DECIPHER Release September 2013

Summary of Changes and New Functionality

The latest release of DECIPHER incorporates significant changes to the service that include the following

- Deposition of sequence variant alongside copy-number variants
- Changes to inheritance categories and parent records
- Changes to existing patient creation and CNV deposition forms
- Improvements to search functionality
- New look to DECIPHER pages

Further details on these changes are described in the sections below

Deposition of Sequence Variant

We are happy to announce that DECIPHER now accepts deposition of sequence variant data for patients with this release. The data entry interface for sequence variant can be found under the "Variants" tab after a patient record has been created. There are two separate sections in this menu that enable the entry of both CNV and sequence variant.

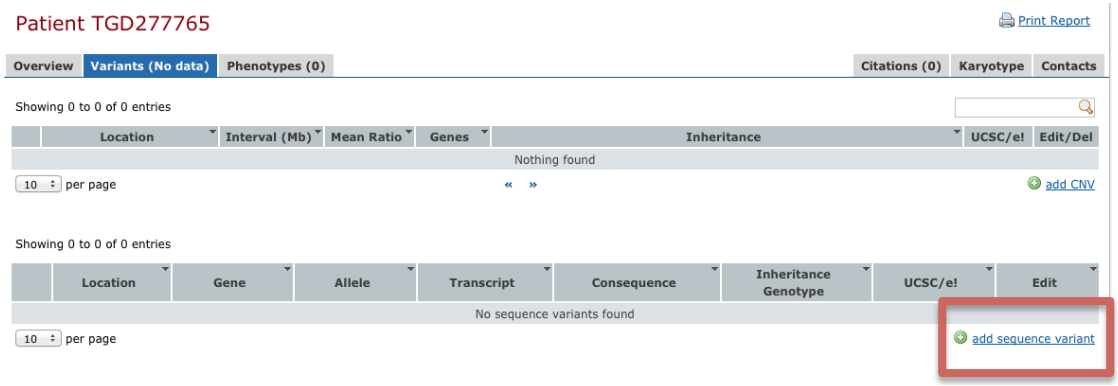


Figure 1: Interface with CNV and Sequence Variant deposition links

Sequence Variant Entry

The sequence deposition form (below) collects information concerning a sequence variant in GRCh37/hg19 assembly coordinates. The minimum items required for deposition of sequence variant are:

- Chromosome – (1-22 or X/Y)
- Start Position – Genomic coordinate position for reference allele.
- Reference Allele – Nucleotide/s starting at the reference position (forward strand)

- Alternate Allele – Indicate alternate allele (or use "." for deletion)
- Transcript – Ensembl or Refseq transcript ID.

The sequence variant entry form validates reference allele and transcript information on submission and will throw an error if the reference allele differs from that expected in the standard genomic assembly or if the transcript does not exist at the given position.

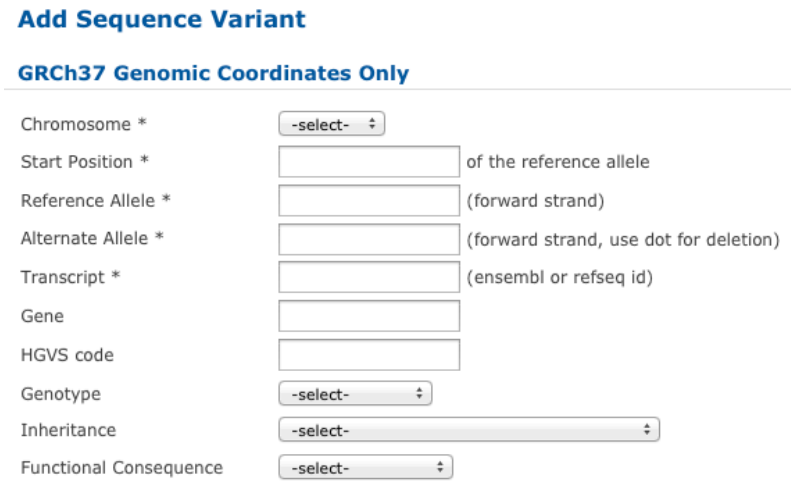


Figure 2: Sequence variant deposition Interface

Examples:

- Mutation of C>G at position 103969467 in Chromosome 7 (Refseq ID: NM_199000.2)

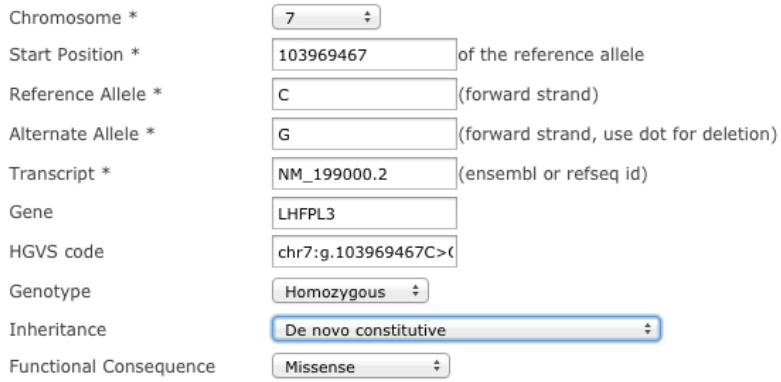


Figure 3: Mutation from C to G

- Insertion of GG after C at position 10369467 in Chromosome 7 (Refseq ID: NM_199000.2)

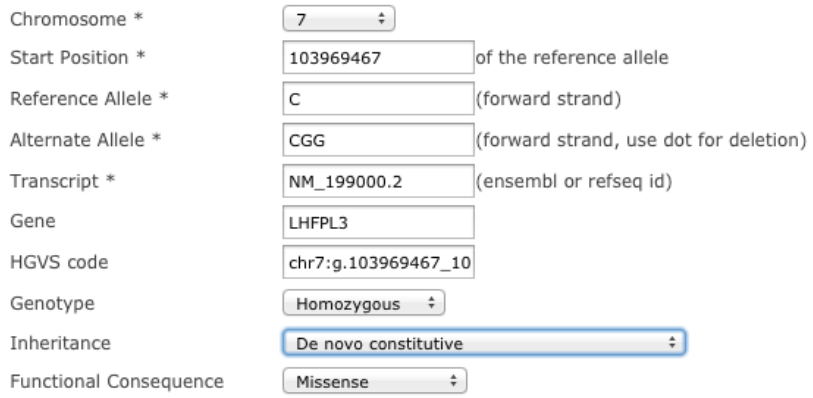


Figure 4: Insertion of GG after C

- Deletion of C at position 10369467 in Chromosome 7 (Refseq ID: NM_199000.2)

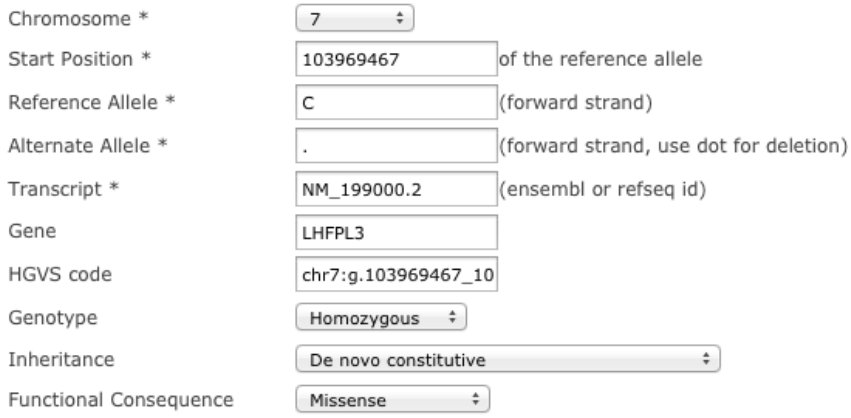


Figure 5: Deletion of C

Viewing Sequence Variants

Upon submission, DECIPHER derives information from the Ensembl Variant Effect Predictor (VEP) and displays a summary of deposited and derived information on the variant pages.

Figure 6: Summary of deposited sequence variant

More information regarding the variant, the gene involved, other patients with overlap at this position as well as the output from Ensembl VEP (including pathogenicity predictions with PolyPhen and SIFT) are available in the tabs below the sequence variant summary.

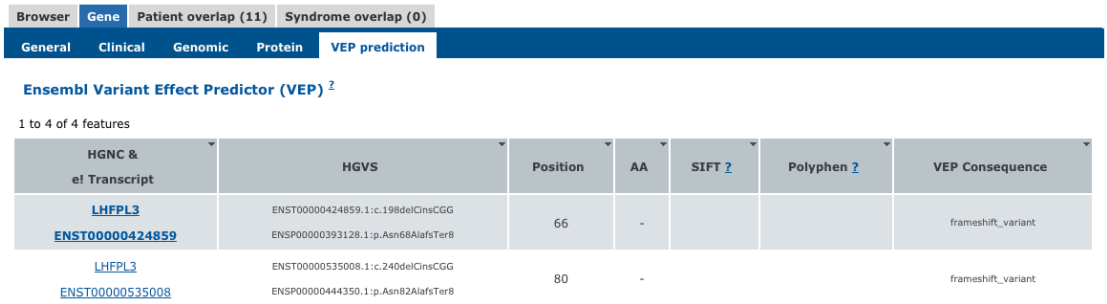


Figure 7: VEP predictions

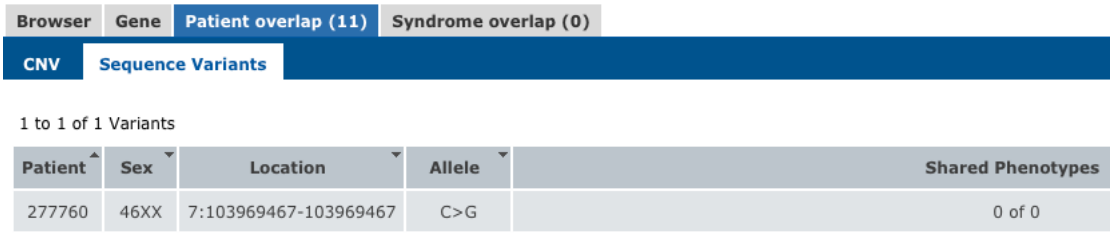
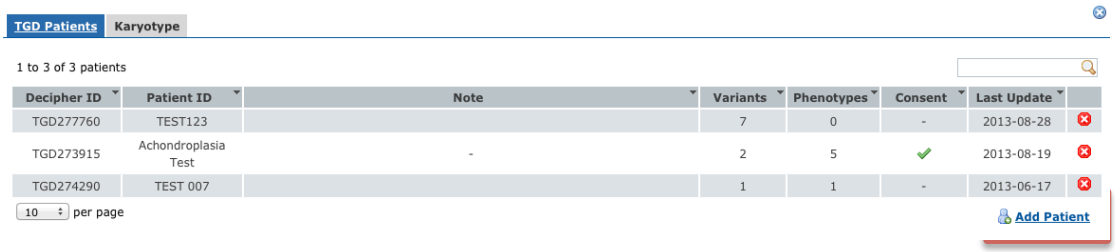


Figure 8: Overlapping patients (Sequence Variants)

Patient Creation

- Re-location of "Add Patient" link for the creation of new patient records. This link has been moved to the bottom right of the "My Patients" table to be consistent with "Add CNV" and "Add Sequence Variant" buttons in DECIPHER



- Patient Creation Form: There are two new mandatory fields in the patient creation form that require information regarding the parents of the patient being entered. We have deprecated the entry of parent information in DECIPHER as a separate patient (more information below). Instead this information is now collected across the patient creation, variant inheritance and mother/father phenotypes.

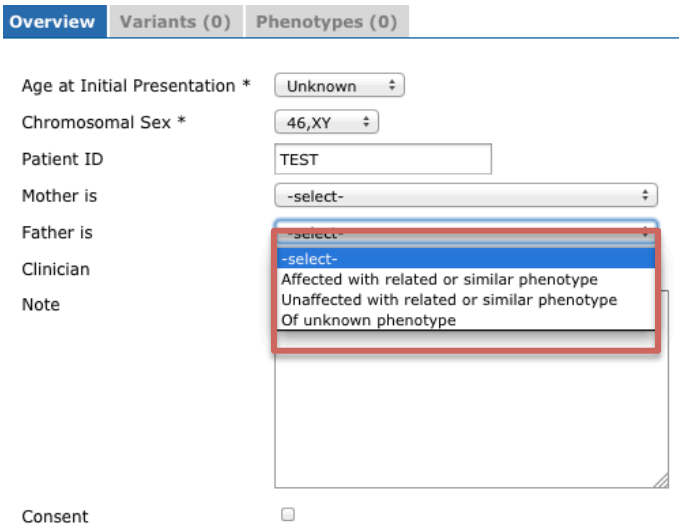


Figure 9: New items in patient creation form

Inheritance categories

We have modified the variant inheritance categories to make the entry of variant and phenotype inheritance more granular. Whether a parent is affected (has a phenotype similar to that of child), unaffected (normal) or Unknown (not known/not analysed) is collected on the patient summary pages. Inheritance of the variant is collected under new categories in the variant entry form.

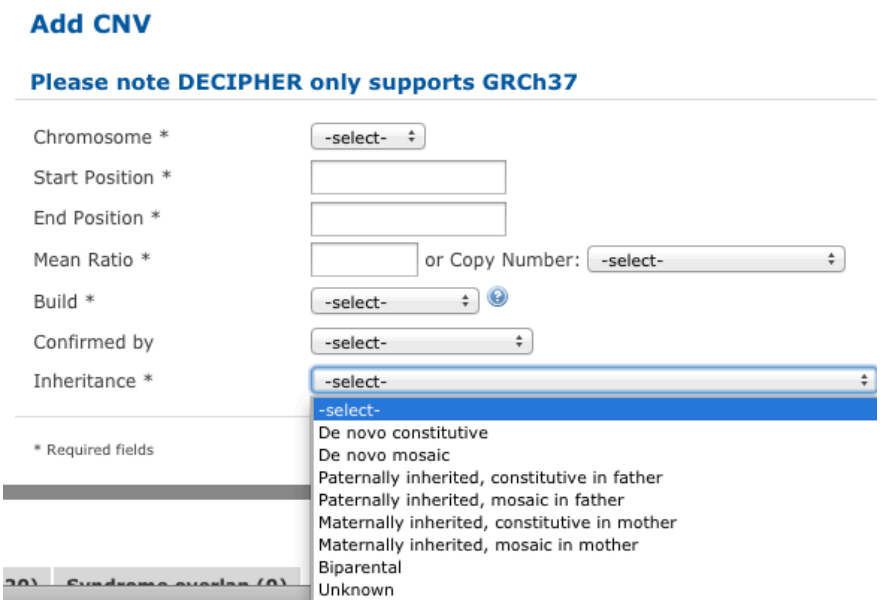


Figure 10: New inheritance categories

Legacy data will continue to have the values previously input, but any future edits for these data will require choosing between any of the newer options.

Parent Records

Earlier versions of DECIPHER did not permit the addition of parental shared phenotypes with the patient record thereby necessitating the upload of patient parent records as separate linked patient records. With the rollout of HPO drag-and-drop phenotyping in DECIPHER earlier this year, parent relevant or shared phenotypes may be entered in the same place as that of the patient. The present release now permits the entry of parent affected status with granular variant level inheritance thus making the parent records redundant in DECIPHER. We have therefore, deprecated all patient parent records in this release. Any data from the patient parent records has been merged within patient pages.

- Parent affected status is now merged in the patient overview page
- Any parent notes have been added under patient notes.
- Parent phenotypes have been added from existing parent data into patient phenotype section under parent phenotype sections.

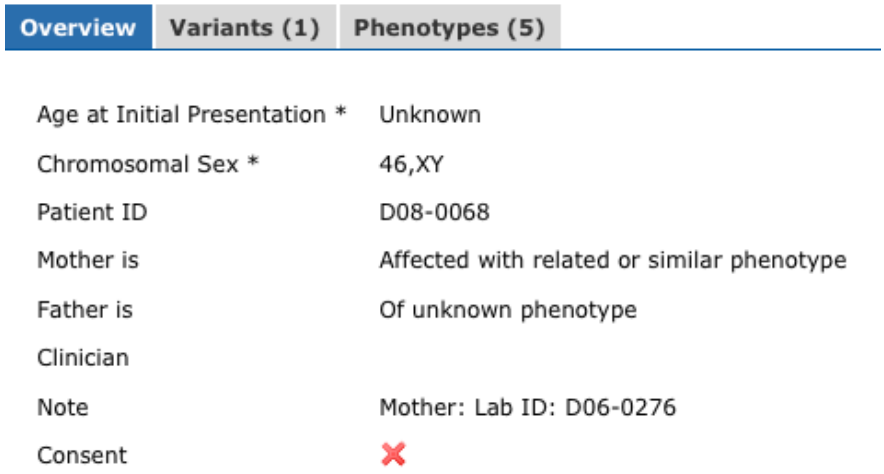


Figure 11: Parent affected status and notes for legacy data

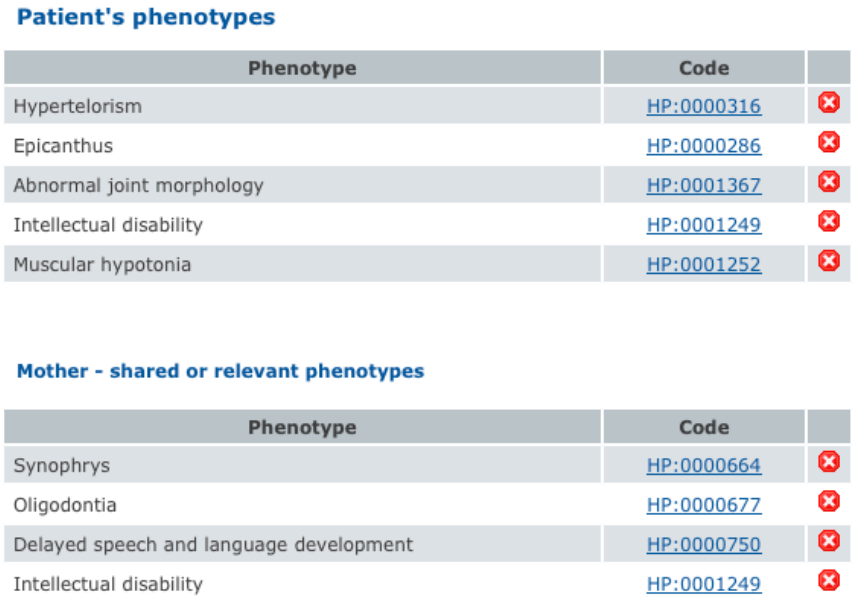
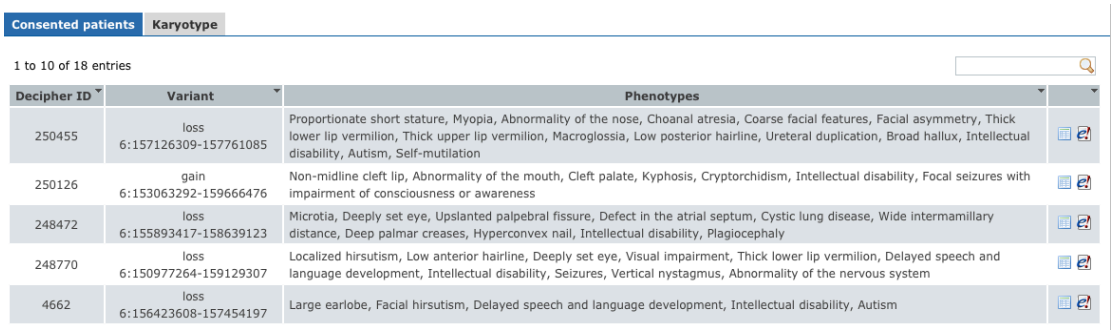


Figure12: Merged mother phenotypes with patient

Improved Search

We have improved DECIPHER search to include phenotypes for patients when queried by gene symbol, location or band. We believe this will make the identification of patients sharing similar genotype-phenotype easier to find and interpret. The new search also includes searches from deposited sequence variants.



Consented patients | Karyotype

1 to 10 of 18 entries

Decipher ID	Variant	Phenotypes	
250455	loss 6:157126309-157761085	Proportionate short stature, Myopia, Abnormality of the nose, Choanal atresia, Coarse facial features, Facial asymmetry, Thick lower lip vermilion, Thick upper lip vermilion, Macroglossia, Low posterior hairline, Ureteral duplication, Broad hallux, Intellectual disability, Autism, Self-mutilation	
250126	gain 6:153063292-159666476	Non-midline cleft lip, Abnormality of the mouth, Cleft palate, Kyphosis, Cryptorchidism, Intellectual disability, Focal seizures with impairment of consciousness or awareness	
248472	loss 6:155893417-158639123	Microtia, Deeply set eye, Upslanted palpebral fissure, Defect in the atrial septum, Cystic lung disease, Wide intermamillary distance, Deep palmar creases, Hyperconvex nail, Intellectual disability, Plagiocephaly	
248770	loss 6:150977264-159129307	Localized hirsutism, Low anterior hairline, Deeply set eye, Visual impairment, Thick lower lip vermilion, Delayed speech and language development, Intellectual disability, Seizures, Vertical nystagmus, Abnormality of the nervous system	
4662	loss 6:156423608-157454197	Large earlobe, Facial hirsutism, Delayed speech and language development, Intellectual disability, Autism	

Figure 13: Search results for gene ARID1B

New Look

We have extended the default page width for all DECIPHER pages to account for improved screen resolution in modern displays. This also means that we may now be able to include more data on our tables than previous as well as provide a wider screen for our interactive genome browser. We have also changed the look-and-feel of DECIPHER to provide a cleaner, more open look to our pages.