LETTER OF SUPPORT

VariantValidator: Creation of novel, intuitive and freely available software significantly improving accuracy and precision diagnosis of genetic disorders

I am a Senior Bioinformatician working with COSMIC (Catalogue of Somatic Mutations in Cancer) at the Wellcome Sanger Institute. COSMIC is the most detailed and the most comprehensive resource for exploring the effect of somatic mutations in human cancer. Our mission is to be the primary resource in cancer genetics and support research, diagnostics and pharmaceutical efforts in target identification and drug resistance. A big part of our work involves annotating and validating variants using third-party software. We intend to use VariantValidator as part of our curation and annotation system in order to help us achieve a high standard in variant representation.

As part of our standardisation effort, we have recently started the process of re-annotating all our variants. Owing to the nature of the data, our curators often come across variants reported with minimal information, for example, only the protein change without an accompanying genomic or transcript reference. VariantValidator can work with such variants, accepting a protein reference and validating the given variant. This is a gap we have struggled to fill using existing variant annotator tools and an area where VariantValidator excels. VariantValidator is able to annotate variants according to HGVS guidelines, which is one of the key requirements in variant representation in COSMIC.

We have met with Prof Raymond Dalgleish and Dr Peter Freeman where they answered many questions on VariantValidator and have agreed to continue to support VariantValidator for our use. They have also offered to add more features and functionality that would be particularly useful for our work at COSMIC. One such request was that they support Ensembl identifiers, as we work very closely with Ensembl data. This request was met with enthusiasm from Dr Causey-Freeman and we were assured that this work will be underway soon.

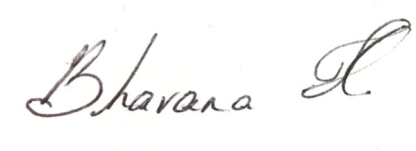
Dr Freeman has subsequently shared with us a development version of the python API to query their service. We have found that this will work particularly well when we integrate VariantValidator into our in-house curation system.

Using VariantValidator as part of our curation and quality-control processes will ensure that the data we're sharing with our users are of a high standard.
The following features of VariantValidator work particularly well for us:

- Can annotate variants reported on a protein reference only
- Can report variants according to HGVS guidelines
- Is free and open-source
- Has a user-friendly web interface suitable for use by non-bioinformaticians and an API for large-scale bioinformatics use

VariantValidator is a brilliant tool which offers many unique features. At COSMIC and the Wellcome Sanger Institute, we are keen to encourage free and open-source software like VariantValidator. We hope to continue our collaboration with the team behind VariantValidator and look forward to seeing more functionality added to the tool.

Yours sincerely,



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