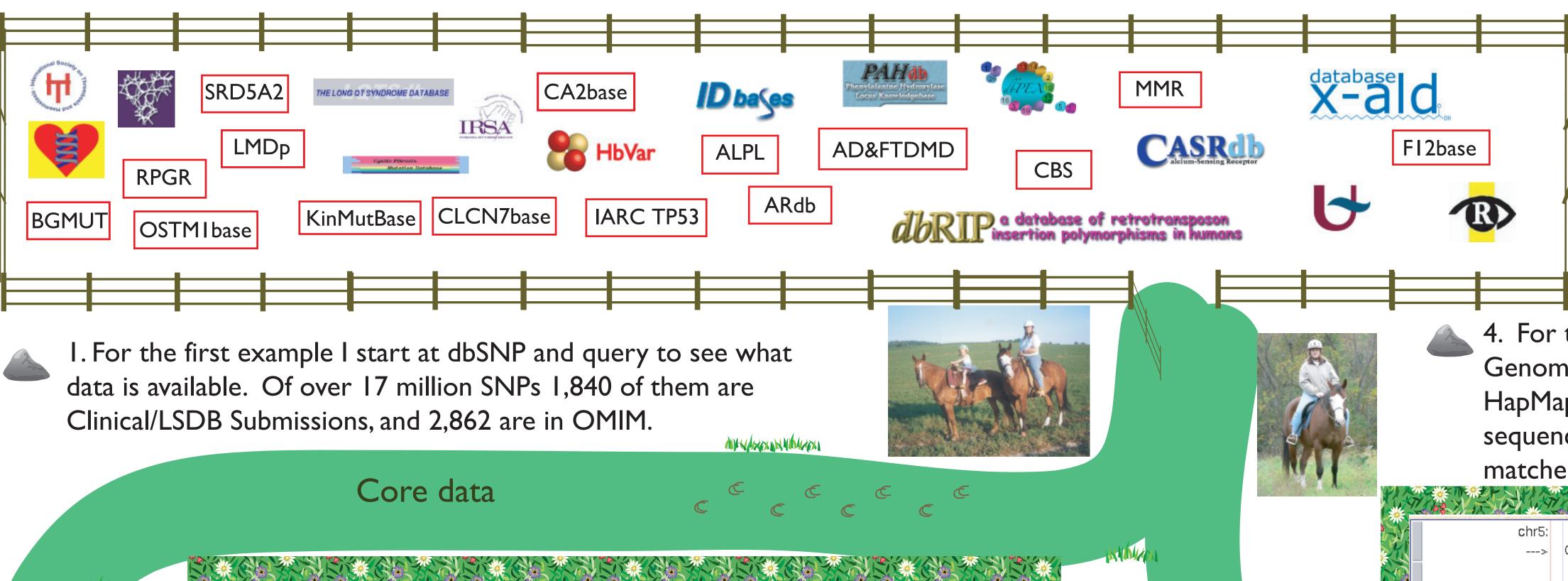
# Two Paths from LSDBs: Core versus Deeper Data

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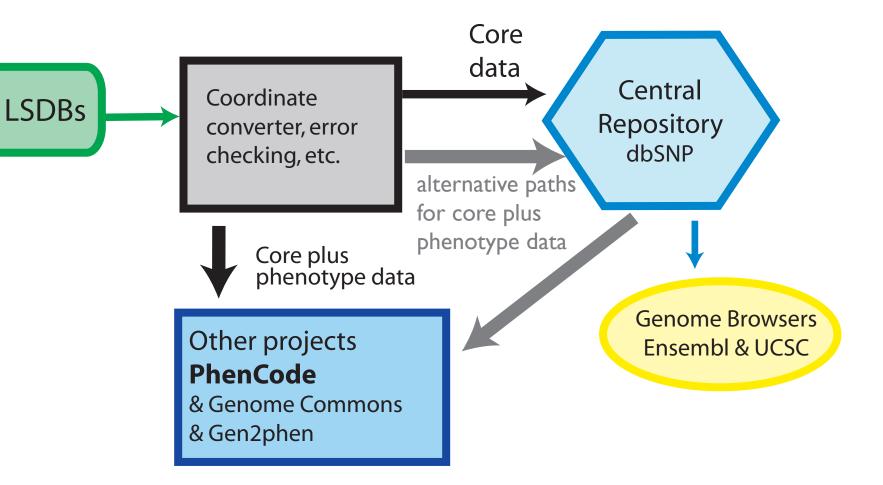
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phencode.bx.psu.edu

Data Sources



## Data flow



187284465

D. A.M. (DA)

4. For the second example I browse personal genomes in the UCSC Genome Test Browser. The mutant form of this variant is found in the YRI HapMap population, Dr. James Watson, and the reference chromosome sequence. The LSDB uses a different reference where the wildtype matches the other species shown in the multiple alignment.

137234460



#### .0006 FRIEDREICH ATAXIA [FXN, MET1ILE] dbSNP

In 3 independent families, Zuhlke et al. (1998) found that affected individuals with Friedreich ataxia (229300) were compound heterozygotes for the repeat expansion (606829.0001) and an ATG-to-ATT (met1-to-ile; M1I) mutation of the start codon of the FXN gene. Haplotype analysis using 6 polymorphic chromosome 9 markers showed complete identity of haplotype in 2 of the 3 chromosomes with the point mutation; the third case showed partial conformity and may represent a single recombination event. A common ancestor was suspected. An M1I start codon mutation has been described in the HBB gene (141900.0430) as the cause of beta-0-thalassemia, in the OAT gene (258870.0001) as the cause of gyrate atrophy, in the PAH gene (261600.0048) as the cause of phenylketonuria, and in the PLP gene (312080.0015) as the cause of Pelizaeus-Merzbacher disease, but in all of these instances the nucleotide change represented an ATG-to-ATA transition.

2. Following hyperlinks to OMIM, we learn that this variant alters the translation start codon. Mutations of the start codon are associated with pathology in other genes.



### Deeper data

137234455



5. To find out whether this variant is associated with a pathology, I followed the hyperlinks to the source LSDB, LMDp. Here we learn that the pathogenicity of this variant is unknown.

HANK

3. How often are translation start codons mutated in disease-associated alleles? By querying at PhenCode I found several additional examples.

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#### Result links

X64594.1(RHAG):c.3G>T CFTR:c.3G>A CFTR:c.3G>T U78027.1:g.46199G>T D0067:g.3276G>A PAH c.3G>A GC1:c.3G>A GC1:c.3G>C ABCD1:c.3G>A HBB:c.3G>A HBB:c.3G>C HBB:c.3G>T HBA2:c.231G>A HBA2:c.99G>A EMD:c.3G>A FKRP:c.3G>T

Query form | Query history

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# Query history 1. LSDB variants and attribute like (M1I, Met1Ile) (11 variants) 2. LSDB variants and attribute like (M1I, Met1Ile, Met>Ile) (16 variants) 3. LSDB variants and name like c.1A or c.2T or c.3G (57 variants)

Database Leiden Muscular Dystrophy pages Myotilin (Titin immunoglobulin domain) (MYOT)

Variants X Submitters X Submit X Documentation

View unique variants Search unique variants View all contents Full database search Variant listing based on patient origin Switch gene

### LOVD - Variant listings

#### 2 public entries 100 entries per page Path. S Exon S DNA change

	Path. 😣 📿	Exon 🕸 📿	DNA change	<u>Protein</u> ⊗⊘ ,	DNA remark	Reference 80	Origin 80	1.	Detection/
e-			c.220C>A					<u> </u>	
	?/?	02	c.220C>A + DES (1)	p.(Gln74Lys)	-	<u>Bar 2007</u>	sporadic		DNA
	+/?	02	c.220C>A	p.(Gln74Lys)	not in 200 control chomosomes	Olive 2005	sporadic		DNA

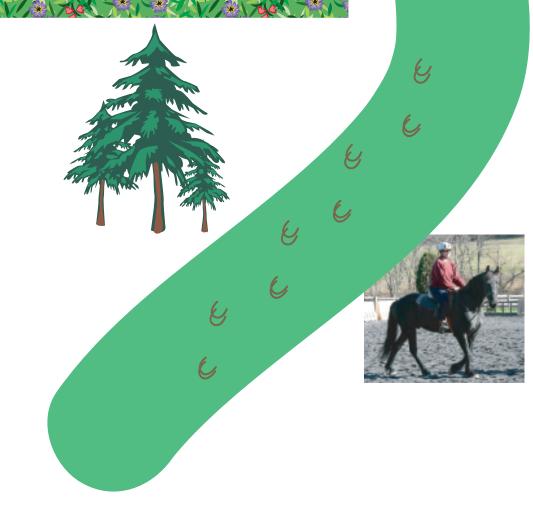
#### Legend: [ MYOT full legend ]

1 - 2

Sequence variations are described basically as recommended by the Ad-Hoc Committee for Mutation Nomenclature (AHCMN), with the recently suggested additions (den Dunnen JT and Antonarakis SE [2000], Hun **Path.**: Variant pathogenicity, in the format Reported/Concluded; '+' indicating the variant is pathogenic, '+?' probably pathogenic, '-' no known pathogenicity, '-?' probably no pathogenicity, '?' effect unknown. **Exe** Variation at protein level. **MYOT DB-ID**: <u>Database IDentifier</u>; When available, links to OMIM ID's are provided. **DNA remark:** DNA remark **DNA\_reported:** DNA\_reported **Reference:** Reference **Origin:** Origin **F Disease:** Disease phenotype, as reported in paper/by submitter, unless modified by the curator. **Reference:** Reference describing the variation, "Submitted:" indicating that the mutation was submitted directly to t

While the core data is useful the deeper data is also needed in a central location to make full use of the data.

The LSDBs are also useful for providing information that is specific to the locus and more specialized query access.



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