

Publication in Human Mutation

Using homologous relationships of protein domains in the human genome to interpret genetic variation

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A study titled "Aggregation of population-based genetic variation over protein domain homologues and its potential use in genetic diagnostics" was recently accepted for publication in Human Mutation.

his work was a collaborative effort between <u>Christian Gilissen</u>, Department of Human Genetics, and Gert Vriend, Centre for Molecular and Biomolecular Informatics.

This publication is part of the PhD project of Laurens van de Wiel and shows how homologous protein domain relations may be used to interpret normal and pathogenic variation at a much finer scale than previously possible. "We developed a framework that maps population variation and known pathogenic mutations onto 2,750 "meta-domains." These meta-domains consist of 30,853 homologous Pfam protein domain instances that cover 36% of all human protein coding sequences. We find that genetic tolerance is consistent across protein domain homologues, and that patterns of genetic tolerance faithfully mimic patterns of evolutionary conservation. Furthermore, for a significant fraction (68%) of the meta-domains high-frequency population variation re-occurs at the same positions across domain homologues more often than expected. In addition, we observe that the presence of pathogenic missense variants at an aligned homologous domain position is often paired with the absence of population variation and vice versa."

Publication: link



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