

Data Flow Chart for the DECIPHER Database

DECIPHER – Private domain for individual genetics department

In this part of the project, DECIPHER is used exclusively as a clinical tool to aid in the interpretation of an investigation.

The data is held in a linked anonymised form within the closed, password protected domain of an individual clinical genetics department that is affiliated to DECIPHER as a submitting centre.

Data held here is only visible to nominated clinicians/genetic or research scientists within that centre who have legitimate access to the data and are logged into DECIPHER.

The patient's clinician arranges for a high resolution genomic analysis eg. Microarray/exome or whole genome analysis as part of routine clinical investigation or an REC approved research study. A genomic variant (copy number or sequence change) is identified. Without analysis via DECIPHER the significance of this finding may be unknown. As part of routine clinical data management within the closed domain of an individual clinical genetics department, linked anonymised data is entered into the closed, password protected DECIPHER domain for that department in order to determine:

- (i) The genomic location of the variant
- (ii) The size of the deletion/duplication, or position of the sequence variant
- (iii) To generate a report for the laboratory record and to aid discussion of the genomic finding with the patient's clinical geneticist

The clinical or research scientist enters:

- (i) Clinical or laboratory reference number
- (ii) Whether the sample is from a patient with an abnormal phenotype or from a family member (eg. parent) with a normal phenotype
- (iii) Technical details about the genomic analysis eg. the type of array or sequencing used
- (iv) The genomic coordinates of the variant and whether it is a gain/loss (CNV) or the nucleotide change(s) (SNV)

The clinical geneticist enters:

- (i) Chromosomal sex eg. 46,XX / 46,XY / other
- (ii) Patient's age in years
- (iii) DECIPHER reference number for samples derived from the same family unit (eg. where parental samples have been analysed to determine whether a genomic variant is 'de novo' or inherited)
- (iv) The phenotype of the patient using restricted terms derived from the Human Phenotype Ontology

Using DECIPHER, the clinician is then able to:

- (i) Generate a report delineating the gene(s) affected by a genomic variant and see immediately if there are genes of known clinical significance eg. tumour suppressor genes in the region
- (ii) View the region of the genomic variant in a genome browser to see whether there are any known pathogenic or benign variants in the region or any patients known to DECIPHER with very similar genomic variants of the same region and if so, what their phenotype is and how this compares with the phenotype of their own patient. This is crucial for clinical interpretation and determining whether a variant of interest is likely to be a benign variant (e.g. polymorphism), or pathogenic and the likely cause of the patient's phenotype (ie. the correct diagnosis). At this stage the patient's own data remains secure within the password protected individual departmental domain

Using DECIPHER as a clinical tool in this way, the clinician is now equipped to counsel his/her patient about their result and its likely significance and implications. At this stage, the clinician invites the patient to consider allowing their data to be passed into DECIPHER-Ensembl view to:

- (i) Aid other clinicians in interpreting genomic data and advising their patients
- (ii) Help towards the delineation of new syndromes

Consent

If a clinical centre or research group has permission to share variants in a limited fashion to improve interpretation without explicit additional written consent, data may be shared with some or all centres in DECIPHER where it will only be visible to bona fide logged-in users of DECIPHER.

If additional written informed consent is given, the clinical geneticist or research nurse checks the 'Consent for view in Ensembl' box and a coloured bar becomes visible in Ensembl showing the location and nature of the genomic variant to which are attached the phenotype terms (eg. short stature, cleft-lip) and the DECIPHER ID code (eg. 0790045).

Clinicians registered with DECIPHER who are logged in would be able to identify the location of the submitting centre for a given patient. They could then contact the designated DECIPHER clinical contact in the submitting centre quoting the patient's DECIPHER ID code. The clinical contact could then obtain the laboratory reference number of their patient and identify them in their own clinical records. Clinicians could then seek to collaborate by exchanging more detailed data on individual consented patients for any ethically approved studies or consented publications. For example, the clinician could contact their patient to explain that a patient with a similar chromosomal finding has been identified in another centre and enquire whether the patient wishes their clinical information to be shared with the clinical team in the other centre eg. to produce a report defining a new microdeletion / microduplication syndrome.

Managed access

Linked-anonymised data held here is visible within the DECIPHER to some or all centres

DECIPHER/Ensembl view

Linked-anonymised data held here is visible within the Ensembl genome browser and other similar genome browsers and databases and can be accessed by users who elect to turn on the DECIPHER track. Only registered members will be able to identify the centre submitting the patient. To anyone else visiting the site, the visible data would be linked-anonymized with no global location.