Ontologies tutorial for MSc Genomics Medicine, Bioinformatics module

Finding and browsing ontologies and ontology relevant information

1) Open a browser and search for the BioPortal service that provides access to all sorts of biomedical ontologies; search for SNOMED CT and Human Phenotype Ontology (HPO) and answer the following questions:
    1) How many classes/concepts does the current version possess?

        SNOMED CT: 316013; HPO: no metrics available

    2) How happy are users with this ontology?

        SNOMED CT: users not happy with formality; HPO: no reviews available

    3) When was the latest version released?

        SNOMED CT: 06/09/2015; HPO: 13/01/2016

    4) Was there a peak period of downloads and if, when was it?

        SNOMED CT: May 2015; HPO: April 2015

    5) Which projects are actively using these ontologies?

        SNOMED CT: Kino, ICDMap, ARRS Goldminer, … ; HPO: Gemma, Neurocarta, SKELETOME, ...

    6) For SNOMED CT, find the concept "*Adrenal gland hematoma*"; what are the synonyms given for this concept and which ID does it possess? What are the parent classes/concepts (ancestors) of this concept?

        Syns: Adrenal gland hematoma (disorder), Adrenal gland haematoma; ID: 262832002; ancestors: Adrenal hemorrhage, Retroperitoneal hematoma, Adrenal mass

2) Now search for the Ontology Lookup Service (OLS) provided by European Bioinformatics Institute (make sure that you use the old version of the service); select HPO and choose the concept "*Adrenal insufficiency*"; answer the following question:
    1) How many direct children (descendants) exist for this concept?

    2) In what other resources does this concept exist?

    3) How many classes are in between this concept and the root term "*All*"? What does this tell us?

4 classes in between; it's not a high level term, so provides some more detail; but, at the same time, it's probably not very specific either

4) Did you see SNOMED CT on the list for selecting the ontology?

   No, OLS checks for OBO Foundry ontologies, which SNOMED doesn't belong to

3) Find the OBOFoundry web page; reading up on it, what do you think this is? What download formats for ontologies are provided? Can you see other services this one is referencing to? If so, which ones is it linking to?

   It's a union of Ontology Developers that try to ensure good quality of ontologies. They have defined a subset of criteria an ontology has to fulfil in order to be called a OboFoundry ontology. One can download a variety of ontologies in OBO and OWL format and it links to things like OntoBee, AberOwl, OLS, BioPortal.

Assigning annotations to patient data

1) Find the online tool PhenoTips; navigate to "*Learn more*". Reading through this information, what do you think the tool will provide you with? Where do you see the usefulness in this tool (please elaborate)? If it's available, have a look at the Playground and see whether you can confirm your findings. Also, have a look at http://monarch-initiative.blogspot.co.uk/2015/01/how-to-annotate-patients-phenotypic.html for more information on annotating patient data.

   Tool to elaborately annotate patients that can then also be shared with others; genotype as well as phenotype information; almost like an EHR, just with additional family tree of disorders ...

2) Can you find another tool online that would allow you to assign phenotype annotations?

   That's a bit hard. There's another tool called Phenote (http://www.bioontology.org/phenote) specific phenotypes. There's also PhenomeCentral, but this relies on PhenoTips.

3) Which HPO concepts would you choose to annotate the following text passage:

   "Angelman (1965) reported 3 'puppet children,' as he called them. Angelman (1965) emphasized the abnormal cranial shape and suggested that the depressed occiput may reflect a cerebellar abnormality. (Harry Angelman pronounces his name as though it means 'male angel;' in other words, he uses a 'long a' and a 'soft g.') Bower and Jeavons (1967) coined the name 'happy puppet' syndrome for the condition that they observed in 2 patients. Clinical features included severe motor and intellectual retardation, ataxia, hypotonia, epilepsy, absence of speech, and unusual facies characterized by a large mandible and open-mouthed expression revealing the tongue. The French refer to the syndrome as that of the 'marionette joyeuse' (Halal and Chagnon, 1976) or 'pantin hilare' (Pelc et al., 1976). Williams

and Frias (1982) suggested use of the eponym Angelman syndrome because the term 'happy puppet' may appear derisive and even derogatory to the patient's family. ”

HP:0001251 Ataxia

HP:0011344 Severe global developmental delay

HP:0011398 Central hypotonia

HP:0001250 Epilepsy

HP:0001344 Absent speech

HP:0000303 Large mandible

HP:0002648 Abnormality of calvarial morphology

HP:0011217 Abnormal shape of occiput

HP:0000194 Open mouth

Using patient annotations for browsing and associations

1) Navigate to the DECIPHER database provided by the Wellcome Trust Sanger Institute; search for all patients with “*Microcephaly*”
    1) How many patients are in DECIPHER with this phenotype?

        1183 including descendant terms; 1053 with this exact phenotype

    2) How many syndromes are relevant for this phenotype?

        11

    3) How many variants have been associated with this phenotype based on the DDD project?

        0

    4) Pick patient with ID 610: How many other phenotypes have been assigned? What do we know about the genotype of this patient? What do we know about the parents of this patient? If you were interested in learning more about this patient, what could you do?

        Another 4 phenotypes; nothing known of parents, they either don't show phenotype or haven't been investigated

    5) Go back to the overview and select syndromes; choose “*Cri du Chat Syndrome*”: What is know about the genetic basis of this syndrome? How many different phenotypes are assigned to this particular syndrome? Judging from your own expertise or reading up on the Online Mendelian in Man (OMIM) database, do

you think that the provided phenotypes are sufficient to characterise this syndrome in all its detail?

3 phenotypes; no, not sufficient detail in phenotype annotations from DECIPHER (project relies on people entering this information which is usually limited by their time …)

2) Find the OrphaNet database for rare diseases; search for some diseases you may know and take a look. Then go to "*Search by sign*" and select "*Microcephaly*" and "Strabismus squint" from the Thesaurus as mandatory signs. Select "*Angelman syndrome*" from the list and have a look at the "*Clinical Signs*" section. Do you find this more or less informative as the respective section on OMIM? If so, why?

   While OMIM has more detailed listings, the occurrence probabilities are hidden within the text. So OrphaNet offers in addition to the clinical signs, an occurrence weight for each of the phenotypes (occasional, frequent, very frequent), which may help in diagnosis process to determine the importance of a patient characteristic you are looking at.