Minutes

2025-06-02 HVNC Bi-monthly Regular Meeting

Attendees: Johan T den Dunnen, Alex Wagner, Ivo Fokkema, Jeroen Laros, Matthew Stachowiak, Gwendolyn Bennett, Ros Hastings, Timothy Hefferon, Marina DiStefano, Hencher Lee
Absent: Reece Hart
Regrets: Rachel Taylor

Agenda

1. Opening and Confirm Agenda

2. Confirm minutes from prior meeting

3. Review action items from previous meeting

4. Announcements
   a. anonymized minutes from February meeting were made
   b. update on Parentheses Task Force
   c. changes to committee membership
      i. Rachel Taylor notified the committee she is leaving leaving EMQN, and HVN
      ii. we will reach out to EMQN for replacements
   d. August and October meeting reschedule request
      i. approved to move both meetings up one week, to July 28th and September 29th, respectively.

5. Introduce a resolution to issue #147
   a. c hanges were suggested to the nomenclature website to clarify that we'll be using capital bases A, C, G, and T for RNA, instead of a, c, g, and u. These changes have not been accepted yet. The pull request is #213.
   b. the proposal is summarized. The website should list an example where the intron is included in a duplication, so users can see what to do in that case.
   c. a community consultation page for this proposal will be created (assigned SVD-WG011).

6. Proposal to resolve the various interpretations of NC(NM) reference sequences
   a. the proposal is summarized. The double colon is not a popular choice.
   b. do we know what the most common understanding of the NC(NM) notation is Often, for intronic variants, the genomic background is specified in text or not specified at all, and only the NM is used for gene-level notations. This could mean the most commonly used interpretation of NC(NM) would be the second interpretation, where the NM provides the exonic sequence. So, perhaps NC(GENE) should be redefined, instead. Group decision request: should we redefine NC(GENE) or NC(NM) and create a new syntax?
      i. maybe create a syntax for annotating references with gene symbols, e.g., as used in ClinVar and for mitochondrial genes. This format can be used for both of these cases.
      ii. it seems more complex than this since mitochondrial genes do not have transcript identifiers. In NM(GENE), the gene symbol is redundant annotation, but with the NC(GENE):c. the gene symbol cannot be removed because it defines the coordinates. We can not use the same notation for these two uses.
      iii. Decided to first create a new proposal to describe transcript-level variants for

mitochondrial genes (currently using the NC(GENE) syntax); this is a specific problem caused by the NCBI not annotating transcript reference sequences on the MT DNA, and we should solve this in a different way. After that, we can redefine the NC(NM) proposal; this will then be reversed; NC(NM) will refer to interpretation 2 (the NM provides the exonic sequence), and an alternative notation needs to be found for interpretation 1 (the NC provides all of the sequence). Action item.

7. Proposal for positions upstream and downstream of transcripts
   a. iInclude in the examples that the g. variant description is mandatory; the c. variant description is additional annotation.
   b. additionally search website for “promoter” or other keywords where updates are needed (ex: https://hgvs-nomenclature.org/stable/recommendations/DNA/substitution/?h=promoter#discussion)
   c. after this update, we’re ready to move to the community consultation step. Action item.

8. HGVS Validation Test Suite
   a. it would be useful to have a test set of valid and invalid variant descriptions, which allows tools to check their conformance to the HGVS nomenclature. We can focus on the syntax level first and add semantic checks later. It will also improve the documentation, as it forces us to check all examples given.
   b. there is a test set of valid and invalid variant descriptions, created by a student and used in the past to test tools.
   c. there are also thousands of transcribed & translated HGVS variant tests, but this will be more of a test for the inner workings of tooling.
   d. (not discussed: Tools like the LOVD HGVS syntax checker, Mutalyzer, and VariantValidator likely also have test sets.)
   e. the committee agrees that this will be useful. Action item.

9. Changes to the HGVS Nomenclature website since the last release
   a. a last commit to main, which was an error, will be removed. After that, we can create a new patch release of the website. Action item.

   (end of time) - the chair ends the meeting

   Not discussed (first on next meetings'agenda).

   b. although SVD-WG010 has been rejected, references to the proposal have not been removed yet. Several PRs have unresolved issues (e.g., PR #215).

10. Review the suggested changes to clarify that the restriction that a repeat’s sequence length should be divisible by three does not apply to intronic sequences in coding transcripts. See PR #231.

11. AOB