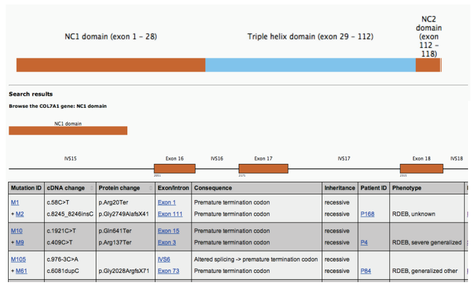
PathoKB:

a pathogenicity-focused mutation knowledge base providing clinical utility

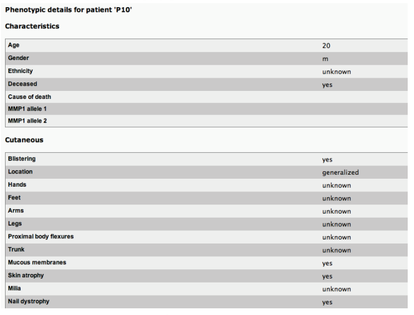
Despite excellent progress in disease research and diagnostics, little of the clinically relevant new knowledge reaches the patient or their doctor in a convenient and useable format. This is particularly true for causative mutations, which underlie Mendelian disease, where pathogenicity interpretation presents a major obstacle. One reason for this is that key reference data (mutation screening data, reports of similar patients, etc.) are either not shared in a structured electronic format, or are dispersed across multiple sites, often with complex and burdensome access mechanisms. After developing Locus Specific Databases (LSDBs) and exchange systems like Café Variome and Vario-ML to support research endeavours, the GEN2PHEN project is now creating a new level of functionality connecting research and clinical activities. The system is now sufficiently mature to hand on to expert consortia interested in specific disease areas (e.g., breast cancer, colon cancer, neurogenetic disorders, etc.) for beta-testing and data management within their projects to ensure this project develops to provide valuable support for clinical diagnostics activities in genetic disease and clinical practice.

Pathogenecity data portals

Genome centric



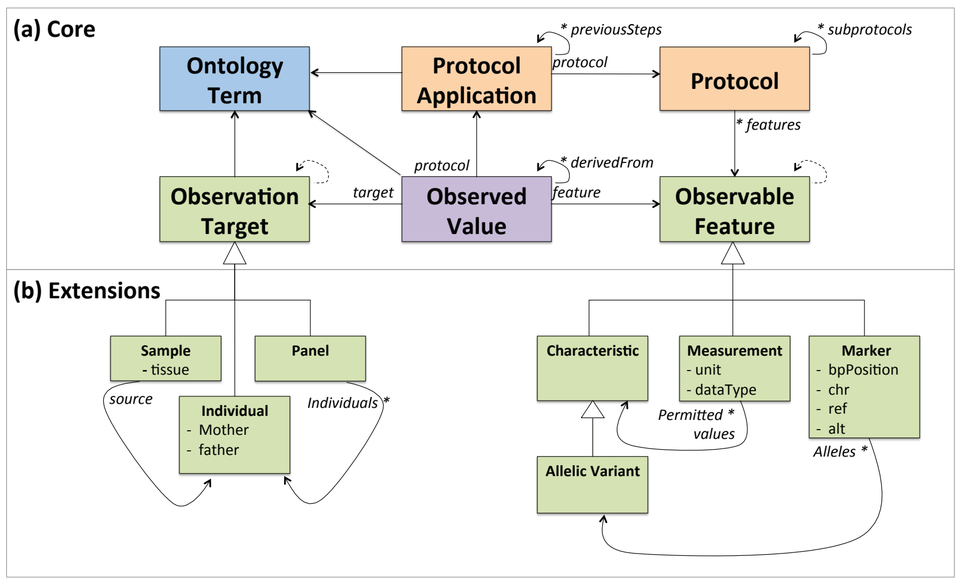
Patient centric



Pathogenecity centric

With model and database in place, we are currently developing pathogenicity-focused mutation knowledge displays relevant to assigning and recording pathogenicity of DNA sequence variants to enable disease consortia to collate, integrate and deliver the clinically useful knowledge required in healthcare.

Flexible model for all patient data modalities



A highly flexible data model (Observ-OM) has been generated (Adamusiak et al, 2012, Human Mutation) and extended for PathoKB to handle all relevant data modalities within the phenotype, sequence and pathogenicity domains — together enabling the capture and repurposing of any and all clinically useful mutation data and supporting evidence/analyses.

Free and open source software

The model has been used as the basis of a reference database implementation, building on the MOLGENIS suite consisting of LSDB, multi-omics, model organism, gwas, whole genome sequencing and biobank databases (www.molgenis.org) and GEN2PHEN expertise, resulting in a complete web-based database application.

Please email us to test PathoKB:

Morris A. Swertz[1] *m.a.swertz@rug.nl*
Sirisha Gollapudi[2]
Raymond Dalgleish[2]
Trebor Rengaw[1]
Pieter Neerincx[1]
Rolf Sijmons[1]
Myles Byrne[3]
Michael Cornell[4]
Andrew Devereau[4]
Juha Muilu[3]
Anthony J Brookes[2]* *ajb97@leicester.ac.uk*

http://www.molgenis.org/wiki/PathoKB

1. *Genomics Coordination Center • Department of Genetics University Medical Center Groningen • Netherlands*
2. *Department of Genetics • University of Leicester Leicester • United Kingdom*
3. *Institute for Molecular Medicine Finland (FIMM) • University of Helsinki Helsinki • Finland*
4. *NGRL Manchester • Genetic Medicine • St Mary's Hospital Manchester • United Kingdom*

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www.gen2phen.org