Proposal for LRG as a reference standard for variant reporting

The system and its features

The HGVS nomenclature system for the reporting sequence variation has been endorsed by the HVP as a Recommended System (RSS001). This nomenclature requires that variants be described with respect to reference sequences and recommendations have been made with respect to accuracy and stability of such sequences.

The Locus Reference Genomic (LRG) sequence format has been designed for the specific purpose of gene variant reporting. The format builds on the successful National Center for Biotechnology Information (NCBI) RefSeqGene project and provides a single-file record containing a uniquely stable reference DNA sequence along with all relevant transcript and protein sequences essential to the description of gene variants. In principle, LRGs can be created for any organism, not just human. In addition, the need is recognised to respect legacy numbering systems for exons and amino acids and the LRG format takes account of these. It is hoped that widespread adoption of LRGs – which will be created and maintained by the NCBI and the European Bioinformatics Institute (EBI) – along with consistent use of the Human Genome Variation Society (HGVS)-approved variant nomenclature will reduce errors in the reporting of variants in the literature and improve communication about variants affecting human health.

As of 22 May 2013, LRG records have been created for 734 human genes.

Further information can be found on the LRG web site (http://www.lrg-sequence.org).

The extent to which the system is currently being utilised

The LRG standard is supported by the LOVD LSDB software system which has been adopted by HVP as a Recommended System (RSS003) and by Mutalyzer (https://mutalyzer.nl/) which is currently under review (RSS002) for adoption. The commercial variant interpretation software package Alamut (http://www.interactive-biosoftware.com/software/alamut/overview) provides support for the LRG standard.

The HVP Standards and Guidelines with which the system is compliant

LRG is fully compliant with the HGVS variant nomenclature system and its XML schema is fully extensible to accommodate any future needs.

Access and license terms and conditions under which the system is made available

There are no restrictions placed on the use of the LRG reference standard and the XML schema is freely available for download from the LRG web site.

Summary

LRG (Dalgleish *et al.*, 2010) provides a stable reference sequence standard which is well suited for the reporting of sequence variants. The creation of LRG sequence records and the development of the schema for the LRG standard are undertaken jointly by EBI and NCBI. This will ensure the permanence of LRG as a reference standard.

Dalgleish R, Flicek P, Cunningham F, Astashyn A, Tully RE, Proctor G, Chen Y, McLaren WM, Larsson P, Vaughan BW, Béroud C, Dobson G, Lehväslaiho H, Taschner PEM, den Dunnen JT, Devereau A, Birney E, Brookes AJ, Maglott DR (2010) Locus Reference Genomic sequences: an improved basis for describing human DNA variants. Genome Medicine 2: 24

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