Novel collaborative bioinformatics platform for gene identification in Hereditary Spastic Paraplegia

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Abstract

Novel genes are now identified at a rapid pace for Hereditary Spastic Paraplegia using next-generation sequencing (NGS) approaches. However, new challenges have also become evident: (1) effectively managing larger exome and/or genome datasets, especially for smaller labs; (2) direct hands-on analysis and contextual interpretation of variant data in large genomic datasets; and (3) many small and medium-sized clinical and research-based investigative teams around the world are generating data that, if combined and shared, will significantly increase the opportunities for the entire community to identify new genes. To address these challenges we have developed GEnomes Management Application (GEM.app), a software tool to annotate, manage, visualize, and analyze large genomic datasets (https://genomics.med.miami.edu/). GEM.app currently contains ~1,700 whole exomes from 50 different diseases studied by 45 principal investigators from 17 different countries. Hereditary Spastic Paraplegia exomes represent the largest share with nearly 400 datasets. The focus of GEM.app is on user-friendly analysis for non-bioinformaticians to make NGS data directly accessible. Yet, GEM.app provides

powerful and flexible filter options, including single family filtering, across family/ phenotype queries, nested filtering, and evaluation of segregation in families. In addition, an opt-in choice is available to share genomic variation on a gene-by gene basis with the worldwide community of scientists. This approach has already let to the collaborative identification of a number of novel HSP genes and will further our abilities to diagnose patients.