Supplementary Data for Wilson Disease Example Use Case

Step 1: Search for proteins associated with Wilson disease

Here the *Variation* service was used to find any protein that is associated with Wilson disease and any associated variants. Figure 1 (a and b) shows the Swagger User Interface (UI) for the *Variation* service with Wilson disease added to the disease search field. Figure 1b illustrates the results after execution of the search in the response body, with a Curl command defined that is also available in Figure 2 with Figure 3 defining a Python script to execute this search.

	variation		Show/Hide List O	perations	Expand Operations
	GET /variation			get var	riation by search
	Implementation Notes with query feature type a	nd query terms			
Protoine	successful operation	~/			
Protoins ins. issforms	Model Example Value				
Froteris Inc. Isolomis	"alterna	tiveSequence": "string",			
Features	"begin":	"string", string".			
Variation	"xrefs":	[
Proteomics	(e", "string",			
Antigen	"id"	: "string",			
roteomes	From 3	t. tasalaat			
faxonomy	Response Content Type	pplication/json \$			
Coordinates	Parameters				
	Parameter	Value	Description	Parameter Type	Data Type
	sourcetype		Filter for variants from a specific sourceType. Options include: uniprot, large_scale_study and mixed, or individual data source such as exac, cosmic curated, esp, 1000genomes.	query	string
	consequencetype		Filter for variants with a specific consequenceType. Options include: missense, stop gained or stop lost	query	string
	wildtype		Search by specific wildType amino acid. Options: Any single letter amino acid and * for stop codon.	query	string
	alternativesequenc	e	Filter by specific alternativeSequence amino acid. Options: Any single letter amino acid and * for stopcodon and - for deletions.	query	string
	location		Filter by amino acid position in the sequence(s). Options: any valid amino acid position within the length of the protein sequence	query	string
	accession		search for accession, can be a list separated by ','	query	string

Figure 1a: Variation service Swagger UI top.

	dicesce		Occurs for a single sta	011001		
	0126926	Wilson disease	by disease name or acronym. For example: alzheimer disease 1 or AD1. Partial names allowed.	query	string	
teins oteins inc. isoforms	omim		Search for variants by MIM identifier. For example: 104300	query	string	
ariation roteomics	evidence		Search for variants by PubMed identifier. For example: 22472873	query	string	
itigen leomes	taxid		Organism taxonomy id	query	string	
nomy	offset	0	Off set, page starting point	query	integer	
	size	100	Page size	query	integer	
	Request URL https://www.phi.ac.uk/proteins/ani/wariation2disease.Wileon&20disease6offect=06siya=100					
	Response Body	uk/proteins/api/variationroisea	SC=#1(500420015085	eauriset	-605126=100	
	<pre>{</pre>	P35670°, NTF78_EUHAN", LISKLEITPRAHEPANEKSFAFDINYOYEGU ULSKLEITPOPILOPEDLENYINDHIFEALIKS GANIFKOVINIETEN IOGLIOVISIOHEIALIKS GANIFKOVISIOTEILIAIAMIKTELLIKS SERGETPRIOVIGOTEILIAIAMIKTELIAIPPULOISE SERGETPRIOVISIOTEILIAIAMIKTELIAIPPULOISE SERGETPRIOVISIONIAINII POLSILAIPPULOISE PSEIPROSVIDINII IOLSILAIPPULOISE SERGETPRIOVISIONII IDLIAIPPULOISE SERGETPRIOVISIONII IDLIAIPPULOISE	DGLOPSSQVATSTVRILG ASHPSRSLPAQEAVVKLR KVAPLSLGPIDIERLQGT KTAQVKYDPSCTSPVALQ EINIEGLEXOTSPVALU EINIEGLEXAVNED EINFIGLEXAVNED EIGFIALAQRIFYAMH VOLLOGHYFYVQAYKSL	MTCQSCVKS VEGMTCQSC NPKRPLSSA RAIEALPPO AEGTATVLY XSPQSTRAV YAGSDGNIE LDHKMEIKQ RERSANMDV VVTLGEDNI	LIEDRIS VSSIEG NONFNN NFFVSL NPSVIS VAPQKCF LLITOM MKKSFL LIVLAT JIKEEQ	
	Response Code					
	200					
	Response Headers					
	<pre>{ "x-pagination-tot "link": "<http: <htt="" chttp:="" disease="wilson+diseaseaseaseaseaseaseaseaseaseaseaseaseas</td" rel='\"first\",' www.ebi.ac.=""><td>alrecords": "1", www.ebi.ac.uk/proteins/api/vari ase&offset=@&size=100>; rel=\"s uk/proteins/api/variation?disea pi//www.ebi.ac.uk/proteins/api/ ase&offset=@&size=100>; rel=\"l</td><td>ation? elf\", ss=Wilson+disease& variation? ast\"",</td><td>offset=0</td><td>Ssize=100>;</td></http:></pre>	alrecords": "1", www.ebi.ac.uk/proteins/api/vari ase&offset=@&size=100>; rel=\"s uk/proteins/api/variation?disea pi//www.ebi.ac.uk/proteins/api/ ase&offset=@&size=100>; rel=\"l	ation? elf\", ss=Wilson+disease& variation? ast\"",	offset=0	Ssize=100>;	

Figure 1b: *Variation* service Swagger UI bottom with Wilson disease added to the disease search field. The search has already been executed by clicking on 'Try Out' and the results of the search are available in JSON in the 'Response Body'.

```
curl -X GET --header 'Accept:application/json'
'https://www.ebi.ac.uk/proteins/api/variation?disease=Wilson%20di
sease&offset=0&size=100'
```

Figure 2: Curl command to execute the search for proteins and variants annotated with being associated to Wilson disease. Pagination has been set but as can be seen in Figure 1b this search only returns a single page.

```
import requests, sys
requestURL =
"https://www.ebi.ac.uk/proteins/api/variation?disease=Wilson%20di
sease&offset=0&size=100"
r = requests.get(requestURL, headers={ "Accept" :
"application/json"})
if not r.ok:
   r.raise_for_status()
   sys.exit()
responseBody = r.text
print(responseBody)
```

Figure 3: Python script equivalent to the curl command in Figure 2 for executing the search for proteins and variants annotated with being associated to Wilson disease. Pagination has been set but as can be seen in Figure 1b this search only returns a single page.

Step 2: Searching for positional annotations 'Features' in P35670 that could be affected by Wilson disease associated variants.

The *Features* service was used to find any positional annotations in the region of the Wilson disease associated variant. Figure 4 shows the Swagger UI for the *Features* service with protein accession P35670 added to the accession search field. Figure 5 illustrates the results after execution of the search in the response body, with a Curl command defined that is also available in Figure 6 with Figure 7 defining a Python script to execute this search. An active site feature is annotated at aspartic acid 1027 is coincides with a Wilson disease associated variant p.Asp1027His (COSM307382), Figure 8.

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rsion": "string", ression": "string", tryName": "string", quenceChecksum": "string", teGeneId": "string", ontent Type application/json \$			
r Value	Description	Parameter	Data Type
00 005570	UniProt accession	Type path	string
P33670		-	
	MOLECULE_PROCESSING, TOPOLOGY, SEQUENCE_INFORMATION, STRUCTURAL, DOMAINS_AND_SITES, PTM, VARIANT, MUTAGENESIS; separated by ','	4	,
Provide multiple values in new lines.	filtering by specified a list of feature types: INIT_MET, SIGNAL, PROPEP, TRANSIT, CHAIN, PEPTIDE, TOPO_DOM, TRANSMEM, DOMAIN, REPEAT, CA_BIND, ZN_FING, DNA_BIND, NP_BIND, REGION, COILED, MOTIF, COMPBIAS, ACT_SITE, METAL, BINDING, SITE, NON_STD, MOD_RES, LIPID, CARBOHYD, DISULFID, CROSSLNK, VAR_SEQ, VARIANT, MUTAGEN, UNSURE, CONFLICT, NON_CONS, NON_TER, HELIX, TURN, STRAND, INTRAMEM; separated by ','	query	Array(string)
	prenceChecksum": "string", reGeneId": "string", ontent Type (application/json \$) Value P35670 ies Provide multiple values in new lines. Provide multiple values in new lines.	puenceChecksum": "string", .eGeneId": "string", Image: string application/json () Image: string application/json ()	pueneeChecksum": "string", eeGeneId": "string", intent Type (application/json ¢) intent (application/json ¢)

Figure 4: *Features* service search by accession. Here we are searching for all positional annotations available for the protein P35670 but it is possible to use the optional search fields to restrict to specific types of 'features'.



Figure 5: Results from the search for 'features' in P35670.

curl -X GET --header 'Accept:application/json' 'https://www.ebi.ac.uk/proteins/api/features/P35670'

Figure 6: Curl command to execute the search for protein features dynamically generated by the Swagger UI as illustrated in Figure 5.

```
import requests, sys
requestURL =
"https://www.ebi.ac.uk/proteins/api/features/P35670"
r = requests.get(requestURL, headers={ "Accept" :
"application/json"})
if not r.ok:
   r.raise_for_status()
   sys.exit()
responseBody = r.text
print(responseBody)
```

Figure 7: Python script equivalent to the curl command in Figure 6 for executing the search for proteins features in P35670.

type': "VARIANT",
"description": "[LSS_COSMIC]: primary tissue(s): kidney",
"alternativeSequence": "H",
"begin": "1027",
"end": "1027",
"xrefs": [
"name": "cosmic curated",
"id": "COSM3073B2",
"url": "http://cancer.sanger.ac.uk/cosmic/mutation/overview?id=307382"
}
"evidences": [
{
"code": "EC0:0000313",
"source": {
"name": "cosmic_study",
"id": "COSU:410",
"url": "http://cancer.sanger.ac.uk/cosmic/study/overview?study_id=410"
}
},
{
"code": "EC0:0000313",
"source": {
"name": "PubMed",
": J" . "00000010"

Figure 8: Identification of a variant at residue 1027 that is associated to Wilson disease and a COSMIC cancer associated variant from the large scale study variant data sets. Aspartic acid 1027 has been annotated as the active site residue.

Step 3: Proteomics Search for unique peptides around residue aspartic acid 1027 in P35670.

The *Proteomics* service was used to find any unique peptides in the region of residue Aspartic acid 1027. Figure 9 shows the Swagger UI for the *Proteomics* service with protein accession P35670 added to the accession search field. Figure 10 illustrates the results after execution of the search in the response body, with a Curl command defined that is also available in Figure 11 with Figure 12 defining a Python script to execute this search. Table 1 summarises the seven unique peptides found upstream of the active site at aspartic acid 1027.

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/ith query feature	type and query terms				
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t {	<pre>: "string", a": "string", s": "string", ta": "string", td": "string", sinId": "string", o, ": [": "string", ": "string", ": "string", ": "string", ": "string", ": "string",</pre>				
Parameter	Value	Description	Parameter Type	Data Type	
offset	0	Off set, page starting point, with default value 0	query	integer	
size	100	Page size with default value 10 When page size is -1, it returns records and offset will be ignore), query all id	integer	
accession	P35670	Search for accession, can be a separated by ','	list query	string	
Laxio		Organism taxonomy id	query	string	

Figure 9: *Proteomics* service Swagger UI with 'P35670' entered in to the accession search field.

accession	P35670	Search for accession, can be a list separated by ','	query	string				
taxid		Organism taxonomy id	query	string				
upid		UniProt proteome Id: UP[0- 9]{9}	query	string				
datasource		Proteomics data source, can be list, separated by ','	query	string				
peptide		Proteomics peptide	query	string				
unique	If unique, a peptide is query string mapped to one gene group only. Value can only be true or false.							
Response Messag Try it cut: Hide Request Sample Co Curl Perl Python	Response Messages Show Response Try it out Request Sample Code							
curl -X GET	header 'Accept:application/json' 'http: e=100&accession=035670'	s://www.ebi.ac.uk/protein	s/api/proteom:	ics?				
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Figure 10: Results from executing the search for peptides.

```
curl -X GET --header 'Accept:application/json'
'https://www.ebi.ac.uk/proteins/api/proteomics?offset=0&size=100&accessi
on=P35670'
```

Figure 11: Curl command to execute the search for proteomics peptides dynamically generated by the Swagger UI as illustrated in Figure 10.

```
import requests, sys
requestURL =
"https://www.ebi.ac.uk/proteins/api/proteomics?offset=0&size=100&accessi
on=P35670"
r = requests.get(requestURL, headers={ "Accept" : "application/json"})
if not r.ok:
   r.raise_for_status()
   sys.exit()
responseBody = r.text
print(responseBody)
```

Figure 12: Python script equivalent to the curl command in Figure 11 for executing the search for proteins features in P35670.

Peptide position	LSS proteomics	Peptide sequence
in P35670	sources	
1042 - 1054	MaxQB,	VLLLGDVATLPLR
	PeptideAtlas	
1042 - 1055	MaxQB,	VLLLGDVATLPLRK
	PeptideAtlas	
1056 - 1077	MaxQB,	VLAVVGTAEASSEHPLGVAVTK
	PeptideAtlas	
1106 - 1137	PeptideAtlas	VSNVEGILAHSERPLSAPASHLNEAGSLPAEK
1229 - 1238	MaxQB,	AIATQVGINK
	PeptideAtlas	
1302 - 1315	MaxQB	NDLLDVVASIHLSK
1416 - 1440	PeptideAtlas	ATPWDQVSYVSQVSLSSLTSDKPSR

Table 1: Unique peptides upstream of active site at residue 1027. Sources for the experimental evidence of the peptide are from either MaxQB or PeptideAtlas.

Step 4: Searching for ATP7B orthologues

The *Proteins* service was used to find any orthologues of human APT7B by searching by gene name. Figure 13 shows the Swagger UI for the *Proteins* service with gene name ATP7B added to the gene search field. Figure 14 illustrates the results after execution of the search in the response body, with a Curl command defined that is also available in Figure 15 with Figure 16 defining a Python script to execute this search. Figure 17 summarises the sequence identity of 83.59% between the two protein sequences when aligned by Clustal Omega. The full sequence alignment of the two protein sequences is shown in Figure 18.

```
curl -X GET --header 'Accept:application/xml'
'https://www.ebi.ac.uk/proteins/api/proteins?offset=0
&size=-1&gene=Atp7b'
```

Figure 15: Curl command to execute the search for protein orthologues dynamically generated by the Swagger UI as illustrated in Figure 16. Here due to the large amount of data returned the pagination has been 'switch-off' using the size=-1 option. Users are recommended to use the pagination option in their scripts.

```
import requests, sys
```

```
requestURL =
"https://www.ebi.ac.uk/proteins/api/proteins?offset=0
&size=-1&gene=Atp7b"
```

```
r = requests.get(requestURL, headers={ "Accept" :
"application/xml"})
```

```
if not r.ok:
    r.raise_for_status()
    sys.exit()
```

responseBody = r.text
print(responseBody)

Figure 16: Dynamically generated python script for searching for proteins from the ATP7B gene across all species. Note that in this example pagination has been switched off so all the results can be returned in a single response (size=-1). Users are recommended to use the pagination option in their scripts.

Proteins

The proteins service provides an interface for accessing UniProtKB(?) entries and UniProtKB(?) isoform entries. The features service provides protein functional annotations from UniProt Knowledgebase (UniProtKB) protein entries. The variation, proteomics and antigen services provide annotations imported and mapped from Large Scale data Sources (LSS) such as 1000Genomes, ExAC, PeptideAtlas, MaxQB and HPA along with UniProtKB annotations for these feature types (if applicable).

The Proteins service returns XML, JSON and FASTA formatted results. Features, variation, proteomics and antigen all return XML, JSON and GFF formatted results.

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/proteins				get list of UniPro	t entri
plementation I	Notes				
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xmlns:xs	i="http://www.w3.org/2001/	XMLSchema-instance"			
xsi:sche	maLocation="http://uniprot	.org/uniprot			
xmlns="http://w	w.uniprot.org/support/doc ttp://uniprot.org/uniprot"	<pre>version="108" modifie</pre>	d="2016-05-	11"	
created=	2006-03-07" dataset="Swis	s-Prot"> <accession>Q98</accession>	XB0-3 <td>ssion></td> <td></td>	ssion>	
<name>MX</name>	<pre>S1=3_HUMAN<protein></protein></pre>	<recommendedname><full< td=""><td>Name>Isofor</td><td>m 3 of Meckel</td><td></td></full<></recommendedname>	Name>Isofor	m 3 of Meckel	
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Parameter	Value	Description	Type	Data Type	
offset	0	Off set, page starting	query	integer	
		value 0			
cizo		Deer size with	au 0.00		
5126	-1	default value 100.	query	integer	
		When page size is -1. it returns all			
		records and offset			
		will be ignored			
accession		search for accession	query	string	
		can be a list separated by '.'			
reviewed		Reviewed(true) or not Reviewed (falce)	query	string	
		not neviewed (laise)			
isoform		0 for exclude	query	integer	
		only and 2 for both	1		
		canonical and			
		auronti.			
goterms		GO ontology terms	query	string	
keywords		keyworde	query	string	
		Neywords	danth	samg	
ec		UniProt EC number	query	string	
		11-10-1			
gene	Atp7b	UniProt gene name	query	scring	

Figure 13: *Proteins* service Swagger UI with 'ATP7B' entered in to the gene search field. Note that the search is case insensitive.

ec		UniProt EC number	query	string
gene	Atp7b	UniProt gene name	query	string
protein		UniProt protein name	query	string
organism		Organism name	query	string
taxid		Organism taxonomy id	query	string
pubmed		UniProt reference pubmed id	query	string
Baspansa Mar	Chow Persona			
Try it out!	lide Response			
Request Sample	e Code			
Curl Perl Pyth	ion Ruby Java			
curl -X G 'https://	ETheader 'Accept:application www.ebi.ac.uk/proteins/api/prot	/xml' eins?offset=0&size	=–1&gene=A	tp7b'
Request URL				
https://w	ww.ebi.ac.uk/proteins/api/prote	ins?offset=0&size=	-1&gene=At	:o7b
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nesponse bouy	, ,			
KPDLERY	EAQAHGRMKPLSASQVSVHVGMDDRRRDSPR	ATPWDQVSYVSQVSLSSL1	SDRLSRHGG	MAEDGGDKWSLLLSD
RDEEQCI				
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created	="2000-12-08" dataset="Swiss-Pr	ot">		
<ac< td=""><td>cession>Q64446</td><td></td><td></td><td></td></ac<>	cession>Q64446			
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<:	recommendedName>			
	<fullname>Copper-transporting</fullname>	ATPase 2	•	
	<pre><ecnumber evidence="2">3.6.3.5</ecnumber></pre>	4		
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<	alternativeName>			
	<fullname>Copper pump 2<td>ame></td><td></td><td></td></fullname>	ame>		
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200				
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#
#
#
Percent Identity Matrix - created by Clustal2.1
#
1: P35670 100.00 83.59
2: Q64446 83.59 100.00

Figure 17: Summary of sequence identity between human ATP7B P35670 and mouse ATP7B Q64446 proteins calculated by sequence alignment with Clustal Omega.

CLUSTAL O(1	.2.4) multiple sequence alignment	
P35670 Q64446	MPEQERQITAREGASRKILSKLSLPTRAWEPAMKKSFAFDNVGYEGGL MDPRKNLASVGTMPEQERQVTAKE-ASRKILSKLALPGRPWEQSMKQSFAFDNVGYEGGL *******:**:* ********:** * ** :* :**:******	48 59
P35670 Q64446	DGLGPSSQVATSTVRILGMTCQSCVKSIEDRISNLKGIISMKVSLEQGSATVKYVPSVVC DSTSS-SPAATDVVNILGMTCHSCVKSIEDRISSLKGIVNIKVSLEQGSATVRYVPSVMN * * .***.************************	108 118
P35670 Q64446	LQQVCHQIGDMGFEASIAEGKAASWPSRSLPAQEAVVKLRVEGMTCQSCVSSIEGKVRKL LQQICLQIEDMGFEASAAEGKAASWPSRSSPAQEAVVKLRVEGMTCQSCVSSIEGKIRKL ***: ** ******* **********************	168 178
P35670 Q64446	QGVVRVKVSLSNQEAVITYQPYLIQPEDLRDHVNDMGFEAAIKSKVAPLSLGPIDIERLQ QGVVRIKVSLSNQEAVITYQPYLIQPEDLRDHICDMGFEAAIKNRTAPLRLGPIDVNKLE *****:*******************************	228 238
P35670 Q64446	STNPKRPLSSANQNFNNSETLGHQGSHVVTLQLRIDGMHCKSCVLNIEENIGQLLGVQSI STNLKKETVSPVQISNHFETLGHQGSYLATLPLRIDGMHCKSCVLNIEGNIGQLPGVQNI *** *: * * *: ********::.** ***********	288 298
P35670 Q64446	QVSLENKTAQVKYDPSCTSPVALQRAIEALPPGNFKVSLPDGAEGSGTDHRSSSSHSPGS HVSLENKTAQIQYDPSCVTPMFLQTAIEALPPGHFKVSLPDGVEENEPQSGS :************************************	348 350
P35670 Q64446	PPRNQVQGTCSTTLIAIAGMTCASCVHSIEGMISQLEGVQQISVSLAEGTATVLYNPSVI SQRHQEQGPGRTAVLTISGITCASSVQPIEDMLSQRKGVQQTSISLAEGTGAVLYDPSIV *:* ** *::::*:*:*:*:*:*:*:*:**:**:**	408 410
P35670 Q64446	SPEELRAAIEDMGFEASVVSESCSTNPLGNHSAGNSMVQTTDGTPTSVQEVAPHTGRLPA SLDELRTAVEDMGFEVSVNSETFTINPVRNFKSGNSVPQTMGDIAGSVQKMAPDTRGLPT * :***:*:*****************************	468 470
P35670 Q64446	NHAPDILAKSPQSTRAVAPQKCFLQIKGMTCASCVSNIERNLQKEAGVLSVLVALMAGKA HQGPGHSSETPSSPGATASQKCFVQIKGMTCASCVSNIERSLQRHAGILSVLVALMSGKA ::.*. :::*.* *.* *.* ****:*************	528 530
P35670 Q64446	EIKYDPEVIQPLEIAQFIQDLGFEAAVMEDYAGSDGNIELTITGMTCASCVHNIESKLTR EVKYDPEIIQSPRIAQLIQDLGFEASVMEDNTVSEGDIELIITGMTCASCVHNIESKLTR *:*****:** .***************************	588 590
P35670 Q64446	TNGITYASVALATSKALVKFDPEIIGPRDIIKIIEEIGFHASLAQRNPNAHHLDHKMEIK TNGITYASVALATSKAHVKFDPEIVGPRDIIKIIEEIGFHASLAQRNPNAHHLDHKTEIK ************************************	648 650
P35670 Q64446	QWKKSFLCSLVFGIPVMALMIYMLIPSNEPHQSMVLDHNIIPGLSILNLIFFILCTFVQL QWKKSFLCSLVFGIPVMGLMVYMLIPSSTPQETMVLDHNIIPGLSVLNLIFFILCTFVQF ***********************************	708 710
P35670 Q64446	LGGWYFYVQAYKSLRHRSANMDVLIVLATSIAYVYSLVILVVAVAEKAERSPVTFFDTPP LGGWYFYVQAYKSLRHRSANMDVLIVLATTIAYAYSLVILVVAVAEKAEKSPVTFFDTPP ***********************************	768 770
P35670 Q64446	MLFVFIALGRWLEHLAKSKTSEALAKLMSLQATEATVVTLGEDNLIIREEQVPMELVQRG MLFVFIALGRWLEHVAKSKTSEALAKLMSLQATEATVVTLGEDNLILREEQVPMELVQRG ************	828 830
P35670 Q64446	DIVKVVPGGKFPVDGKVLEGNTMADESLITGEAMPVTKKPGSTVIAGSINAHGSVLIKAT DVIKVVPGGKFPVDGKVLEGNTMADESLITGEAMPVTKKPGSIVIAGSINAHGSVLLKAT *::**********************************	888 890
P35670 Q64446	HVGNDTTLAQIVKLVEEAQMSKAPIQQLADRFSGYFVPFIIIMSTLTLVVWIVIGFIDFG HVGNDTTLAQIVKLVEEAQMSKAPIQQLADRFSGYFVPFIIIISTLTLVVWIVIGFVDFG ************************************	948 950

P35670	VVQRYFPNPNKHISQTEVIIRFAFQTSITVLCIACPCSLGLATPTAVMVGTGVAAQNGIL	1008
Q64446	VVQKYFPSPSKHISQTEVIIRFAFQTSITVLCIACPCSLGLATPTAVMVGTGVAAQNGVL	1010
-	*******	
P35670	IKGGKPLEMAHKIKTVMFDKTGTITHGVPRVMRVLLLGDVATLPLRKVLAVVGTAEASSE	1068
Q64446	IKGGKPLEMAHKIKTVMFDKTGTITHGVPRVMRFLLLADVATLPLRKVLAVVGTAEASSE	1070

P35670	HPLGVAVTKYCKEELGTETLGYCTDFQAVPGCGIGCKVSNVEGILAHSERPLSAPASHLN	1128
Q64446	HPLGVAVTKYCKEELGTETLGYSTDFQAVPGCGISCKVSNVEGILARSDLTAHPV	1125

P35670	EAGSLPAEKDAVPQTFSVLIGNREWLRRNGLTISSDVSDAMTDHEMKGQTAILVAIDGVL	1188
Q64446	GVGNPPTGEGAGPQTFSVLIGNREWMRRNGLTISSDISDAMTDHEMKGQTAILVAIDGVL	1185
	• • • • • • * ************************	
P35670	CGMIAIADAVKQEAALAVHTLQSMGVDVVLITGDNRKTARAIATQVGINKVFAEVLPSHK	1248
Q64446	CGMIAIADAVKPEAALAIYTLKSMGVDVALITGDNRKTARAIATQVGINKVFAEVLPSHK	1245
	********* ******	
D25670		1200
064446	VARVQELQNRGRAVAMVGDGVNDSPALAQADMGVALGIGIDVALEAADVVLIRNDLLDVV	1305
204440	***************************************	1303
P35670	ASTHLSKRTVRRTRTNLVLALTYNLVGTPTAAGVFMPTGTVLOPWMGSAAMAASSVSVVL	1368
064446	ASIHLSKRTVRRIRVNLVLALIYNMVGIPIAAGVFMPIGIVLOPWMGSAAMAASSVSVVL	1365
2 * *	*****	
P35670	SSLQLKCYKKPDLERYEAQAHGHMKPLTASQVSVHIGMDDRWRDSPRATPWDQVSYVSQV	1428
Q64446	SSLQLKCYRKPDLERYEAQAHGRMKPLSASQVSVHIGMDDRRRDSPRATAWDQVSYVSQV	1425

P35670	SLSSLTSDKPSRHSAAADDDGDKWSLLLNGRDEEQYI 1465	
Q64446	SLSSLTSDRLSRHGGAAEDGGDKWSLLLSDRDEEQCI 1462	
	******* *** *** ** ******** *	

Figure 18: Sequence alignment of human ATP7B protein P35670 and mouse ATP7B protein Q64446 by Clustal Omega. As summarised in Figure 17 the two proteins are 83.59% identical.

Step 5: Gene structure analysis using Coordinates service

The *Coordinates* service was used to retrieve genomic coordinates mapped to both the human APT7B protein P35670 and mouse ATP7B protein Q64446 searching by accession. Figure 19 shows the Swagger UI for the *Coordinates* service with accession P35670 added to the accession search field and the results after execution of the search in the response body, with a Curl command defined that is also available in Figure 20 with Figure 21 defining a Python script to execute this search. The equivalent coordinate search for mouse ATP7B protein Q64446 is shown in Figure 22, with the dynamically generated curl command and python script in Figures 23 and 24 respectively. Both P35670 and Q64446 genes consist of 21 exons with the active site residue in both proteins being found in the fourteenth exon. Therefore, we can be confident that other sequence features are related between the two proteins.

GET /coordina	ates/{accession}		Get Genon	ne Coordinates by accession.
Response Class	s (Status 200)			
successful ope	eration			
Model Examp	ile Value			
acces	sion": "string",			
"name"	: "string",			
"taxid	": 0,			
"seque	nce": "string",			
"prote	in": (
"red	ommendedName": {			
Response Cont	ent Type application/json 🛊			
Parameters				
Paramotor	Value	Description	Parameter	Data Tuno
- arameter	Yanuo	Description	Туре	Data Type
accession	P35670	UniProt accession	path	string
Response Mes	sages Show Response			
Touit out	lide Response			
ity it out:				
Request Sample	a Code			
Curl Perl Pyth	on Ruby Java			
curl -X 6	ETheader 'Accent:application	/ison'		
'https://	www.ebi.ac.uk/proteins/api/coor	dinates/P35670'		
Request LIRI				
noquosione				
https://w	ww.ebi.ac.uk/proteins/api/coord	linates/P35670		
Response Body	,			
-				
"gnCoo	ordinate": [
(· · · ·
	jenomicLocation": {			
	exon i [
	"proteinLocation": (
	"begin": {			
	"position": 1,			
	"status": "certain"			
),			
	"end": {			
	"position": 17,			
	"status": "certain"			
	,			
) e			

Figure 19: *Coordinates* service Swagger UI with the human protein identifier P35670 entered in to the accession search field. The results body contains the protein and matching genomic coordinates for the protein.

```
curl -X GET --header 'Accept:application/json'
'https://www.ebi.ac.uk/proteins/api/coordinates/P3567
0'
```

Figure 20: Curl command to execute the search for mapped genomic coordinates for P35670 dynamically generated by the Swagger UI as illustrated in Figure 19.

```
import requests, sys
requestURL =
"https://www.ebi.ac.uk/proteins/api/coordinates/P3567
0"
r = requests.get(requestURL, headers={ "Accept" :
"application/json"})
if not r.ok:
   r.raise_for_status()
   sys.exit()
responseBody = r.text
print(responseBody)
```

Figure 21: Dynamically generated python script for searching for the genomic coordinates for protein P35670.

GET	/coordinates/{accession}		Get Genon	ne Coordinates by accession.				
Resp suc	onse Class (Status 200) cessful operation							
Mo	Model Example Value							
	<pre>{ "accession": "string", "name": "string", "taxid": 0, "sequence": "string", "protein": { "recommendedName": { } } } </pre>							
Resp	onse Content Type application/json \$							
man	inders	O	Parameter	D. I. X.				
a	cession Q64446	UniProt accession	Type path	String				
Res	vit out							
Curl Perl Python Ruby Java								
curl -X GETheader 'Accept:application/json' 'https://www.ebi.ac.uk/proteins/api/coordinates/Q64446'								
Requ	est URL							
https://www.ebi.ac.uk/proteins/api/coordinates/Q64446								
Resp	https://www.ebi.ac.uk/proteins/api/coordinates/Q64446							
	<pre>{ "accession": "Q64446", "name": "ATP7B_MOUSE", "taxid": 10090, "sequence": "MDPRKNLASVGTMPEQERQVTAKEASRKILSKLALPG SCVKSIEDRISSLKGIVNIKVSLEQGSATVRYVPSVMS MTCQSCVSSIEGKIRKLQGVVRIKVSLSNQEAVITYQP KKETVSPVQISNHFETLGHQGSYLATLPLRIDGMHCKS AIEALPPGHFKVSLPDGVEENEPQSGSSQRHQEQGPGF YDPSIVSLDELRTAVEDMGFEVSVNSETFTINPVRNFF ATASQKCFVQIKGMTCASCVSNIERSLQRRAGILSVLV DIELLITGMTCASCVHNIESKLTRTNGITYASVALATE EIKQWKKSFLCSLVPGIPVMGLMVYMLIPSSTPQETMU</pre>	RPWEQSMKQSFAFDNVGYI ILQQICLQIEDMGFEASAAI YLIQPEDLRDHICDMGFEA SCVLNIEGNIGQLPGVQNII TAVLTISGITCASSVQPI SGNSVPQTMGDIAGSVQKI /ALMSGKAEVKYDPEIIQSI SKAHVKFDPEIVGPRDIIK: JLDHNIIPGLSVLNLIFFI	EGGLDSTSSSI EGKAASWPSRS AAIKNRTAPLR HVSLENKTAQI EDMLSQRKGVQ MAPDTRGLPTH PRIAQLIQDLG IIEEIGPHASI LCTFVQPLGGW	PAATDVVNILGMTCH SSPAQEAVVKLRVEG LLGPIDVNKLESTNL QYDPSCVTPMFLQT QGTSISLAEGTGAVL QGCGHSSETPSSPG JFEASVMEDNTVSEG AQRNPNAHHLDHKT YYFYVQAYKSLRHRS				
Response Code								
2	00							

Figure 22: *Coordinates* service Swagger UI with the mouse protein identifier Q64446 entered in to the accession search field. The results body contains the protein and matching genomic coordinates for the protein.

```
curl -X GET --header 'Accept:application/json'
'https://www.ebi.ac.uk/proteins/api/coordinates/Q6444
6'
```

Figure 23: Curl command to execute the search for mapped genomic coordinates for P35670 dynamically generated by the Swagger UI as illustrated in Figure 19.

```
import requests, sys
requestURL =
"https://www.ebi.ac.uk/proteins/api/coordinates/Q6444
6"
r = requests.get(requestURL, headers={ "Accept" :
"application/json"})
if not r.ok:
   r.raise_for_status()
   sys.exit()
responseBody = r.text
print(responseBody)
```

Figure 24: Dynamically generated python script for searching for the genomic coordinates for protein Q64446.

Step 6: Mouse Q64446 variant search and comparison to P35670

The Variation service was used to retrieve any variants for mouse ATP7B protein Q64446 by searching with the protein accession. Figure 25 shows the Swagger UI for the Variation service with accession Q64446 added to the accession search field. Results after execution of the search are shown in Figure 26, where the mouse variant p.R1040K is shown as it is equivalent to the human p.R1038K Wilson disease associated variant. The curl command to execute the search is defined in Figure 27 with Figure 28 defining a Python script to execute this search.

GET /variation/{accession}		get UniProt va	riation featur	es by accession					
Implementation Notes									
with categories as query par	ameter								
Hesponse Class (Status 200) successful operation									
Model Example Value									
Model Example value									
(
"version": "stri:	ng", sina"								
"entryName": "st:	ring",								
"sequence": "str	ing",								
"sequenceChecksu	n": "string",								
geteseneru i s	cring ,								
Response Content Type app	lication/json \$								
Parameters									
		Parameter							
Parameter	Value	Description	Туре	Data Type					
accession	Q64446	UniProt accession	path	string					
sourcetype		Filter for variants	query	string					
		from a specific sourceType, Options							
		include: uniprot,							
		large_scale_study and mixed, or							
		individual data							
		source such as exac, cosmic curated, esp.							
		1000genomes.							
consequencetype		Filter for variants	query	string					
		with a specific							
		Options include:							
		missense, stop							
		gained or stop lost							
wildtype		Search by specific	query	string					
		Options: Any single							
		letter amino acid and							
		 for stop codon. 							
alternativesequence		Filter by specific	query	string					
		alternativeSequence amino acid. Options:							
		Any single letter							
		amino acid and * for stopcodon and - for							
		deletions.							
location	1	Filter by amino acid	querv	string					
		position in the	danak	ad ing					
		sequence(s). Options: any valid							
		amino acid position							
		within the length of the protein sequence							
Response Messages Show Response									
Try it out!									

Figure 25: *Variation* service Swagger UI with the mouse protein identifier Q64446 entered in to the accession search field.



Figure 26: Results from the *Variation* search with the mouse protein identifier Q64446. In the response body is the mouse equivalent variant p.R1040K to the human p.R1038K Wilson disease associated variant.

```
curl -X GET --header 'Accept:application/json'
'https://www.ebi.ac.uk/proteins/api/variation/Q64446'
```

Figure 27: Curl command to execute the search for variant for Q64446 dynamically generated by the Swagger UI as illustrated in Figure 26.

```
import requests, sys
requestURL =
"https://www.ebi.ac.uk/proteins/api/variation/Q64446"
r = requests.get(requestURL, headers={ "Accept" :
"application/json"})
if not r.ok:
   r.raise_for_status()
   sys.exit()
responseBody = r.text
print(responseBody)
```

Figure 28: Dynamically generated python script for searching for variants for protein Q64446.

Step 7: Mouse proteomics peptide search

The *Proteomics* service was used to retrieve any peptides for mouse ATP7B protein Q64446 by searching with the protein accession. Figure 29 shows the Swagger UI for the *Proteomics* service with accession Q64446 added to the accession search field. Results after execution of the search are shown in Figure 30, where the mouse protein has an equivalent unique peptide between residues 1044-1057 to the unique peptide 1042-1054 in the human ATP7B protein P35670. Where a peptide is defined as unique if it not found in another protein, not including isoforms, in the organisms' proteome. Unique peptides from different species can be the same. The curl command to execute the search is defined in Figure 31 with Figure 32 defining a Python script to execute this search.

ET /proteomic	15	Get proteon	nics peptides (of list of UniProt accessions				
Implementation Notes								
With query feature type and query terms								
Response Class (Status 200)								
successful operation								
Nodel Example Value								
"version": "string",								
"acces	ssion": "string", yName": "string",							
"sequ	ence": "string",							
"gete	GeneId": "string",							
"geteProteinId": "string",								
Response Content Type application/ison 1								
Parameters								
Parameter	Value	Description	Parameter Type	Data Type				
offset	0	Off set, page starting point, with default value 0	query	integer				
size	100	Page size with default value 100. When page size is -1, it returns all records and offset will be ignored	query	integer				
accession	Q64446	Search for accession, can be a list separated by ','	query	string				
taxid		Organism taxonomy id	query	string				
upid		UniProt proteome Id: UP[0-9]{9}	query	string				
datasource		Proteomics data source, can be list, separated by ','	query	string				
peptide		Proteomics peptide	query	string				
unique		If unique, a peptide is mapped to one gene group only. Value can only be true or false.	query	string				
Response Messa	ages Show Response							

Figure 29: *Proteomics* service Swagger UI with the mouse protein identifier Q64446 entered in to the accession search field.



Figure 30: Results from the *Proteomics* search with the mouse protein identifier Q64446. In the response body is the mouse unique peptide starting at residue 1044.

```
curl -X GET --header 'Accept:application/json'
'https://www.ebi.ac.uk/proteins/api/proteomics?offset
=0&size=100&accession=Q64446'
```

Figure 31: Curl command to execute the search for peptides for Q64446 dynamically generated by the Swagger UI as illustrated in Figure 30.

```
import requests, sys
requestURL =
"https://www.ebi.ac.uk/proteins/api/proteomics?offset
=0&size=100&accession=Q64446"
r = requests.get(requestURL, headers={ "Accept" :
"application/json"})
if not r.ok:
   r.raise_for_status()
   sys.exit()
responseBody = r.text
print(responseBody)
```

Figure 32: Dynamically generated python script for searching for unique peptides for protein Q64446.