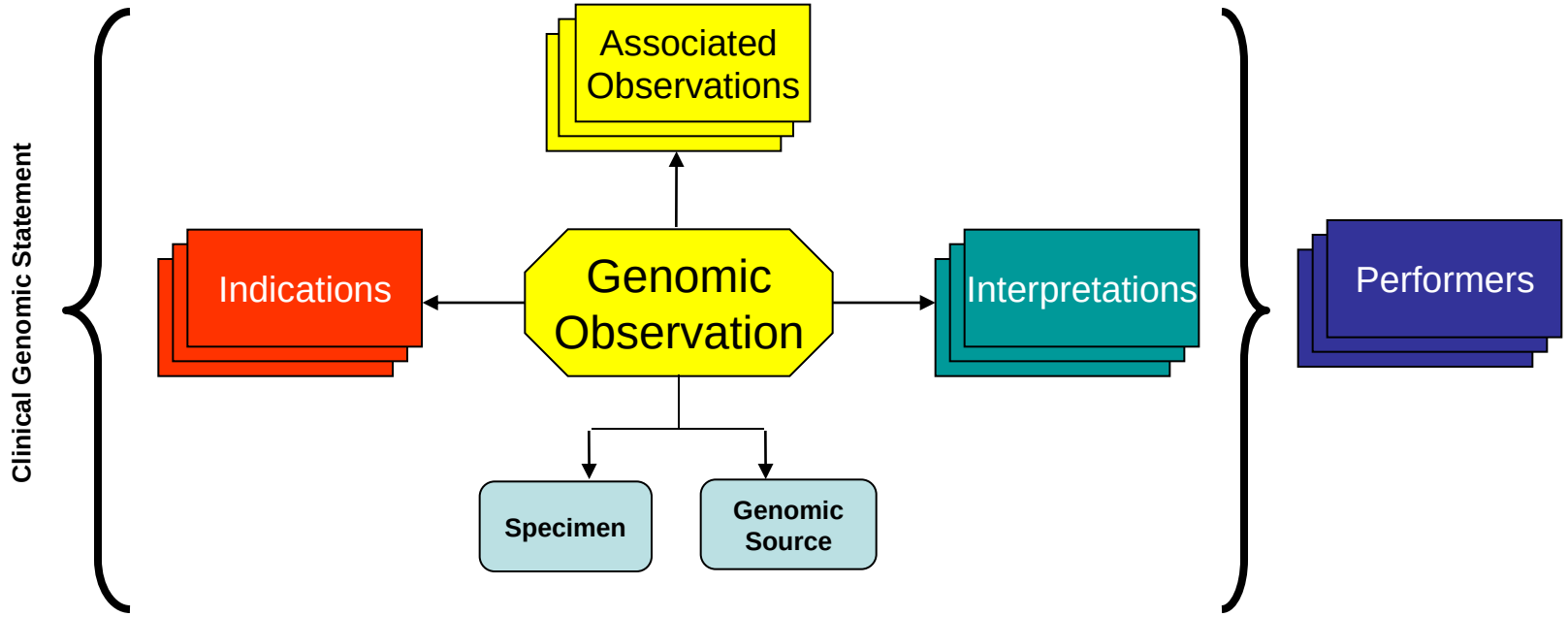
- Define an implementation guide for a genetic testing report that is both human readable and machine-processable
  - Target at all types of GTR producers, e.g., genetic labs, clin. geneticists
  - Readable content is larger in scope
  - E.g., detailed description of the tests performed along with references
  - Machine-processable should be limited, e.g., exclude raw data
- Ballot a Universal IG; then derive → specific types of GTR:
  - Healthcare & Research
  - Realm-specific guides
  - Omic-specific guides
- Developed using the MDHT open source tool (OHT)

GTR - Design Principles

- Follow existing report formats commonly used in healthcare & research
- Emphasize interpretations & recommendations
- Provide general background information on tests performed
- Reference HL7 Clinical Genomics instances (e.g., v3 or v2 GeneticVariation and Pedigree) as the place holders of full-blown raw genomic data and fully-structured family history data
- Utilize patterns of 'genotype-phenotype' associations in the HL7 v3 Clinical Genomics Domain
  - Implement them as 'clinical genomic statement' entry-level templates (see next slide), enabling meaningful use of the data

The Clinical Genomic Statement

- An abstract Clinical Genomic Statement (CGS) template that
  - Has at its core a genomic observation (e.g., a DNA sequence variation)
  - If it's a reportable finding, then it should be associated with indications and interpretations, specimen and genomic source class
  - The major finding can be associated with associated observation (e.g., amino acid change)
  - Optionally, performers may be specified (overriding header performers)
- The CGS abstract template is instantiated by specialized CGS's, e.g., for genetic variations or cytogenetics



Narrative and Structured Data

- All CGS structured data items shall be part of clinical genomic statement (CGS) instances so that parsing applications can find the full semantics explicitly represented in one coherent structure
  - In the case of the overall interpretation, it is part of CGS that has references to the various testing interpretations
- Sub-sections such as Indications, Interpretations and Specimen are mainly for presenting narrative, but they may also contain structured data
  - In this way, it is possible to have less redundant documents, e.g., in the case where all tests reported in a GTR document have the same indication, an Indications section in the Summary section consists of a full-blown indication observation which all CGS indication observations reference
- CGS structured data may point to the respective narrative in sub-sections (by means of XML ID)

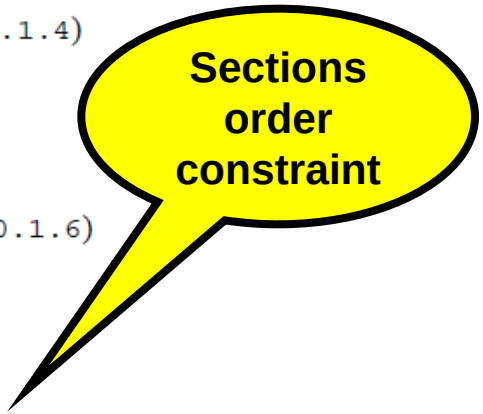
GTR Overall Layout

Genetic Testing Report

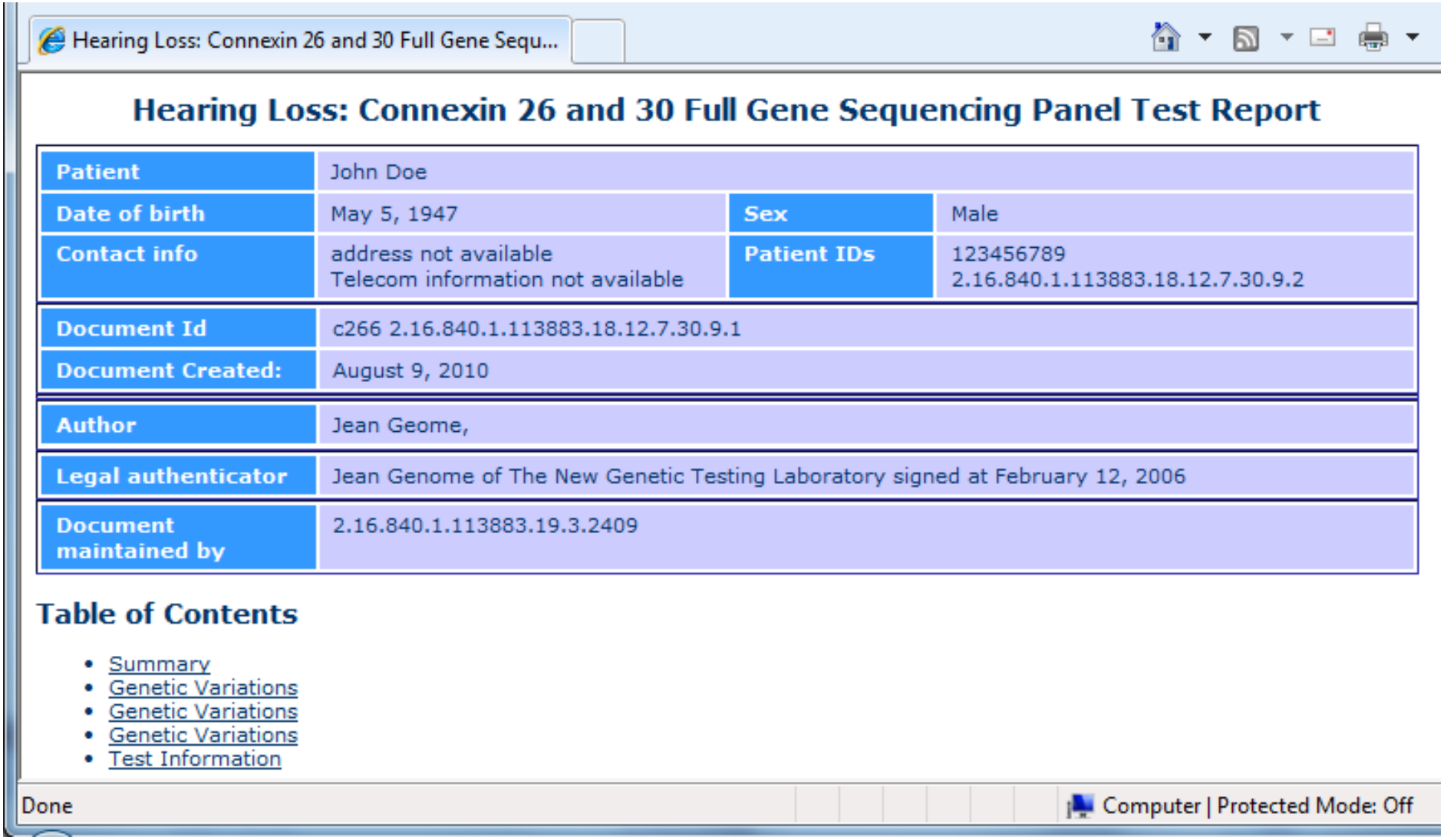
[ClinicalDocument: templateId 2.16.840.1.113883.10.20.20]

The GeneticTestingReport is a document template and thus serves as the root template for the GTR Implementation Guide. Its organization is described in the Approach section of this document. The sub-sections residing here constitute the backbone of the GTR. Most of them share a common structure represented by the Test Details Section which serves as a blueprint for most of the test-oriented sections like genetic variation or gene expression sections.

1. **SHALL** contain exactly one [1..1] **code/@code**="51969-4" *Genetic analysis summary report* (CodeSystem: 2.16.840.1.113883.6.1 LOINC) (CONF-GTR-1)
2. **SHALL** contain exactly one [1..1] **title** (CONF-GTR-7)
   - Default title is "Genetic Testing Report".
3. **SHALL** contain exactly one [1..1] **component**, such that
   a. Contains exactly one [1..1] *Summary Section* (templateId: 2.16.840.1.113883.10.20.20.1.1)
4. **MAY** contain zero or one [0..1] **component**, such that
   a. Contains exactly one [1..1] *Genetic Variations Section* (templateId: 2.16.840.1.113883.10.20.20.1.2)
5. **MAY** contain zero or one [0..1] **component**, such that
   a. Contains exactly one [1..1] *Cytogenetics Section* (templateId: 2.16.840.1.113883.10.20.20.1.4)
6. **MAY** contain zero or one [0..1] **component**, such that
   a. Contains exactly one [1..1] *Gene Expression Section* (templateId: 2.16.840.1.113883.10.20.20.1.3)
7. **MAY** contain zero or one [0..1] **component**, such that
   a. Contains exactly one [1..1] *Other Testing Section* (templateId: 2.16.840.1.113883.10.20.20.1.6)
8. **MAY** contain zero or one [0..1] **component**, such that
   a. Contains exactly one [1..1] *Test Information Section* (templateId: 2.16.840.1.113883.10.20.20.1.9)
9. Sections and subsections **SHALL** have a title and the title **SHALL NOT** be empty.
10. All sections **MAY** occur in any order except for the SummarySection which **SHALL** appear first and TestInformationSection which **SHOULD** appear last. Note that a TestInformationSection can appear in each of the specific test sections.



GTR Rendered – The Header



Draft that has not been clinically validated

GTR Rendered – Summary Section

Favorites | Hearing Loss: Connexin 26 and 30 Full Gene Sequ...

Summary

Indications

- Indication: Profound sensorineural hearing loss

Specimen and Genomic Source Class

- Peripheral Blood
- Genomic source class: Germline

Summary of Tests Performed

- GJB2 Full Gene Test
- GJB6-D13S1830 deletion
- Mitochondrial Hearing Loss Mutation Test

Overall Interpretation

- **Inconclusive.**
- DNA sequencing detected two changes in the GJB2 gene, 79G>A (V27I) and 109G>A (V37I). The V27I change has been reported as a benign variant (references) and is not believed to cause hearing loss. The V37I mutation has been previously reported in patients with hearing loss. This mutation, in homozygosity or combined with another GJB2 disease causing mutation, typically results in a mild to moderate hearing loss (Cryns et al. 2005). Mutations in both copies of the GJB2 gene are necessary to assume that GJB2 is responsible for the hearing loss. Although two mutations were identified in this patient, we would assume that the combination of a benign variant and a mild pathogenic mutation would result in a mild to moderate hearing loss rather than a moderately-severe one, as in this patient. It is most likely that the hearing loss in this patient is the result of the V37I mutation and an unknown second pathogenic mutation. It should be noted that a second mutation is not identified in a large percentage (10-50%) of patients with nonsyndromic hearing loss and GJB2 mutations (del Castillo et al. 2003).
- GJB6-D13S1830 Deletion: A PCR-based analysis of the GJB6-D13S1830 region of chromosome 13 was performed and did not detect the deletion. This test does not assess the DNA sequence of the GJB6 gene or detect other mutations that could affect the expression of the gene.
- Mitochondrial Hearing Loss mutations: Targeted bidirectional sequencing of mitochondrial DNA 1555 and 7445 regions did not detect the presence of these mutations.

Recommendations

- Although some cases may represent a coincidental carrier state, all of the studies have concluded that there are likely to be other genetic mutations that have not yet been identified. Genetic counseling is recommended for this patient and his/her family members.

Draft that has not been clinically validated

GTR Rendered – Genetic Variation Sections

Favorites | Hearing Loss: Connexin 26 and 30 Full Gene Sequ...

Genetic Variations

Tests Performed

- GJB2 Full Gene Test

Findings

- DNA MUTATIONS: Heterozygous 109G>A (V37I), Exon 2, GJB2, Pathogenic
- INCIDENTAL VARIANTS: Heterozygous 79G>A (V27I), Exon 2, GJB2, Benign

Interpretation

- DNA sequencing detected two mutations in the GJB2 gene, 79G>A (V27I) and 109G>A (V37I). The V27I mutation has been reported as a benign variant (references) and is not believed to cause hearing loss. The V37I mutation has been previously reported in patients with hearing loss. This mutation, in homozygosity or combined with another GJB2 disease causing mutation, typically results in a mild to moderate hearing loss (Cryns et al. 2005). Mutations in both copies of the GJB2 gene are necessary to assume that GJB2 is responsible for the hearing loss. Although two mutations were identified in this patient, we would assume that the combination of a benign variant and a mild pathogenic mutation would result in a mild to moderate hearing loss rather than a moderately-severe one, as in this patient. It is most likely that the hearing loss in this patient is the result of the V37I mutation and an unknown second pathogenic mutation. It should be noted that a second mutation is not identified in a large percentage (10-50%) of patients with nonsyndromic hearing loss and GJB2 mutations (del Castillo et al. 2003).

Genetic Variations

Tests Performed

- GJB6-D13S1830 Deletion Test

Findings

- Negative.

Interpretation

- GJB6-D13S1830 Deletion: A PCR-based analysis of the GJB6-D13S1830 region of chromosome 13 was performed and did not detect the deletion. This test does not assess the DNA sequence of the GJB6 gene or detect other mutations that could affect the expression of the gene.

Genetic Variations

Tests Performed

- Mitochondrial Hearing Loss Genes Test

Findings

- Negative.

Interpretation

- DNA sequencing did not detect the presence of any mutations in the MTTS1 and MTRNR1 genes.

Draft that has not been clinically validated

GTR Rendered – Test Information Section

Hearing Loss: Connexin 26 and 30 Full Gene Sequ...

Test Information

Background

- Mutations in the GJB2 (connexin 26) gene are the most common cause of non syndromic hearing loss and are most often seen in a person with hearing loss that was found in early childhood without any other medical problems. The severity of the hearing loss can range from mild to profound. The inheritance pattern is usually autosomal recessive, requiring two mutations, one in each copy of the gene, to cause hearing loss. The GJB6-D13S1830 deletion removes most of the GJB6 gene, which encodes the connexin 30 protein (Cx30). This deletion, when present in two copies or when combined with a single connexin 26 mutation, causes hearing loss. Although the frequency of mitochondrial hearing loss is unknown, studies suggest that mitochondrial mutations play an important role in inherited and acquired hearing impairment.

Methodology

- Exon 1 and the coding region of exon 2 of the connexin 26 (GJB2) gene are amplified using flanking primer sets. PCR products are sequenced using an ABI fluorescence automatic DNA sequencer. This test does not detect large deletions or mutations in non-coding regions that could affect gene expression. This assay is greater than 99.9% accurate in detecting mutations in the sequences analyzed. Polymerase chain reaction (PCR) analysis is performed to detect the presence or absence of a deletion spanning the GJB6-D13S1830 region of chromosome 13.

References

- Azaiez H, Chamberlin GP, Fischer SM, Welp CL, Prasad SD, Taggart RT, del Castillo, I, Van Camp G and Smith RJ. GJB2: the spectrum of deafness-causing allele variants and their phenotype. Hum Mutat. 2004;24(4): 305-11.
- Calvo J, Rabionet R, Gasparini P, Estivill X. Connexins and Deafness Homepage. http://www.crg.es/deafness.
- del Castillo I, Moreno-Pelayo MA, del Castillo FJ, Brownstein Z, Marlin S, Adina Q, Cockburn DJ, Pandya A, Siemering KR, Chamberlin GP, Ballana E, Wuyts W, Maciel-Guerra AT, Alvarez A, Villamar M, Shohat M, Abeliovich D, Dahl HH, Estivill X, Gasparini P, Hutchin T, Nance WE, Sartorato EL, Smith RJ, Van Camp G, Avraham KB, Petit C. and Moreno F. Prevalence and evolutionary origins of the del(GJB6-D13S1830) mutation in the DFNB1 locus in hearing-impaired subjects: a multicenter study. Am J Hum Genet. 2003;73: 1452-1458.
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- Kenneson A, Van Naarden Braun K and Boyle C. GJB2 (connexin 26) variants and nonsyndromic sensorineural hearing loss: a HuGE review. Genet Med. 2002;4 (4): 258-74.
- Park HJ, Hahn SH, Chun YM, Park K, Kim HN. Connexin26 mutations associated with nonsyndromic hearing loss. Laryngoscope. 2000 Sep;110(9):1535-8.
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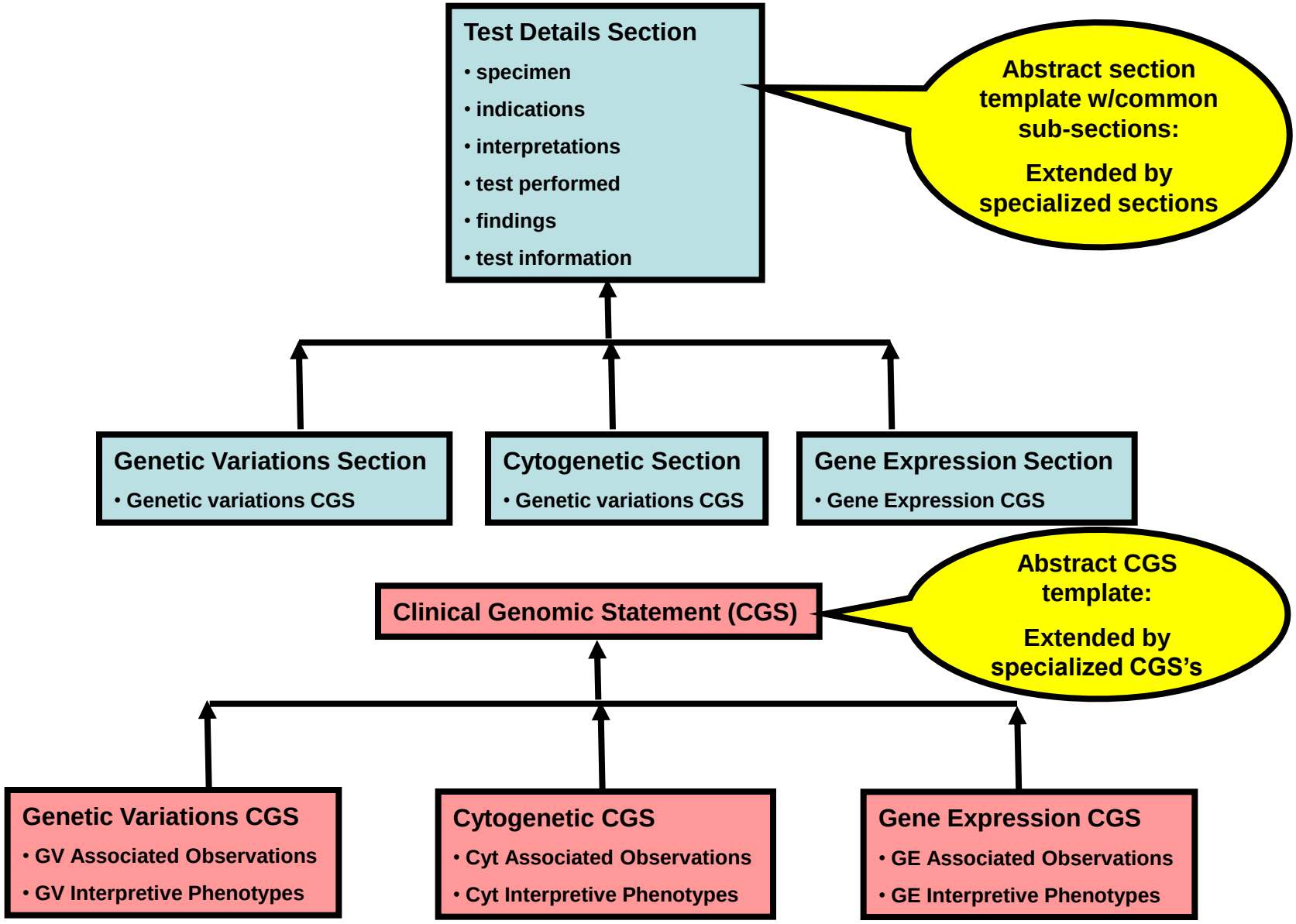
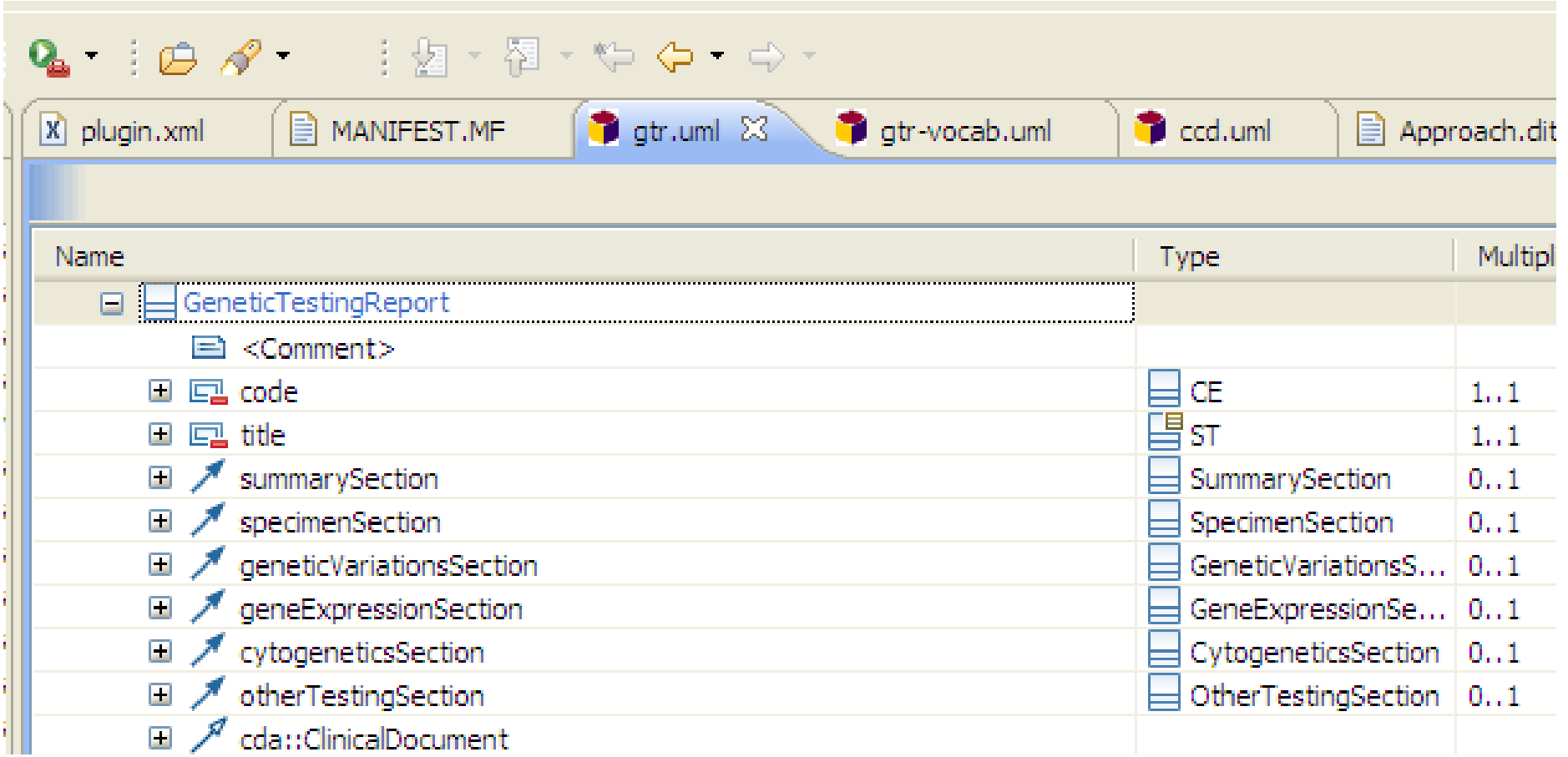
- Snoeckx RL, Huygen PLM, Feldmann D, Marlin S, Denoyelle F, Waligora J, Mueller-Malesinska M, Pollak A, Ploski R, Murgia A, Orzan E, Castorina P, Ambrosetti U, Nowakowska-Szyrwinska E, Bal J, Wiszniewski W, Janecke AR, Nekahm-Heis D, Seeman P, Bendova O, Kenna MA, Frangulov A, Rehm HL, Tekin M, Incesulu A, Dahl H-HM, du Sart D, Jenkins L, Lucas D, Bitner-Glindzicz M, Avraham KB, Brownstein Z, del Castillo I, Moreno F, Blin N, Pfister M, Sziklai I, Toth T, Kelley PM, Cohn ES, Maldergem LV, Hilbert P, Roux A-F, Mondain M, Hoefsloot, LH Cremers CWRJ, Löppönen T, Löppönen H, Parving A, Gronskov K, Schrijver I, Roberson J, Gualandi F, Martini A, Lina-Granade G, Pallares-Ruiz N, Correia C, Fialho G, Cryns K, Hilgert N, Van de Heyning P, Nishimura CJ, Smith RJH, and Van Camp G. A genotype-phenotype correlation for GJB2 (connexin 26) deafness. Am J Med Genet 2005 Dec;77(6):945-57.

GTR Main Hierarchies



GTR UML Model - Section Outline



GTR UML Model - Summary Section

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testsPerformedSection	TestsPerformedSe...	0..1
testInformationSection	TestInformationSe...	0..1
recommendationsSection	Recommendations...	0..1
cda::Section		

OverallInterpretationSection		
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title	ST	1..1
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overallInterpretivePhenotypeObservationPharmacogenomicDrugMetaboli	OverallInterpretiv...	0..1
overallInterpretivePhenotypeObservationGeneticDisease	OverallInterpretiv...	0..1
overallInterpretivePhenotypeObservationGeneticDiseaseCarrier	OverallInterpretiv...	0..1
cda::Section		

GTR Genetic Variation Section

GeneticVariationsSection		
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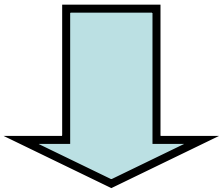

TestDetailsSection		
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title	ST	0..1
specimenSection	SpecimenSection	0..1
indicationsSection	IndicationsSection	0..1
testsPerformedSection	TestsPerformedSe...	0..1
findingsSection	FindingsSection	0..1
interpretationSection	InterpretationSect...	0..1
testInformationSection	TestInformationSe...	0..1
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Clinical Genomic Statement

ClinicalGenomicStatement		
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interpretivePhenotypeObservation	InterpretivePheno...	0..1
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cda::Observation		

Extended by specialized Clinical Genomic Statements

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interpretivePhenotypePharmacogenomicDrugMetabolism	InterpretivePhen...	0..1
geneticVariationAssociatedObservationAminoAcidChange	GeneticVariation...	0..1
geneticVariationAssociatedObservationDNAChange	GeneticVariation...	0..1
geneticVariationAssociatedObservationDNARegionName	GeneticVariation...	0..1
geneticVariationAssociatedObservationZygosity	GeneticVariation...	0..1
{?} value		
gtr::ClinicalGenomicStatement		

Interpretive Phenotype Observation

InterpretivePhenotypeObservationGeneticVariation		
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value	CD	0..1
{?} value		
qtr::InterpretivePhenotypeObservation		

Name	Type	Multiplicity	Annotation
qtr-vocab			
Allelic State			53034-5
Clinical Genomic Statement Genetic Variation Amino Acid Change			48006-1
Clinical Genomic Statement Genetic Variation DNA Change			48019-4
Genetic disease analysis overall interpretation			51968-6
Genetic disease sequence variation interpretation			53037-8
Interpretive Phenotype Observation Pharmacogenomic Drug Efficacy			51961-1
Interpretive Phenotype Observation Pharmacogenomic Drug Metabolism			53040-2
Overall Interpretive Phenotype Observation Genetic Disease Carrier			53039-4
Overall Interpretive Phenotype Observation Pharmacogenomic Drug Efficacy			51964-5
Overall Interpretive Phenotype Observation Pharmacogenomic Drug Metabolism			51971-0
(CodeSystems)			

Genetic disease sequence variation interpretation			53037-8
LA6668-3			Pathogenic
LA6669-1			Presumed pathogenic
LA6682-4			Unknown significance
LA6675-8			Benign
LA6674-1			Presumed benign

GTR XML Snippets – Indications Section

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 Summary Section
**********************************************************************
-->
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                    <title>Summary Section</title>
                    <!--
**********************************************************************
 Indications Section
**********************************************************************
-->
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                                    </item>
                                </list>
                            </text>
                            <entry>
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                                            <reference value="#a2"/>
                                        </originalText>
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                                    </reference>
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                            </entry>
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                    </component>
```

Summary Section

Indication's narrative

Indication's structured data

GTR XML Snippets – Specimen Section

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149   Specimen Section
150  ************************************************************************
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159                                  <item>Peripheral Blood</item>
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162                          </text>
163                          <entry>
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172                                  </entryRelationship>
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174                          </entry>
175                      </section>
176                  </component>
```

Specimen's narrative

Specimen's structured data

GTR XML Snippets – Overall Interpretation Section

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208    Overall Interpretation section
209  ****************************************
210  -->
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214                          <title>Overall Interpretation</title>
215                          <text>
216                              <list>
217                                  <item>
218                                      <content>
219                                          <content styleCode="Bold">Inconclusive.</content> DNA sequencing detected two mutations in the connexin 26 gene,
                                             79G>A (V27I) and 109G>A (V37I). GJB6-D13S1830 Deletion: A PCR-based analysis of the GJB6-D13S1830 region of
                                             chromosome 13 was performed and did not detect the deletion. This test does not assess the DNA sequence of the GJB6
                                             gene or detect other mutations that could affect the expression of the gene. Mitochondrial Hearing Loss Genes: DNA
                                             sequencing did not detect the presence of any mutations in the MTTS1 and MTRNR1 genes. Although this test examines
                                             all regions known to contain pathogenic mutations in these genes, it does not include sequencing of the 5' end of
                                             the MTRNR1 gene. The V27I mutation has been reported as a benign variant (references) and is not believed to cause
                                             hearing loss. The V37I mutation has been previously reported in patients with hearing loss. This mutation, in
                                             homozygosity or combined with another GJB2 disease causing mutation, typically results in a mild to moderate
                                             hearing loss (Cryns et al. 2005). Mutations in both copies of the GJB2 gene are necessary to assume that GJB2 is
                                             responsible for the hearing loss. Although two mutations were identified in this patient, we would assume that the
                                             combination of a benign variant and a mild pathogenic mutation would result in a mild to moderate hearing loss
                                             rather than a moderately-severe one, as in this patient. It is most likely that the hearing loss in this patient is
                                             the result of the V37I mutation and an unknown second pathogenic mutation. It should be noted that a second
                                             mutation is not identified in a large percentage (10-50%) of patients with nonsyndromic hearing loss and GJB2
                                             mutations (del Castillo et al. 2003).
220                                      </content>
221                                  </item>
222                              </list>
223                          </text>
224                          <entry>
225                              <observation classCode="PHN" moodCode="DEF">
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227                                  <statusCode code="completed"/>
228                                  <effectiveTime value="200512011500"/>
229                                  <value xsi:type="CD" code="LA9663-1" displayName="Inconclusive"/>
230                              </observation>
231                          </entry>
232                      </section>
233                  </component>
```

Interpretation's narrative

Structured Interpretation

GTR XML Snippets – Genetic Variation Section

```
373  ************************************************************************
374   Genetic Variations Section: Connexin 26 Full Gene Test
375  ************************************************************************
376  -->
377          <component>
378              <section>
379                  <code code="TBD" codeSystem="2.16.840.1.113883.6.1" codeSystemName="LOINC" displayName="Genetic Variations Section"
380                  <title>Genetic Variations Section</title>
381                  <!-- Structured representation of: Homozygous 109G>A (V37I), Exon 2, GJB2, Pathogenic -->
382                  <entry>
383                      <observation classCode="GEN" moodCode="EVN">
384                          <code code="55208-3" codeSystemName="LOINC" displayName="DNA Analysis Discrete Sequence Variant Panel"/>
385                          <statusCode code="completed"/>
386                          <effectiveTime value="200512011500"/>
387                          <entryRelationship typeCode="SUBJ">
388                              <observation classCode="LOC" moodCode="EVN">
389                                  <code code="48018-6" codeSystemName="LOINC" displayName="Gene Identifier"/>
390                                  <value xsi:type="CD" code="GJB2" codeSystemName="HUGO"/>
391                              </observation>
392                          </entryRelationship>
393                          <entryRelationship typeCode="SUBJ">
394                              <observation classCode="LOC" moodCode="EVN">
395                                  <code code="51958-7" codeSystemName="LOINC" displayName="Transcript Reference Sequence Identifier"/>
396                                  <value xsi:type="CD" code="NM_004004.5" codeSystem="REFSEQ" codeSystemName="NCBI Reference Sequence"/>
397                              </observation>
398                          </entryRelationship>
399                          <entryRelationship typeCode="SUBJ">
400                              <observation classCode="LOC" moodCode="EVN">
401                                  <code code="48003-8" codeSystemName="LOINC" displayName="DNA Sequence Variation Identifier"/>
402                                  <value xsi:type="CD" code="rs72474224" codeSystemName="dbSNP"/>
403                              </observation>
404                          </entryRelationship>
405                          <entryRelationship typeCode="SUBJ">
406                              <observation classCode="LOC" moodCode="EVN">
407                                  <code code="48004-6" codeSystemName="LOINC" displayName="DNA Sequence Variation"/>
408                                  <value xsi:type="CD" code="109G>A" codeSystemName="HGVS nomenclature for the description of sequence variations"/>
409                              </observation>
410                          </entryRelationship>
411                          <entryRelationship typeCode="SUBJ">
412                              <observation classCode="LOC" moodCode="EVN">
413                                  <code code="48019-4" codeSystemName="LOINC" displayName="DNA Sequence Variation Type"/>
414                                  <value xsi:type="CD" code="LA6690-7" codeSystemName="LOINC" displayName="Substitution"/>
415                              </observation>
416                          </entryRelationship>
417                          <entryRelationship typeCode="SUBJ">
418                              <observation classCode="LOC" moodCode="EVN">
419                                  <code code="48005-3" codeSystemName="LOINC" displayName="Amino Acid Change"/>
420                                  <value xsi:type="CD" code="Val37Ile"/>
```

Genetic Variation

Genetic Variation associated observations

GTR XML Snippets – Genetic Variation Section (cont.)

```
                    </observation>
                </entryRelationship>
                <entryRelationship typeCode="SUBJ">
                    <observation classCode="GEN" moodCode="EVN">
                        <code code="48006-1" codeSystemName="LOINC" displayName="Amino acid change type"/>
                        <value xsi:type="CD" code="LA6698-0" displayName="Missense"/>
                    </observation>
                </entryRelationship>
                <entryRelationship typeCode="SUBJ">
                    <observation classCode="LOC" moodCode="EVN">
                        <code code="47999-8" codeSystemName="LOINC" displayName="DNA Region Name"/>
                        <value xsi:type="ST">Exon 2</value>
                    </observation>
                </entryRelationship>
                <entryRelationship typeCode="SUBJ">
                    <observation classCode="GEN" moodCode="EVN">
                        <code code="53034-5" codeSystemName="LOINC" displayName=" Allelic State"/>
                        <value xsi:type="CD" code="LA6705-3" codeSystemName="LOINC" displayName="Homozygous"/>
                    </observation>
                </entryRelationship>
                <!-- pointing to the indication of performing this variation testing-->
                <entryRelationship typeCode="RSON">
                    <observation classCode="OBS" moodCode="EVN">
                        <id root="2.16.840.1.113883.18.12.7.30.9.2.1"/>
                        <code/>
                    </observation>
                </entryRelationship>
                <!-- interpretation of the variation observation (should consider if MFST=manifistation as the code here) -->
                <entryRelationship typeCode="SPRT">
                    <observation classCode="PHN" moodCode="DEF">
                        <code code="53037-8" codeSystemName="LOINC" displayName="Genetic disease sequence variation interpretation"/>
                        <value xsi:type="CD" code="LA6668-3" codeSystemName="LOINC" displayName="Pathogenic"/>
                    </observation>
                </entryRelationship>
            </observation>
        </entry>
```

Genetic Variation indication

Genetic Variation interpretation

CDA GTR Ballot Status

- Balloted as DSTU and passed in October 2010
- Still under ballot to refine & reconcile ballot comments
- Main issues:
  - Vocabulary:
    - Universal spec vs. Realm (e.g. mandate the use of LOINC code?)
    - Binding syntax (align with new vocabulary spec and the respective SDWG guidance for CDA IGs)
  - Layout:
    - Semantics – compare to recommended layouts in the literature
    - Syntactic – works closely with MDHT developers to adhere to SDWG guidelines
  - Sections specific to every type of genetic test (derived from abstract)
  - Section and Entry level template ids registration (when layout agreed)
  - Suggestion to add drug safety template

The End

- Thank you for your attention… ☺
- Questions?