Variant Effect Prediction Training Course

Johor (Malaysia), August 27-30, 2018

Human Phenotype Ontology (HPO)

There are several standards to describe, and store in databases, phenotypic characteristics of an individual (patient). The Human Phenotype Ontology (HPO) is a standard which recently gained a lot of traction and it is used by many databases.

The aim of this task is gaining experience in using the Human Phenotype Ontology (HPO) to describe phenotypes using tools/resources available on the internet. Experience will be gained by visiting a few sites and performing some simple tasks/queries. Note there are many more sites where similar information/tools can be found. Feel free to try others as well. Ultimately, use the one you like best, i.e. easiest to work with to get the results you need!

Our advise is to try;

- Ontobee HPO browser (http://www.ontobee.org/ontology/HP)
  Ontobee includes some other standards as well
- HPO website (http://human-phenotype-ontology.github.io/),
- Phenotips (http://phenotips.org/)

When you are new to HPO it might be good to first get a feeling about HPO and its structure. Using the resources mentioned, try to find the HPO description and code of some standard phenotypic characteristics. While working, note the tree-based structure of HPO with less detail above and more detail below.

When you have some experience, or want a more demanding task, please ask for a manuscript containing detailed phenotype descriptions, find the respective HPO codes and mail the result to the LOVD-team (LOVD@JohanDenDunnen.nl, lsdbs@lovd.nl). Your work will then be used to update the respective database records in the "Global Variome shared LOVD" (http://databases.lovd.nl/shared) with the detailed descriptions you generated.

For all **ToTry's** note that you can query the resource for anything you are interested in. The examples we give is just for those that lacking inspiration. We encourage participants to bring their own cases, get to HPO-based phenotype descriptions and submit them to e.g. the "Global Variome shared LOVD".

Beginners

ToTry: just take some phenotype descriptions you know/work with and see how specific they are or check how many descriptions are linked to term.

Browsing phenotype characteristics

1) go to Ontobee and using the "Keywords" query box try: big head
- what is the associated HPO term,?
- what the HPO code?
- check the class hierarchy, are there sub-classes?

2) now try: macrocephaly
- note you now immediately get the more detailed subclasses, how many?

3) try some other terms like "scoliosis", "intellectual disability"

4) try "abnormal nose" and "nose" and compare the results

- how many hits do you get with the query "nose"?

5) try some other general terms like "mouth" and "lip"/"lips"

6) go to the HPO website (http://compbio.charite.de/hpoweb/showterm?id=HP:0000118#id=HP_0000118), try the same queries and compare the results
- what do you notice?

Generating a HPO-based phenotype description

Alternative for 7) and 8)
ask for a manuscript containing phenotype descriptions. For features checked but not present use "no scoliosis (-HP:0002650)", for features which are not known use "loss ability to walk not known (?HP:0006957)" The disadvantage of this task is we cannot quickly give the "correct" answer, the advantage is you help us to improve the phenotype descriptions in the GV shared database.

7) an individual has coronal craniosynostosis (left and right), hypertelorism, a grooved nasal tip, down slanting palpebral fissures, a high arched palate, agenesis of the corpus callosum, a mild learning disability, Sprengel deformity, grooved nails, brachydactyly, syndactyly of the 2nd and 3rd left toes, low set ears, wiry hair, ptosis (left eye only), undescended testes (left and right), mild pectus excavatum, duplication of the distal phalanx of the right thumb, postaxial polydactyly and an inguinal hernia.
- what are the HPO codes for these features?

- can all features be described using HPO?

- can all features be described down to the detail you have?

8) go to the PhenoTips website, select the “Playground”, the “Create new patient”, select “None” for “Please select one of the available studies” and click “Select”. Enter the features described for the individual under 7). Save your result.

- which matching disorders (OMIM) does PhenoTips suggest?

- remove or add a few phenotypic features. Look at the list of matching disorders. More phenotypes do not necessarily narrow the possible diseases/genes. Playing around with the order of the HPO terms shows which terms are in favor for or against a specific disease. **NOTE:** the algorithm does not "exclude" a disease completely if one or more terms do not fit, it allows for some "false" HPOterms (the individual could also have two diseases).

- which matching Genes does PhenoTips suggest

- save the result, open the file (unfortunately the HPO codes are not given).
You can use the result to submit your data to a gene variant databases or to include in a manuscript.

9) go to the Phenomizer website (compbio.charite.de/phenomizer/) and try the same exercise.
The results are similar but different. There is no "gold standard" for prioritizing diseases/genes with HPO.

Andreas Laner & Johan den Dunnen, August 2018