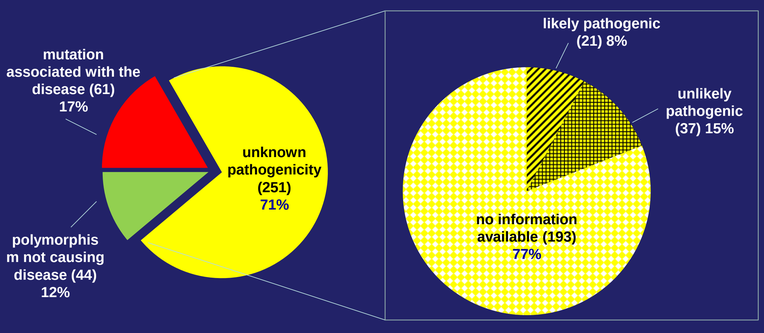
Creation of a locus-specific database (LSDB) for *AIP* mutations

F Begum[1,2], G Trivellin[2], P Gabrovska[2], K Wertheim-Tysarowska[3], M Jones[4], K Stals[5], S Ellard[5], S Radian[2], M Korbonits[2]

[1]King's College London, UK; [2]Department of Endocrinology, Queen Mary University of London, UK; [3]Department of Medical Genetics, Institute of Mother and Child, Poland; [4]University of Bristol, UK; [5]Department of Molecular Genetics, Royal Devon and Exeter Foundation Trust, UK

Introduction: Locus-specific databases (LSDBs) have been recently developed in response to the increasing number of sequence variations reported in the human genome and the consequent necessity to establish their clinical significance. Several genes causing endocrine syndromes have LSDBs available (e.g. *MEN1*, *VHL*, *RET*, *GNAS, PRKAR1A*, the *SDH* subunits). Germline mutations in the *AIP* gene are found in about 20% of familial isolated pituitary adenoma (FIPA) patients. The majority of these variants are of unknown pathogenicity.

Aim: To create a LSDB for *AIP* by collecting all available variants found worldwide in FIPA patients accompanied by their clinical information.



- The human *AIP* gene is located at 11q13, consists of 6 exons and encodes a 330 amino acid cytoplasmic co-chaperone protein
- 356 variants identified until March 2013 in *AIP*

Methods:

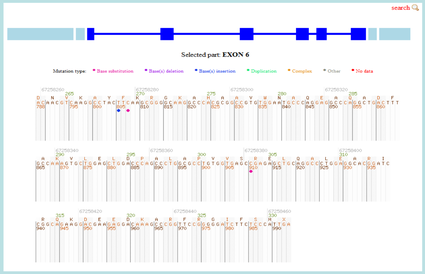
A free-to-use *AIP*-LSDB was created and registered in Orphanet, the reference portal for rare diseases

AIP variants are named according to LRG_460, a standard reference sequence generated in collaboration with the NCBI and EBI, following HGVS recommendation

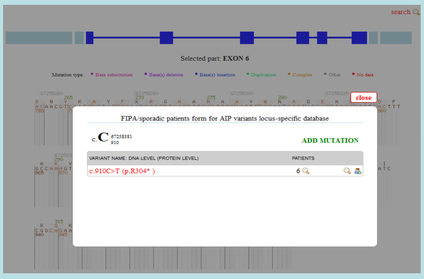
Variants submission by other centres is allowed after free registration via a provided clinical description form

*LRG= locus reference genomic, HGVS= Human Genome Variation Society

Results:



The core of the database is a graphic view of the *AIP* gene structure divided in exons and introns



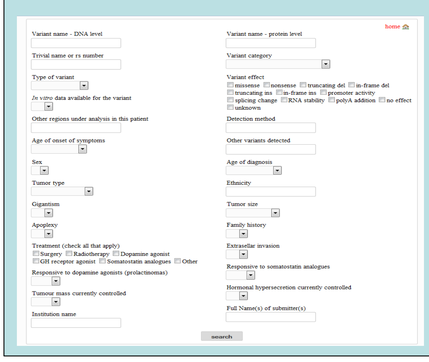
Clicking on each dot enables to see all the genetic and clinical details available for that variant

c.910C>T (p.R304*): Patient #4

Other patients with this mutation: Patient #5 Patient #6 Patient #7 Patient #8 Patient #9

Variant name (according to HGVS guidelines) - DNA level	c.910C>T
If YES please specify (check all that apply)	no data
Variant name (according to HGVS guidelines) - protein level	p.R304*
If other family members are affected please provide a unique family identifier	FA2
Trivial name and/or rs number	AM236344
Variant category	mutation associated with disease
Type of variant	Base substitution
Variant effect	nonsense
In vitro data available for the variant	Yes
Age of onset of symptoms	no data
Age of diagnosis	19-30
Sex	M
Ethnicity	UK
Tumor type	GH-secreting
Tumor size	micro Φ < 1cm
Gigantism	Yes
Family history	Yes
Apoplexy	No
Extracellular invasion	no data
Treatment (check all that apply)	Surgery
Responsive to somatostatin analogues	N/A
Responsive to dopamine agonists (prolactinomas)	N/A
Hormonal hypersecretion currently controlled	No
Tumour mass currently controlled	no data
Institution name	Barts and the London Medical Schoo
Country	UK
Telephone	+442078826238
Fax	+442078826197
E-mail adress	m.korbonits@qmul.ac.uk

The database allows for the addition of data from patients with the same variant



Search module: The database allows individuals to search the data using numerous variables

A flexible data selection tool for statistical analysis will be implemented, but users can also download all data in a CSV format for further statistical analyses

Summary: This database will aid easier interpretation of variants in *AIP* mutated patients for both clinicians, who are better able to provide genetic counselling and reduce unnecessary testing, and researchers in examining the structure-function and genotype-phenotype correlations.

Database available soon at http://aip.fipapatients.org/

Correspondence: m.korbonits@qmul.ac.uk