JOHNS HOPKINS
UNIVERSITY

Institute of Genetic Medicine
733 N. Broadway
BRB Suite 551/Room 559
Baltimore, MD 21205
PHONE: 410-955-1773/FAX: 410-614-0213
EMAIL: gcutting@jhmi.edu

Garry R. Cutting, MD
Professor, Pediatrics and Medicine

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Prof Raymond Dalgleish
Department of Genetics and Genome Biology
University of Leicester
University Road
Leicester, UK

Dear Raymond,

I am writing to offer my support for your effort to further develop VariantValidator into a tool to visualize sequence variants and to generate HGVS-compliant variant descriptions. Such a tool will have global application in clinical-diagnostic and research laboratories and its development, as free and open-source software, will ensure that its benefits are maximized.

I am already grateful to the VariantValidator developers for producing a software tool that has made a significant contribution to the authentication of human-genome sequence variant descriptions. As you are aware, in my capacity as Editor of the journal *Human Mutation* and Co-Chair of the International Scientific Advisory Committee of the Global Variome project, I am chairing a committee to evaluate and implement a process to ensure that sequence variants are correctly reported in leading journals in the field of human/medical genetics. The committee enjoys the support of the following journals: American Journal of Human Genetics, PlosGenetics, Human Molecular Genetics, Genetics in Medicine, Journal of Medical Genetics, Human Genome Variation and Human Genetics. VariantValidator has been endorsed by the committee as a tool for verifying compliance of variants with the universally accepted HGVS variant nomenclature standard prior to acceptance of manuscripts. The goal of the committee is to extend the procedure to all journals in the biomedical sphere, not just those that focus on human genetics.

You are also aware that I direct the CFTR2 database (https://www.cftr2.org/) which is interpreting the consequences of all variants in the *CFTR* gene that have been found in ~89,000 individuals with cystic fibrosis. VariantValidator has proven to be a valuable tool in helping us

confirm the correctness of variant descriptions, as well as identifying a number of invalid descriptions that appear from time to time in the literature.

The use of VariantValidator in assessing *CFTR* gene variant data gives us confidence that the variant descriptions in our database, on which genetic diagnostic labs depend, are robust and that continued use of the software will ensure that they remain so in the future. Furthermore, I am confident that promoting the use of VariantValidator in the biomedical community will markedly improve the reporting of sequence variation in the scientific literature. These efforts will undoubtedly lead to tangible improvements in patient care.

I am pleased to confirm that I will provide guidance to the project in respect of the need to ensure that VariantValidator remains the cutting-edge tool that it is and that it develops in a way that properly addresses unmet needs in the field of genetic data analysis in the clinical setting.

Sincerely,

Garry R. Cutting, M.D.
Professor of Pediatrics and Medicine
Aetna/U.S. Healthcare Professor of Medical Genetics
Director, DNA Diagnostic Laboratory