

A quick guide to... Genomic Entities on PanelApp



8th June 2018 PanelApp Release 2.2.0

An introduction to Short Tandem Repeats (STRs) in PanelApp



https://panelapp.genomicsengland.co.uk/

- An interpretation pipeline for STRs in whole genome sequences has been developed and validated by Genomics England in order to allow these variant types to be reported back to Genomic Medicine Centers.
- In order to incorporate the STRs into the bioinformatics pipeline and ensure that particular STRs are only analysed in genomes for patients recruited for certain diseases, STRs have been added to the appropriate panels within PanelApp.
- In **PanelApp Release v2.2.0**, we have expanded the scope of PanelApp to allow curation and review of STRs that are disease causing when a particular number of repeats is present.
- Genes and STRs are now termed genomic 'entities' and can be added to panels, reviewed and curated.
- Green genes and Green STRs on a version 1+ panel will be used for genome interpretation for the 100,000 Genomes Project. These are deemed to have a high level of evidence for disease causation.
- An 'Entities' page has replaced the 'Genes' page to allow users to search for genes and STRs that are included in panels.
- Nomenclature: There is currently no defined nomenclature for STRs. Currently all the STRs in PanelApp are associated with a gene. We have named the STRs added to PanelApp using the associated gene symbol (HGNC-approved symbol) and nucleotide repeat - for example HTT_CAG.
- How to find STRs: STRs can be found by searching for the associated gene on the 'Entities' page. By clicking on the STR, this will take the user to the gene page where panels that include the gene or the associated STRs are displayed. From there, users can click on the panel or STR of interest.

18/06/18

Information provided for STRs

Chromosome and genomic coordinates for the start and the end of the nucleotide repeats in the human reference genome for Build 37 and 38

The repeated nucleotide sequence

The maximum number of repeats that are considered non-pathogenic/normal (equal to or less than)

The minimum number of repeats that are considered pathogenic/disease causing (equal to or more than)

The mode of inheritance for the pathogenic number of repeats that is required to cause disease

The disease caused by the pathogenic number of repeats (phenotype)

Information about the associated gene, including links to Ensembl

The source – "Expert list" has been used to indicate that these STRs are from the Genomics England pipeline.

Whether penetrance is incomplete (default is complete)

The tag 'STR'

LRRK2	4	Reviews (2) D	etails	History
MAPT	2	Details		
OPA3	1			
PANK2	2	Name HTT_CAG		
PARK7	2	Chromosome		
PINK1	2	4		
PLA2G6	2	GRCh37 Coordin 3076604-3076666	ates	
PRKRA	2	GRCh38 Coordin	ates	
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TUBB4A	2	Tags		
VPS13A	2	SIR		

Example of the HTT_CAG STR in the Parkinson Disease and Complex Parkinsonism panel (version 1.40) https://panelapp.genomicsengland.co.uk/panels/39/str/HTT_CAG/#!details



How to find STRs...

PanelApp Panels Entities Activity

Genomics England PanelApp

A crowdsourcing tool to allow gene panels to be shared, downloaded, viewed and evaluated by the Scientific Community

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PanelApp Release v2.2.0: We have expanded the scope of PanelApp to allow curation and review of Short Tandem Repeats (STRs) associated with disease

Go to

Genes and STRs can be found from our 'Entities' page. We are in the process of adding these to the appropriate gene panels on PanelApp, and will release more detailed documentation on STRs shortly.





Log in Register

Click on 'Entities'





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Genes and STRs can be found from our 'Entities' page. We are in the process of adding these to the appropriate gene panels on PanelApp, and will release more detailed documentation on STRs shortly.

Genomic Entities page



PanelApp Panels Entities Activity 4350 entities Image: Second Seco	PanelApp Panels Entities Activ	Filter the list of genes STRs by typing the ass gene you would like to	and ociated o review	Log in Register
Find an entity				
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ABCB11 ABCB4 ABCB6 AB B7 ABCC2 ABCC6	V 🛛 Genes 🖉 STRS			cnvs curated-variant-list
ACADVL ACAN ACAT1 ACBD5 ACBD6 10				currently-ngs-unreportable
ACP5 ACSF3 ACSL4 ACSL6 ACTA1 ACTA2 AC	HTT HTT_CAG HTT_CAG HTT_CAG			de novo deletions
ACTN1 ACTN2 ACTN4 ACVR1 ACVR2B ACVRL1				drug-contraindication drug-dosing
ADAMTS13 ADAMTS17 ADAMTS18 ADAMTS2 AD				drug-efficacy drug-indication
ADCY5 ADCY6 ADD1 ADD2 ADD3 ADGRA3 AD				drug-toxicity duplication
ADM ADNP ADRA2B ADSL AEBP1 AFF2 AFF3				early-onset epigenetics
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Genomic Entities page



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DM ADNP ADRA2B ADSL AEBP1 AFF2 AFF3 GMO AGO1 AGPAT2 AGPS AGRN AGT AGTR1 JFM1 AIMP1 AIP AIPL1 AIRE AK1 AK2 AKAP1 JKR1C2 AKR1D1 AKR1E2 AKT1 AKT2 AKT3 AL		Panel Filter paper Filter pape	Reviews	Mode of inheritance MONOALLELIC, autosomal or pseudoautosomal, NOT imprinted	Details Sources Expert Review Red Expert Review Phenotypes Huntington disease 143100 Tags Courrently-ngs-unreportable nucleotide-repe	7 panel: at-expansion
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Find STRs on the associated



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STR

Find STRs on the associated



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STR reviews



PanelApp Panels	Entities Activity		Scroll down the page to view
Panels / Parkinson I	Disease and Complex Parkinsonism / HTT_CAG		reviews for a STR
Genes in panel	Parkinson Disease and Complex Parkinsonism		
♠ Prev Next ↓	STR: HTT_CAG		
• PRKN 4	Green List (high evidence)		
• ATP13A2 2			
• ATP1A3 2	Chromosome: 4 GRCh37 Position: 3076604-3076666		
C19orf12 2	GRCh38 Position: 3074877-3074939	• LRRK2 4	Reviews (2) Details History
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DNAJC6 3	Pathogenic Number of Repeats: = or > 36	PANK2 2	Arianna Tucci (Genomics England Curator)
	HTT (huntingtin)	PARK7 2	Comment on list classification: changed to green as diagnostic for HD
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Submit a review



LRRK2	4	Reviews (2) Details History Log in to make a review for a
MAPT OPA3	2	Review STR
PANK2	2	Rating: 🕑
PARK7	2	Provide rating
PINK1	2	Mode of Inheritance: 🕑
PLA2G6	2	Provide a mode of inheritance
• PRKRA	2	Publications (PMID: 1234;4321):
RAB39B	3	Publications (PMID: 1234;4321)
SLC30A10	2	Phenotypes (separate using a semi-colon - ;):
SLC39A14	1	Phenotypes (separate using a semi-colon - ;)
SLC6A3	2	Current diagnostic: 🕑
SNCA	2	Current diagnostic
 SPC11 	-	Interruptions are clinically relevant:
• SPGTT	2	 Interruptions are clinically relevant
SPR	2	Comments:
SYNJ1	3	Comments
• тн	2	
TUBB4A	2	

Add an STR to a panel as a reviewer



Red C9orf72_GGGC	Add review 1 green	MONOALLELIC, autosomal or pseudoautosomal, NOT imprinted	Sources • Expert list Phenotypes • Frontotemporal dementia and/or amyotrophic lateral sclerosis 1 105550 Tags STR
Red JPH3_CTG	1 review Add review 1 green	MONOALLELIC, autosomal or pseudoautosomal, NOT imprinted	Sources • Expert list Phenotypes • Huntington disease-like 2 606438 Tags STR
Red TBP_CAG	1 review Add review 1 green	MONOALLELIC, autosomal or pseudoautosomal, NOT imprinted	Sources • Expert list Phenotypes • Spinocerebellar ataxia 17 607136 Tags
+ Add a STR to this panel	Log in to add a panel	STR to the	

-ind a panel			englan
PanelApp Panels Entities Activity	Go to the 'Panel filter for key wo the disease	ls' page ar rds relate	nd d to _{Jister}
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Compare two panels	Evaluated gapes	Paviowars	Actions
Compare two panels Panel parkinson	Evaluated genes	Reviewers	Actions 1 panel



Panels

Entities

Activity

List ↑

Parkinson Disease and Complex Parkinsonis Once on the panel, scroll 1.37)

Reviews

Level 3: Neurodegener Level 2: Neurology and

Relevant disorders: Co

PanelApp

57 genes 57 reviewed, 32 green

Gene

down the page to view the list of genes and STRs on a panel. Genes are listed first, then

Register

Log in

familial Parkinson's Di Previous code: 58078	Filter gen	nes	6 ST	Rs	STRS.			
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			List ↑	STR	Reviews	Mode of inheritance	Details	
This panel was created by c (Version 0.51) gene panel ar			Filter S	TRs				6 genes
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18/06/18			Red	C9orf72_GGGGCC	1 review 1 green	MONOALLELIC, autosomal or pseudoautosomal, NOT imprinted	Sources Expert list Phenotypes Frontotemporal dementia and/or amyotrophic 105550 	ateral sclerosis

Mode of inherita

Downloads



Downloads

Download lists

- Whole panel
- Green list (high evidence)
- Green and Amber Genes
- Amber Genes
- Red list (low evidence)

Download Version

Download

Panel version, for examp

Scroll down the page to download the panel – the download will include genes and STRs

Acknowledgements



- STR development: Kristina Garikano, Arianna Tucci, Katherine Smith, Oleg Gerasimenko
- Participants & Partners of the 100,000 Genomes Project
- PanelApp Reviewers; many of whom are from GMCs
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- PanelApp Curators (past & present): Ellen McDonagh, Sarah Leigh, Rebecca Foulger, Louise Daugherty, Olivia Niblock, Eleanor Williams, Arianna Tucci, Helen Brittain, Rachel Jones, Eik Haraldsdottir, Alice Gardham, Ellen Thomas, Richard Scott, Caroline Wright, Emma Baple, Damian Smedley, Chris Boustred, Kirsty McCaffrey, Chris Campbell.
- Other contributers to PanelApp creation, documentation, outreach: Augusto Rendon, Katherine Smith, Clare Turnbull, Jo Whittaker, Mina Ryten, Tom Fowler & members of the V&F GeCIP Domain, Mark Caulfield, Verity Fryer, Corey Johnson, Lisa Carr, PanelApp collaborators & Users.

Any questions?

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