Variant View

Visualizing Sequence Variants in their Gene Context

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BioIT World, Data Visualization and Exploration Tools Track

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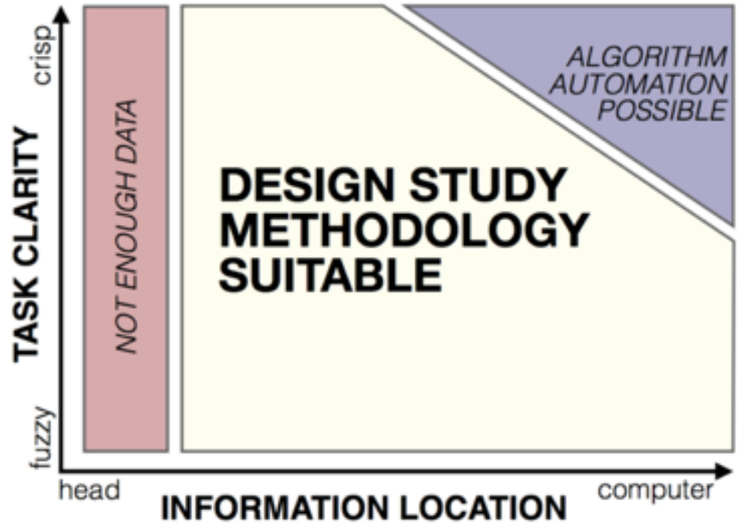
http://www.cs.ubc.ca/~tmm/talks.html#bioit14

Variant View: Visualization *Design Study*

- a specific real-world problem
  - real users and real data,
  - collaboration is (often) fundamental
- design a visualization system
  - implications: requirements, multiple ideas
- validate the design
  - at appropriate levels
- reflect about lessons learned
  - transferable research: improve design guidelines for vis in general
    - confirm, refine, reject, propose

more at:
A Nested Model of Visualization Design and Validation.
Munzner. IEEE TVCG 15(6):921-928, 2009 (Proc. InfoVis 2009).

more at:
The Nested Blocks and Guidelines Model.
Meyer, Sedlmair, Quinan, Munzner. Information Visualization Journal, 2014, to appear.



Design Study Methodology

Reflections from the Trenches and from the Stacks

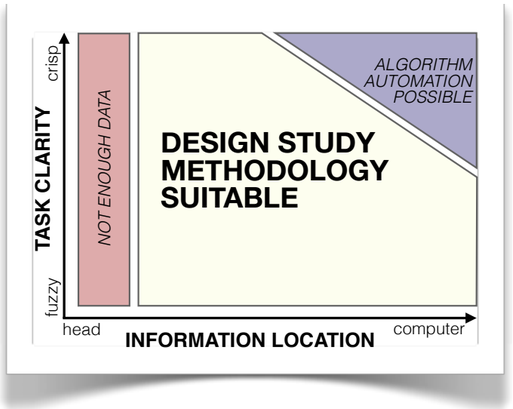
joint work with:
Michael Sedlmair, Miriah Meyer

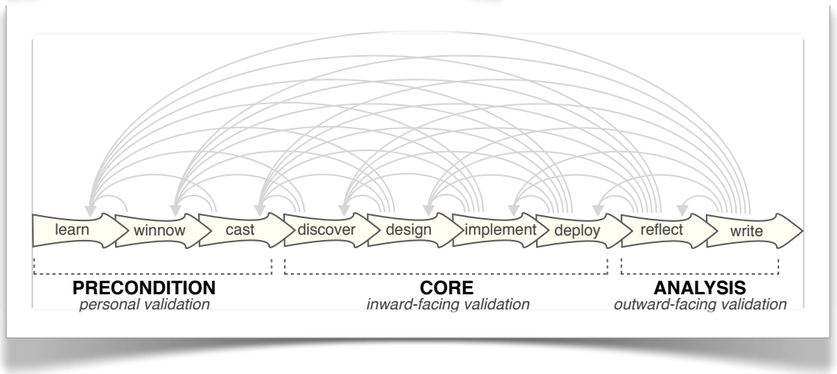
http://www.cs.ubc.ca/labs/imager/tr/2012/dsm/

Design Study Methodology: Reflections from the Trenches and from the Stacks.
Sedlmair, Meyer, Munzner. IEEE TVCG 18(12): 2431-2440, 2012 (Proc. InfoVis 2012).

How To Do Design Studies

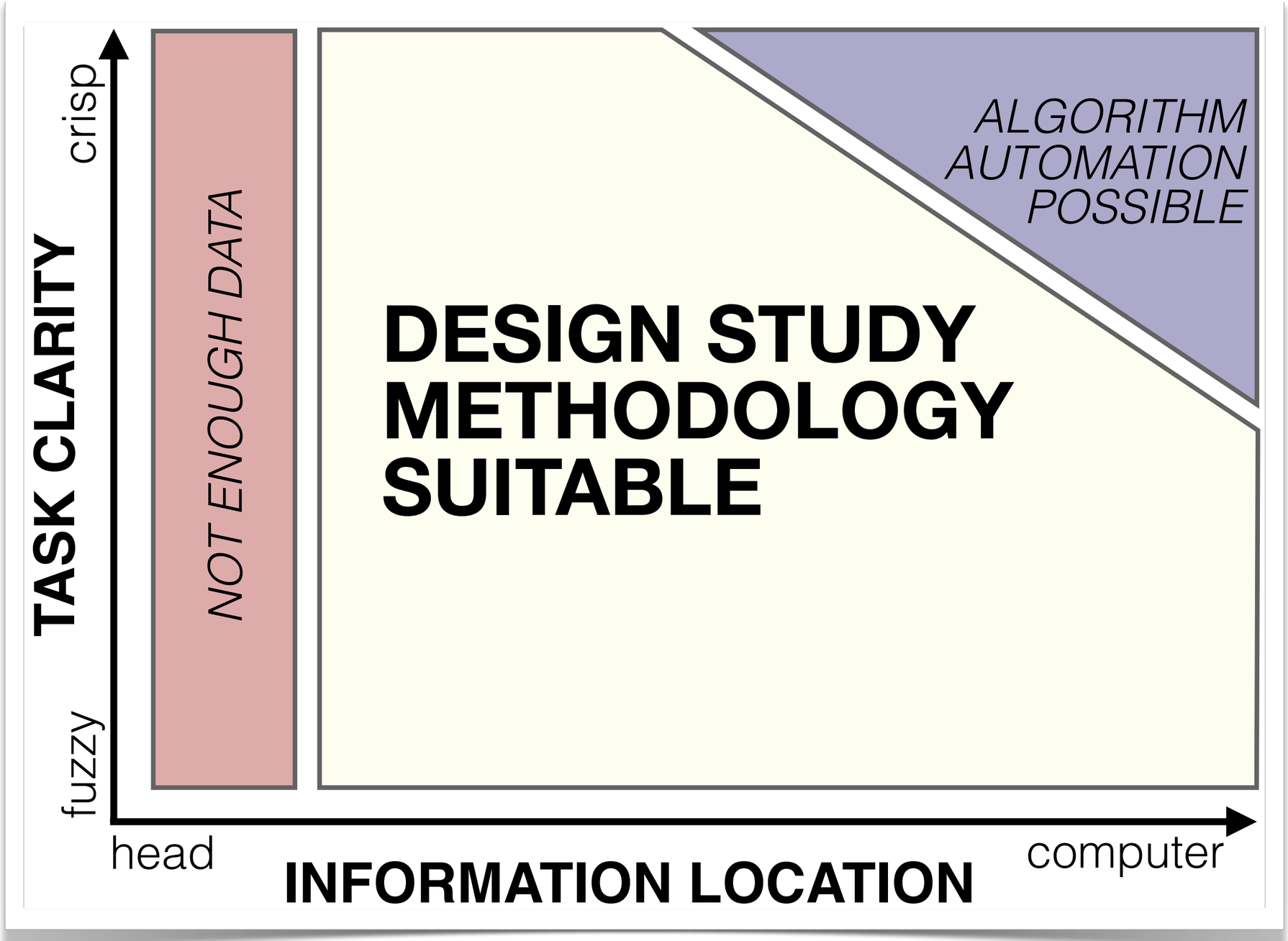
- definitions
- 9-stage framework
- 32 pitfalls and how to avoid them



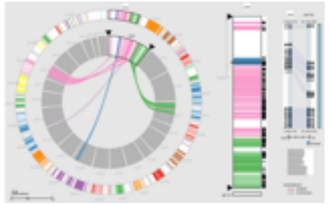


PF-1	premature advance: jumping forward over stages	general
PF-2	premature start: insufficient knowledge of vis literature	learn
PF-3	premature commitment: collaboration with wrong people	winnow
PF-4	no real data available (yet)	winnow
PF-5	insufficient time available from potential collaborators	winnow
PF-6	no need for visualization: problem can be automated	winnow
PF-7	researcher expertise does not match domain problem	winnow
PF-8	no need for research: engineering vs. research project	winnow
PF-9	no need for change: existing tools are good enough	winnow

When To Do Design Studies

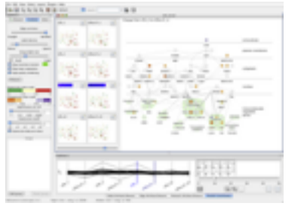


Design Studies: Lessons learned after 21 of them

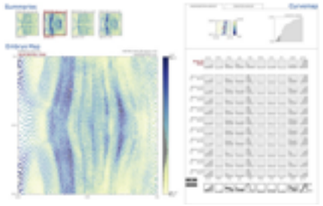


MizBee
genomics

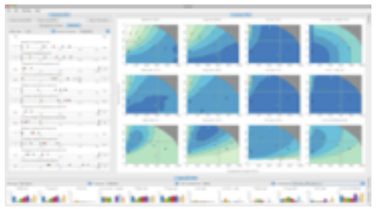
Pathline
genomics



Cerebral
genomics



MulteeSum
genomics

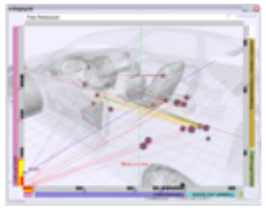


Vismon
fisheries management

QuestVis
sustainability

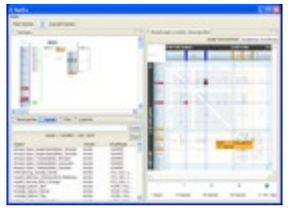
WiKeVis
in-car networks

MostVis
in-car networks



Car-X-Ray
in-car networks

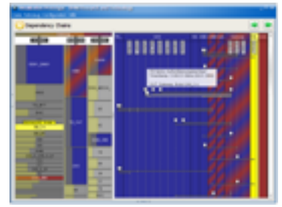
ProgSpy2010
in-car networks



RelEx
in-car networks

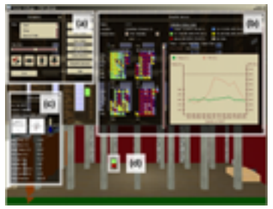
Cardiogram
in-car networks

AutobahnVis
in-car networks

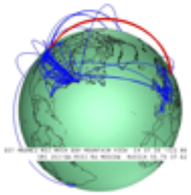


VisTra
in-car networks

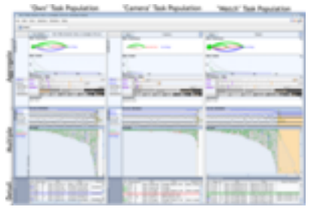
Constellation
linguistics



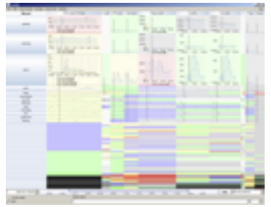
LibVis
cultural heritage



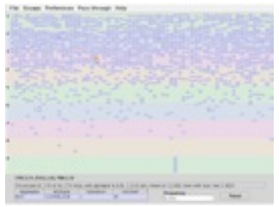
Caidants
multicast



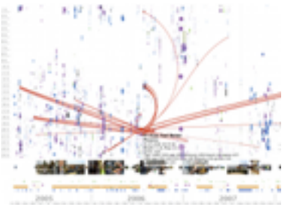
SessionViewer
web log analysis



LiveRAC
server hosting



PowerSetViewer
data mining

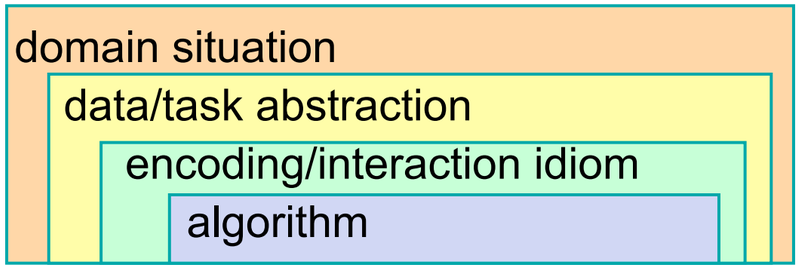


LastHistory
music listening

- commonality of representations cross-cuts domains!

Abstractions and Idioms

- abstractions
  - translate from specifics of domain to vocabulary of vis
    - task abstraction: **why** they're looking at it
    - data abstraction: **what** to draw
  - transform data into form useful for task at hand
    - don't just draw what you're given; decide what is the right thing!
- idioms
  - visual encoding idiom: **how** to draw
  - interaction idiom: **how** to manipulate
- focus today: two mappings
  - from domain to abstraction
  - from abstraction to idiom



A Nested Model of Visualization Design and Validation.
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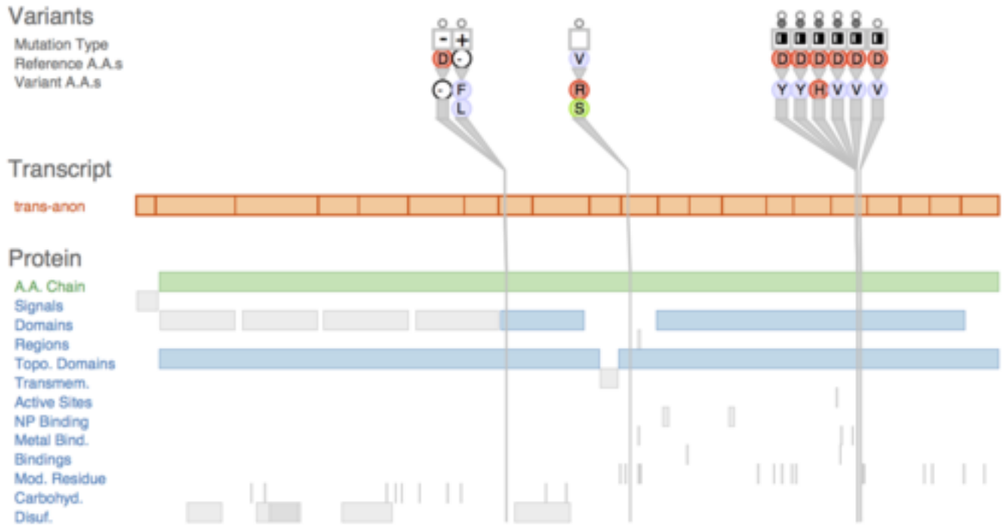


Variant View

Visualizing Sequence Variants in their Gene Context

joint work with:

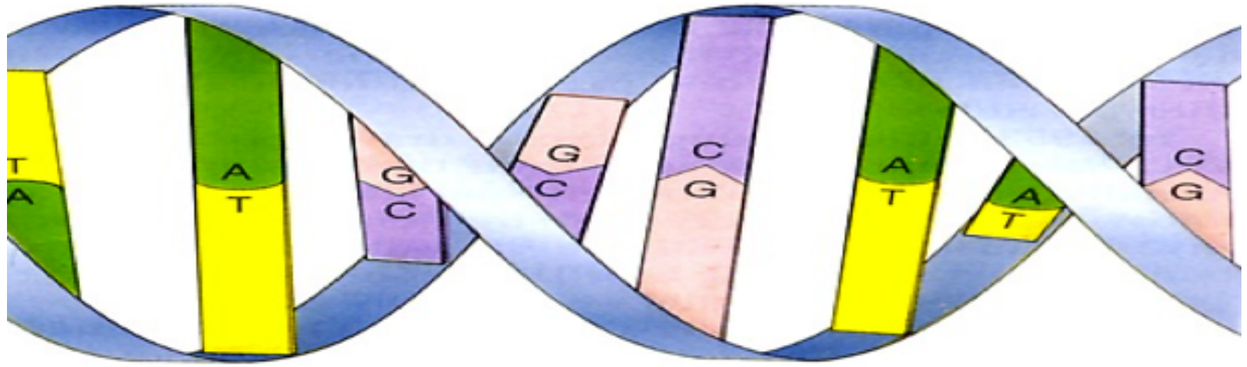
Joel Ferstay, Cydney Nielsen

http://www.cs.ubc.ca/labs/imager/tr/2012/VariantView/

Variant View: Visualizing Sequence Variants in their Gene Context.
Ferstay, Nielsen, Munzner. IEEE TVCG 19(12): 2546-2555, 2013 (Proc. InfoVis 2013).

Sequence Variant Definition

- Sequence variants
  - Difference between reference and given genome



Reference Genome DNA: ATA TGA TCA ACA CTT

Sample 1 Genome DNA: ATA TGG TCA ATA CTT

Sample 2 Genome DNA: ATA TGA TGA ACA CCT

Harmful?

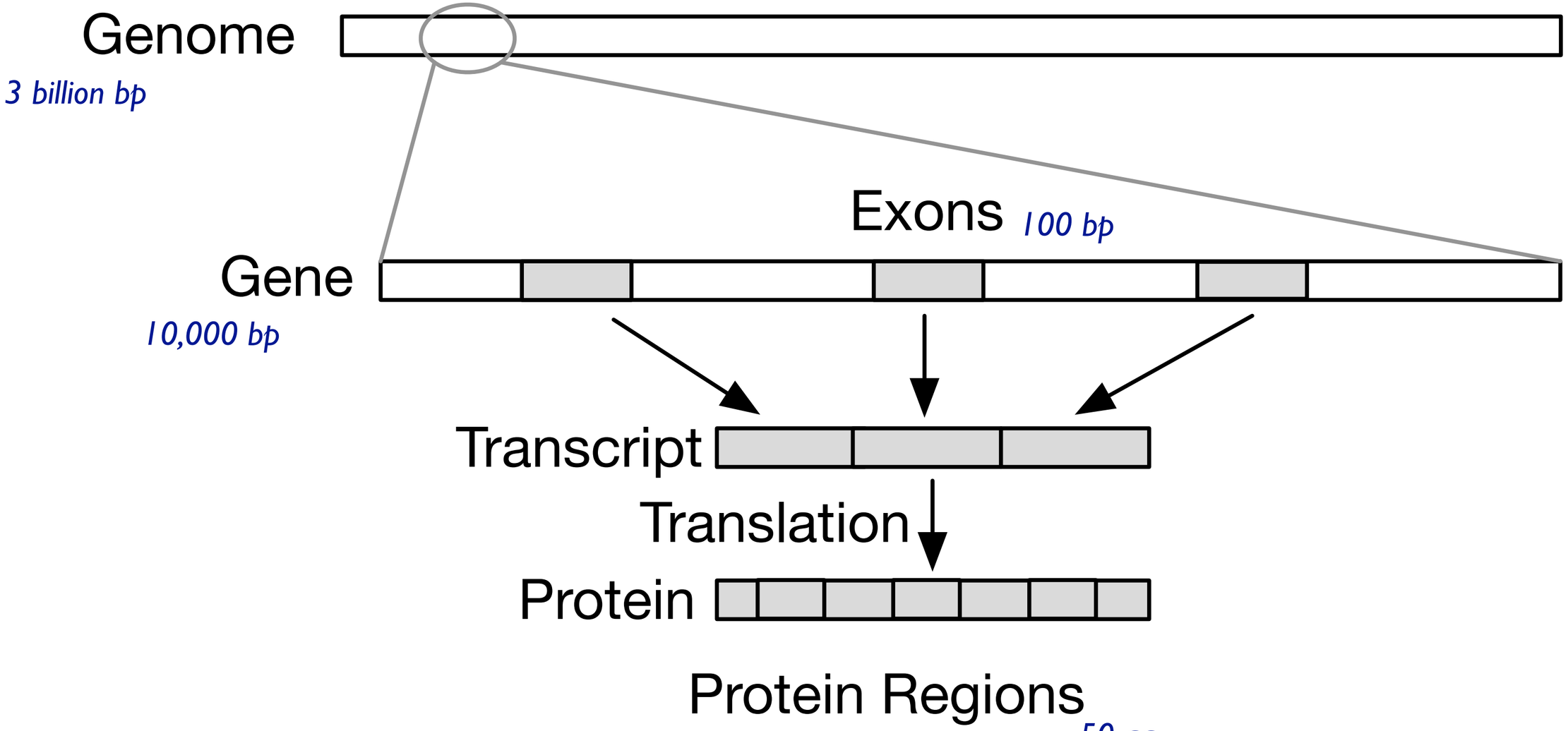
Harmless?

Cancer Research

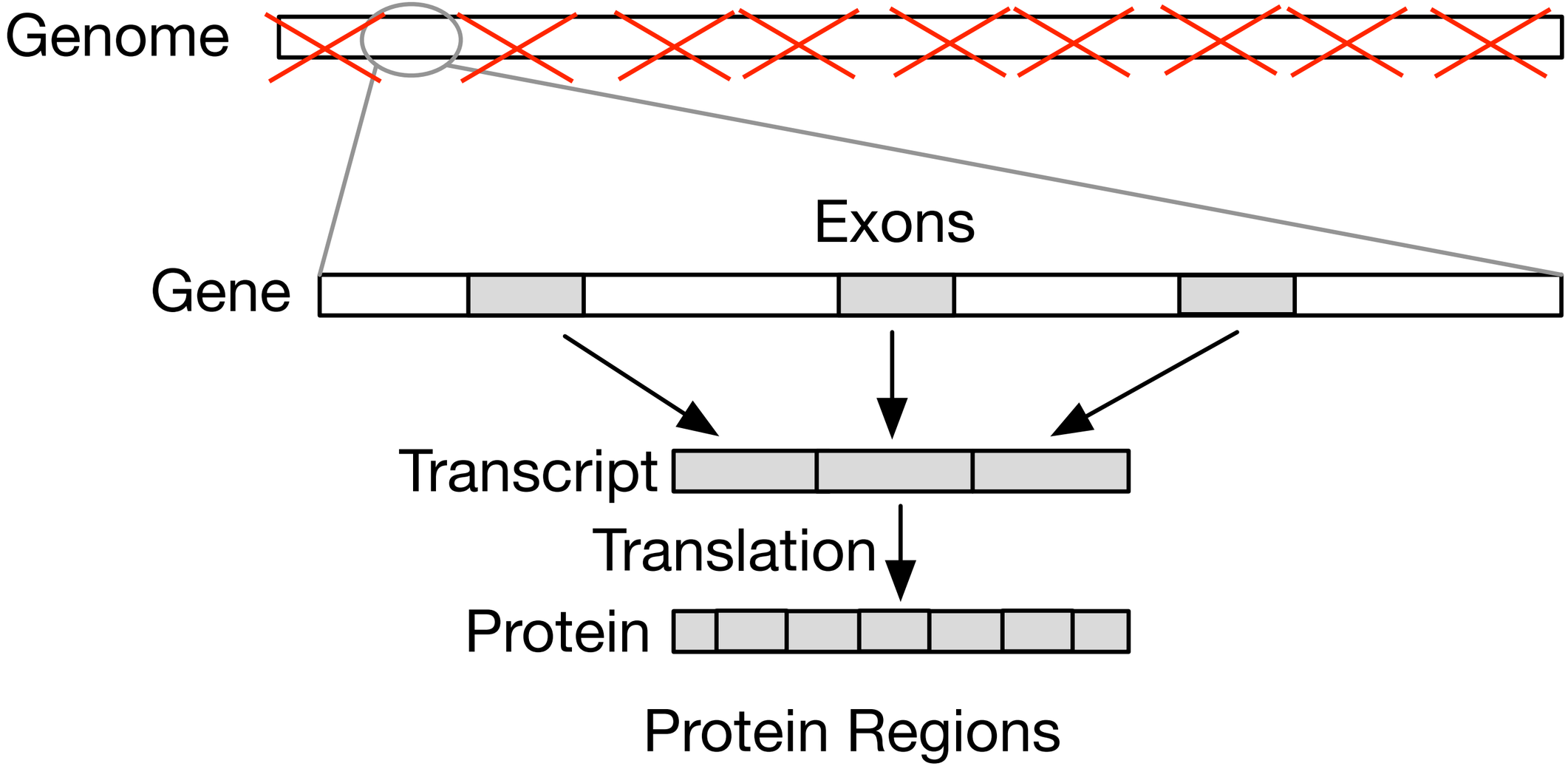
- collaboration with analysts at BC Genome Sciences Center
  - studying genetic basis of leukemia
- driving task
  - discover new candidate genes with harmful variants
- two big questions
  - what to show
    - data abstraction
    - challenge: enormous range of scales in the data
  - how to show it
    - visual encoding idiom

Abstractions

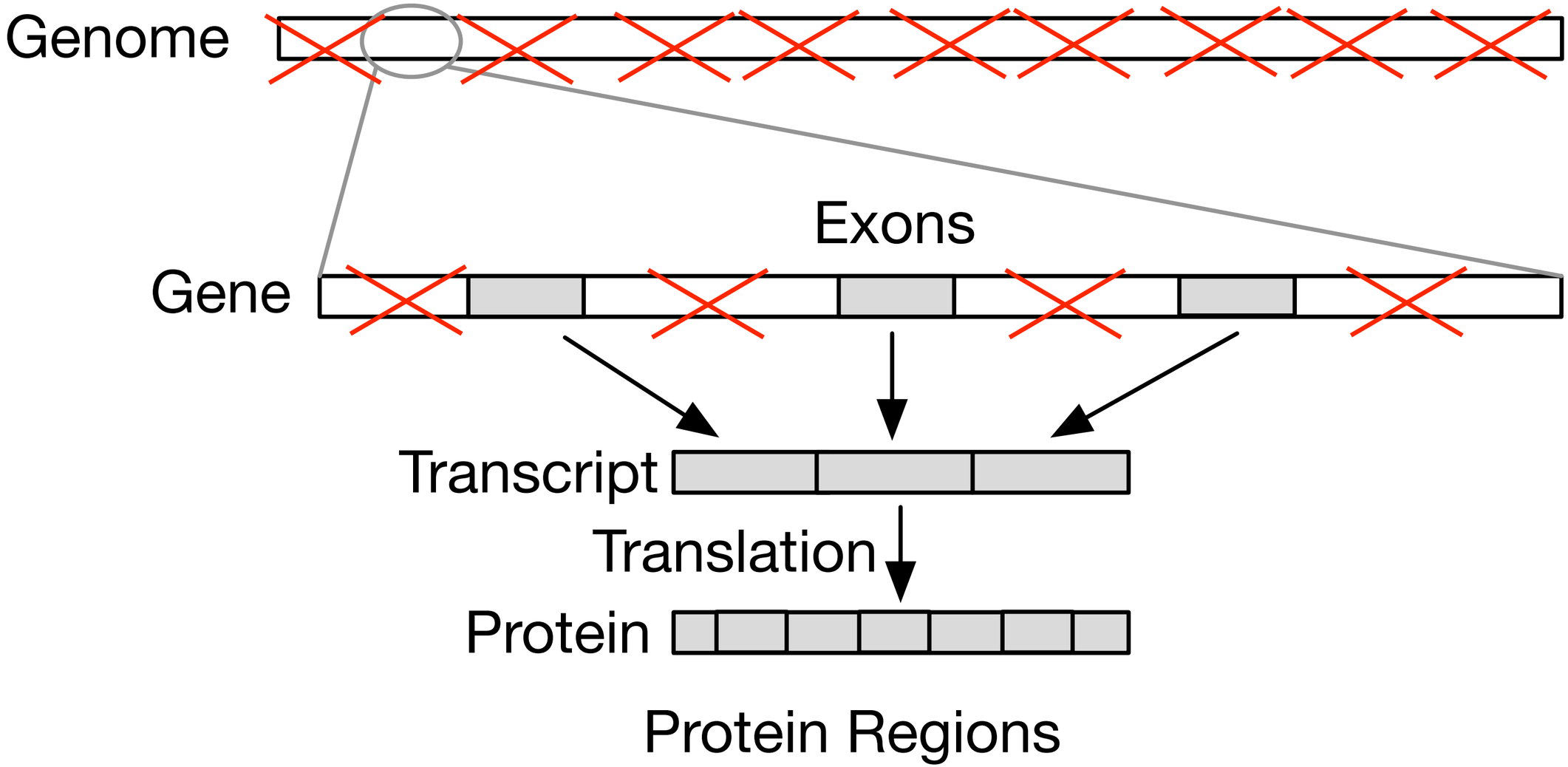
Data: Filtering to relevant biological levels and scales



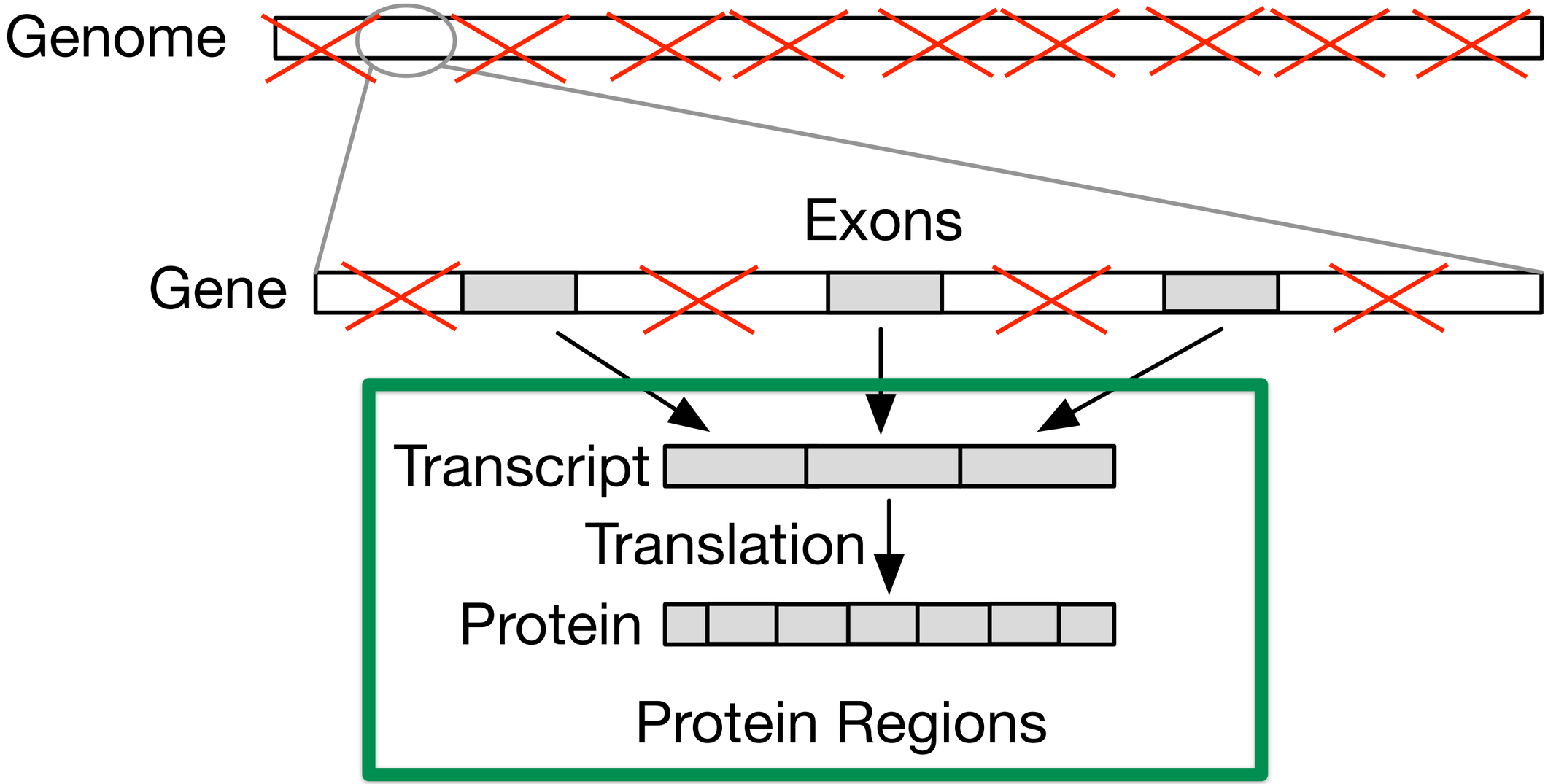
Filter out whole genome; keep genes



Filter out non-exon regions

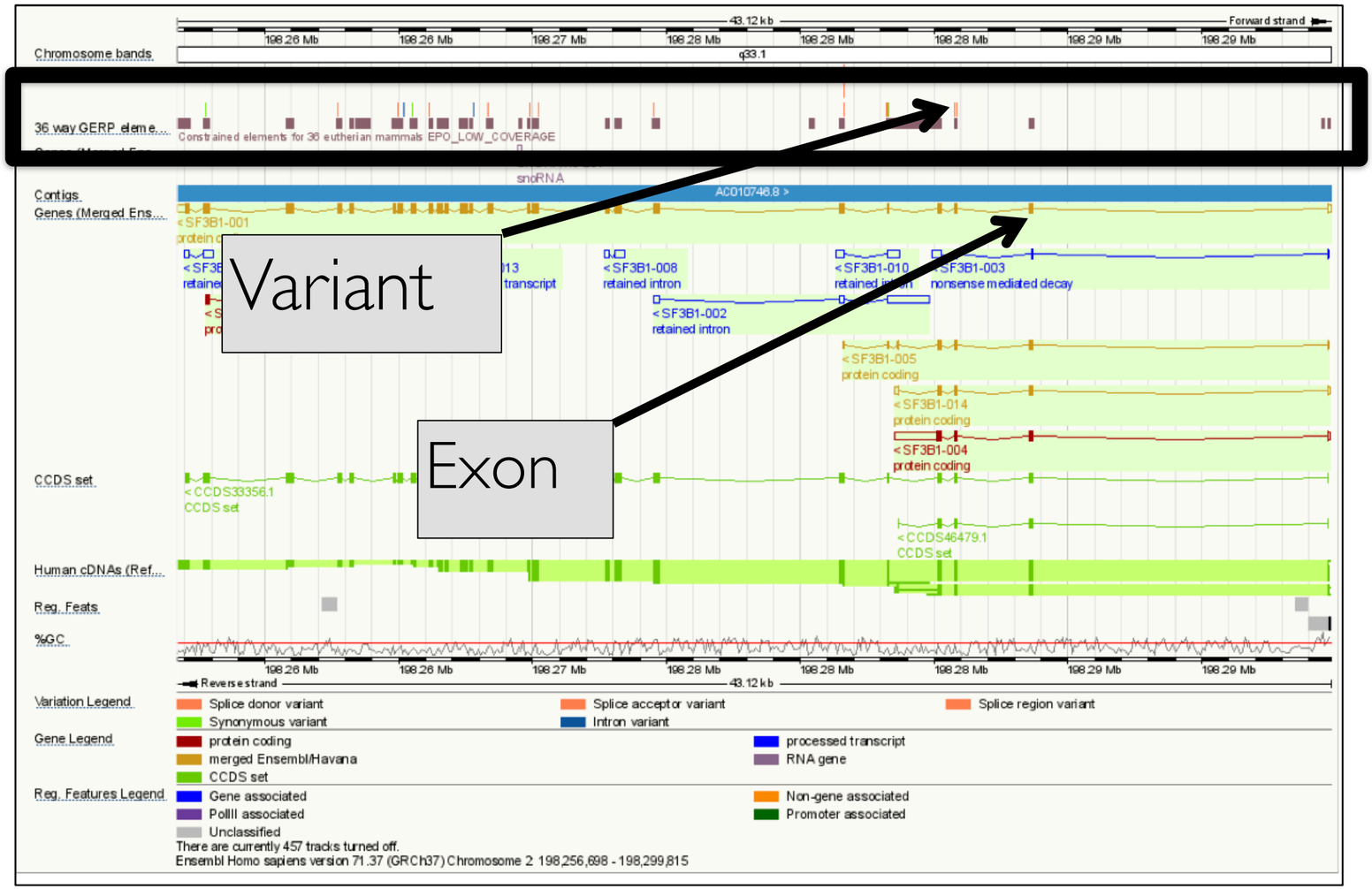


Data abstraction: highly filtered scope



Dominant paradigm: genome browsers

- strengths: flexible and powerful
  - horizontal tracks: user data
  - shared coordinate system: genome coordinates (bp)
- problems
  - tiny features of interest spread out across large extent
    - must zoom far in to inspect known feature, then zoom out and pan to locate next
    - high cognitive load for interaction
    - must already know where to look

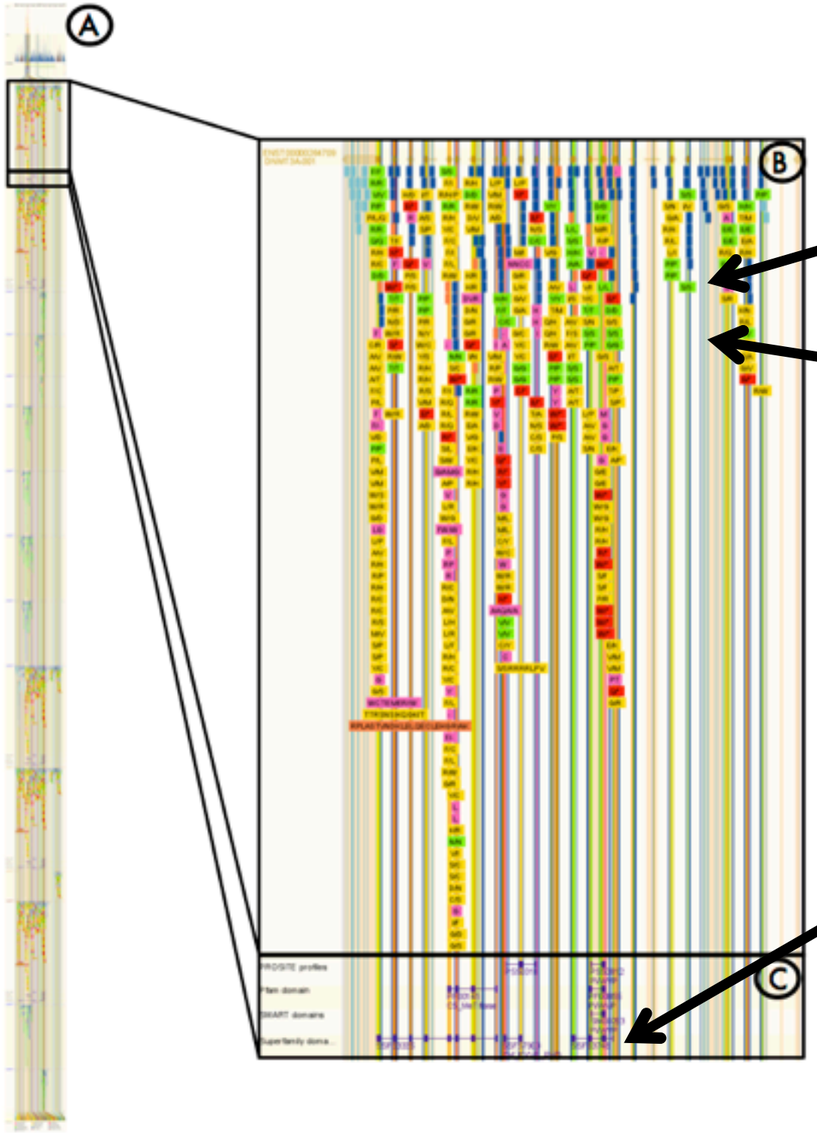


representative example: Ensembl

Chen et al, BMC Bioinformatics 2010.

Features of interest small even in variant-specific view

1st Screen



Exon regions small

Color coding difficult to see

Protein regions overlap on same track

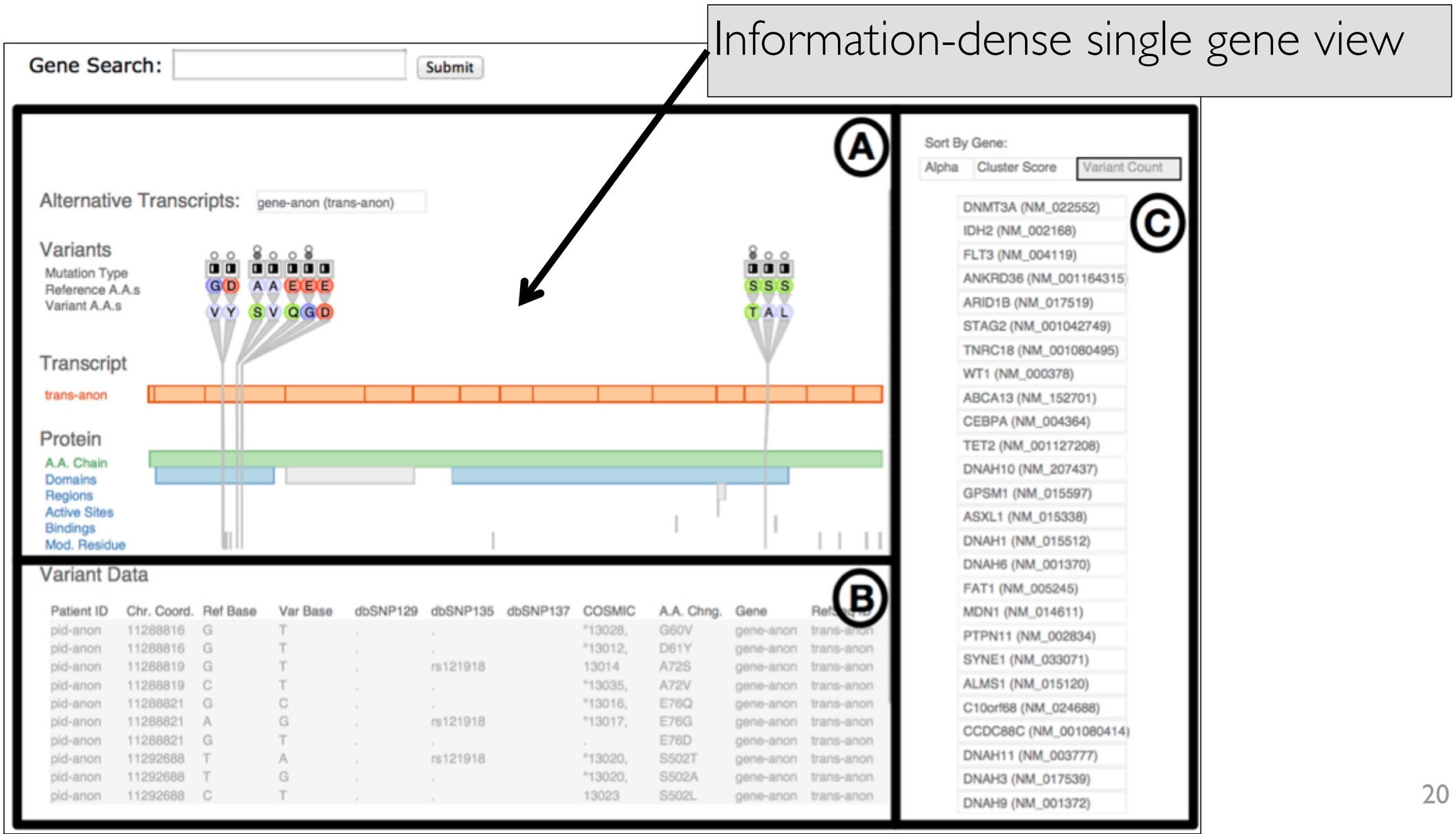
Ensembl Variant Image

Chen et al, BMC Bioinformatics 2010.

Idioms

Variant View

Variant View



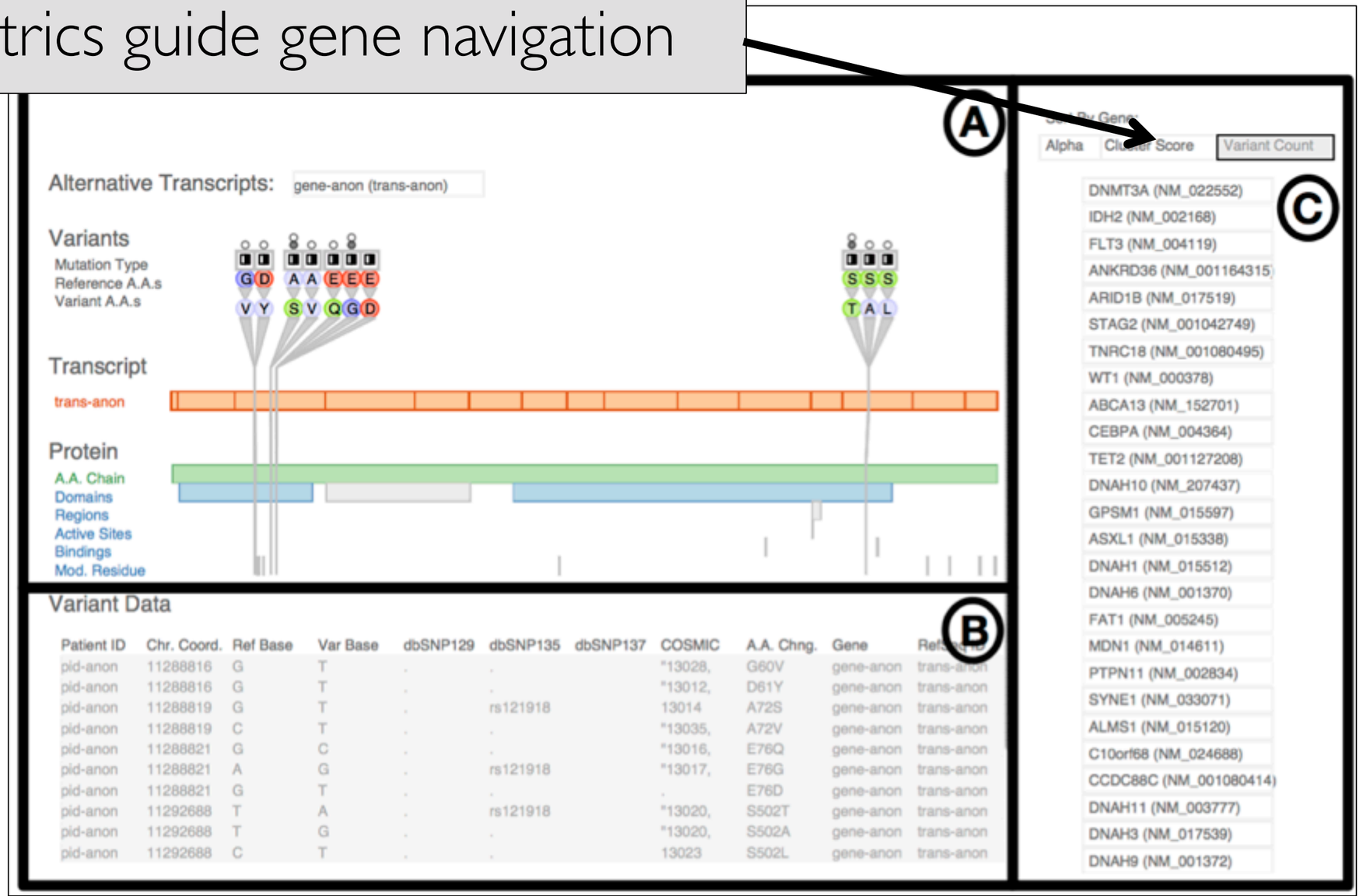
Variant View

Information-dense single gene view

No need for pan and zoom

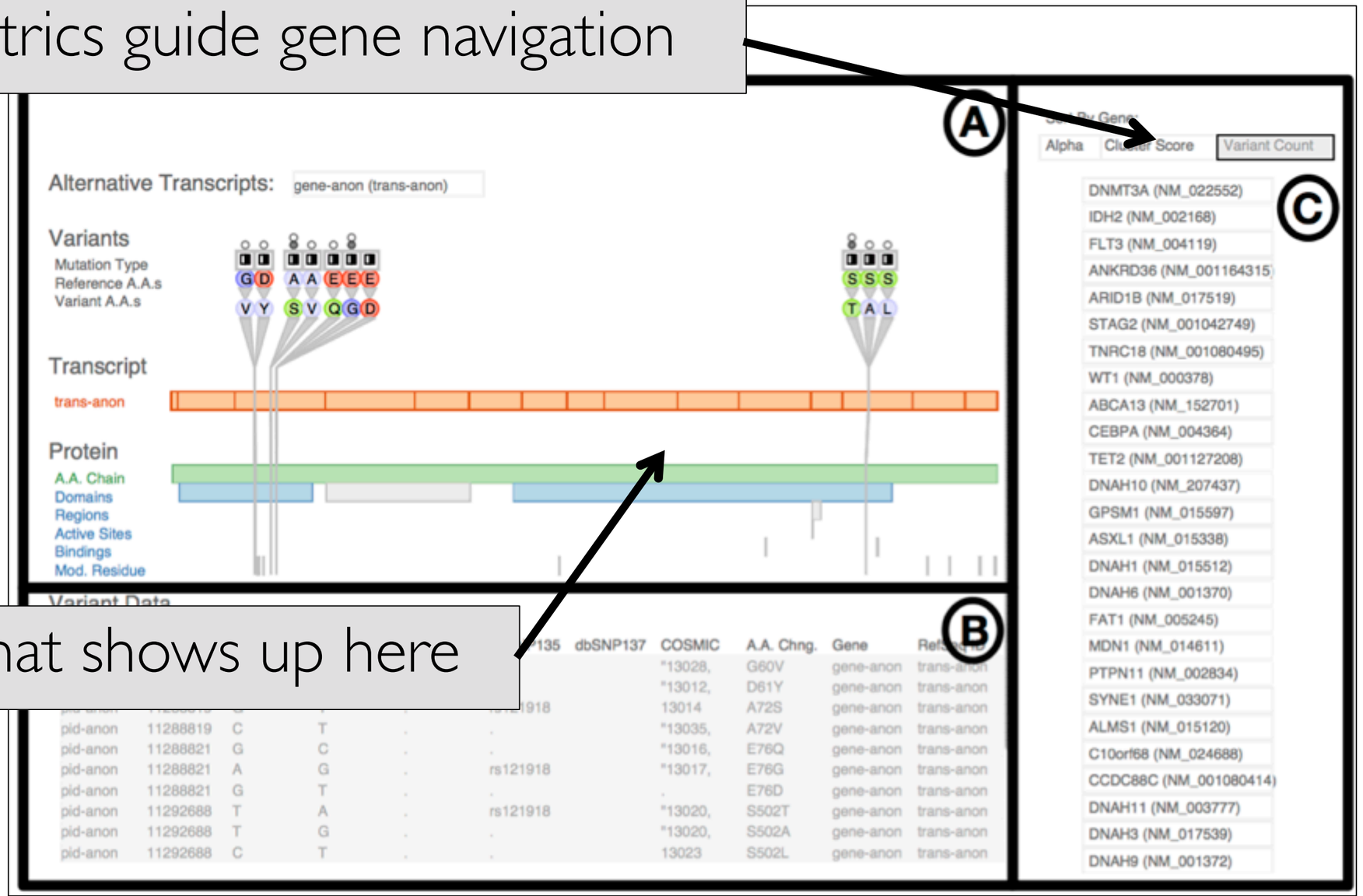
Variant View

Sorting metrics guide gene navigation



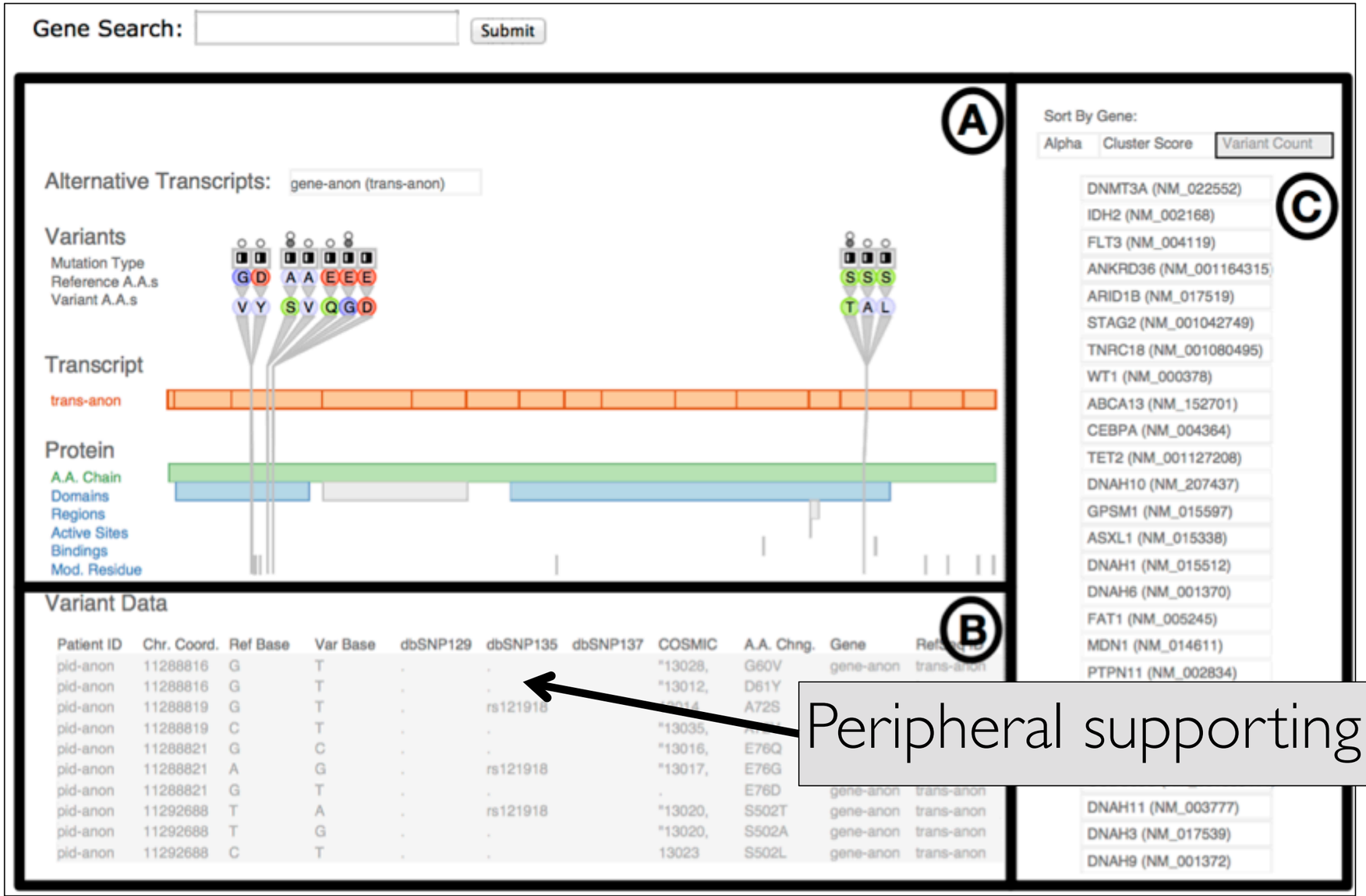
Variant View

Sorting metrics guide gene navigation



Control what shows up here

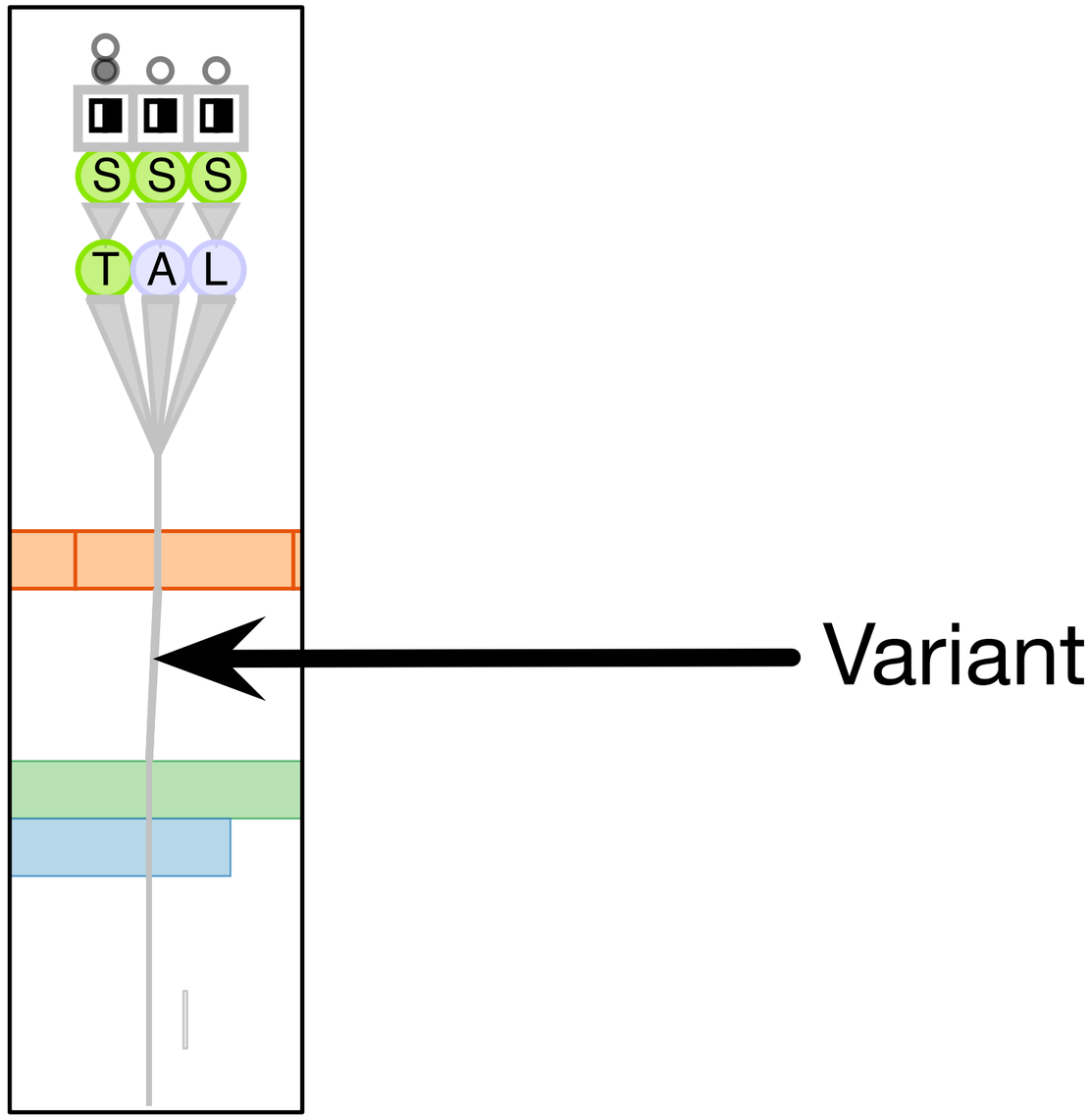
Variant View



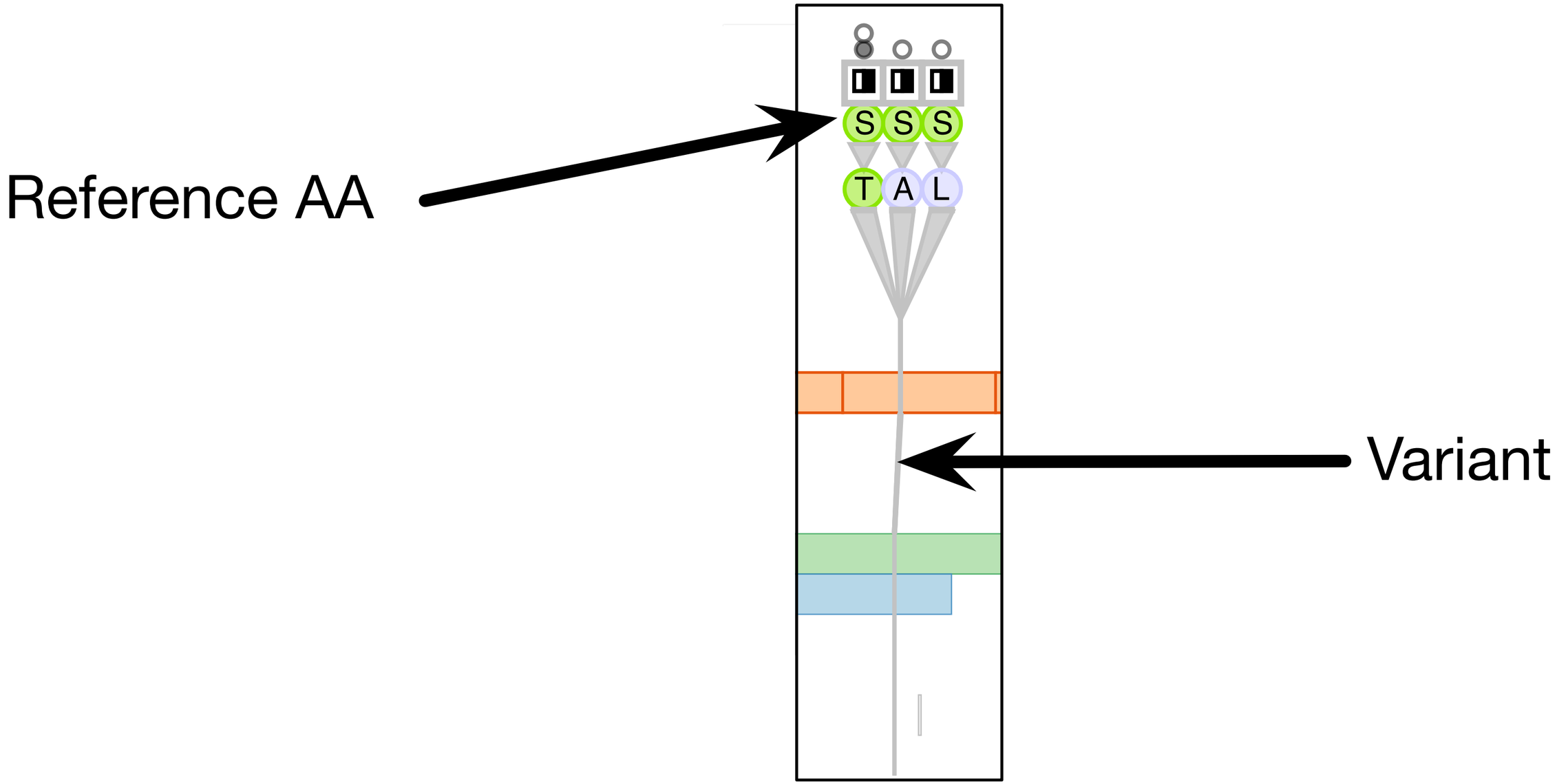
Peripheral supporting data

Design information-dense visual encoding

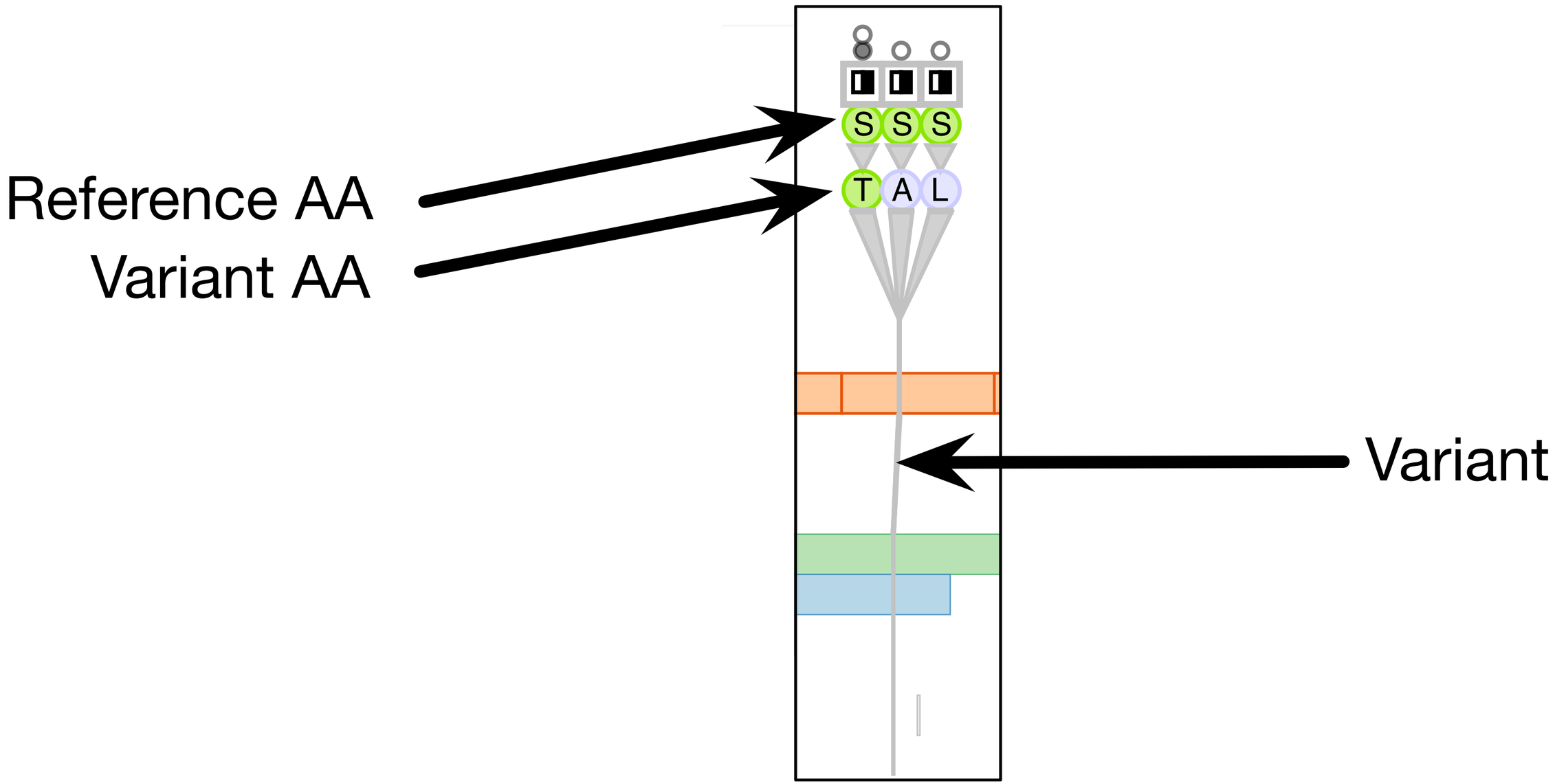
- show all attributes necessary for variant analysis
  - match salience with importance for analysis task
- variant not just a thin line!
- emphasize with high salience
  - collocated variants fan out at top
  - grey variant vertical stroke intersects horizontal colored protein regions



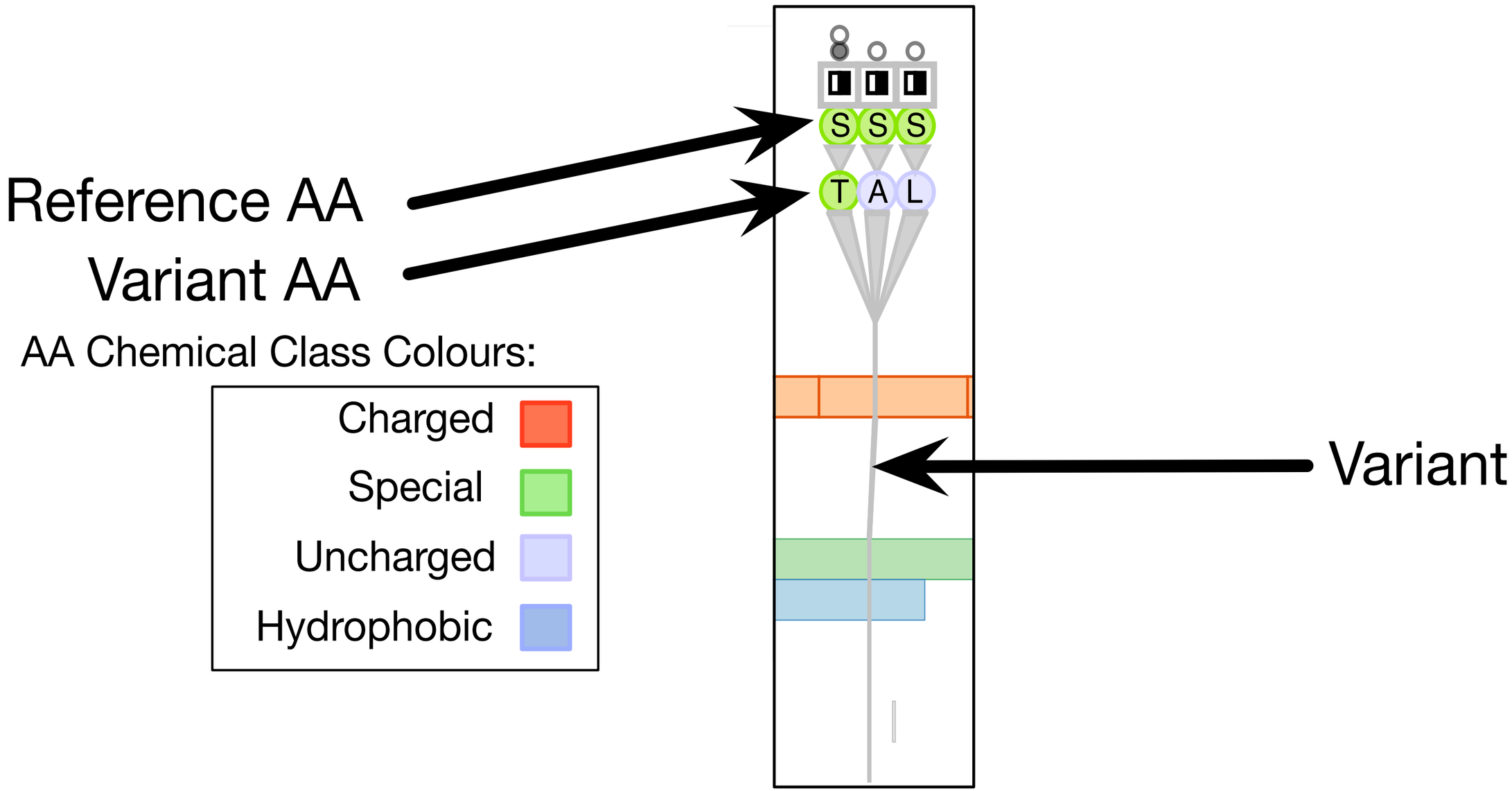
Design information-dense visual encoding



Design information-dense visual encoding



Design information-dense visual encoding



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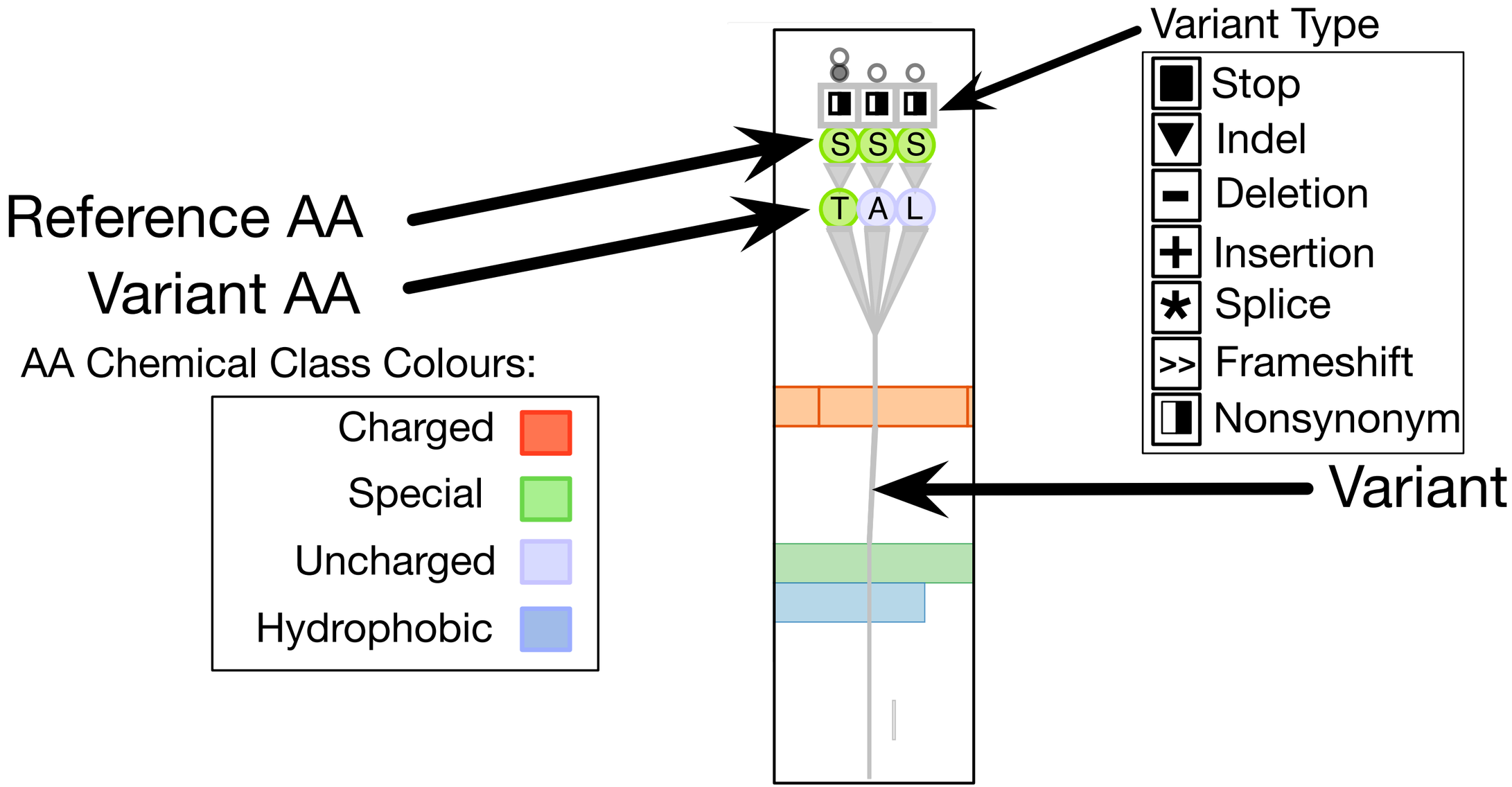

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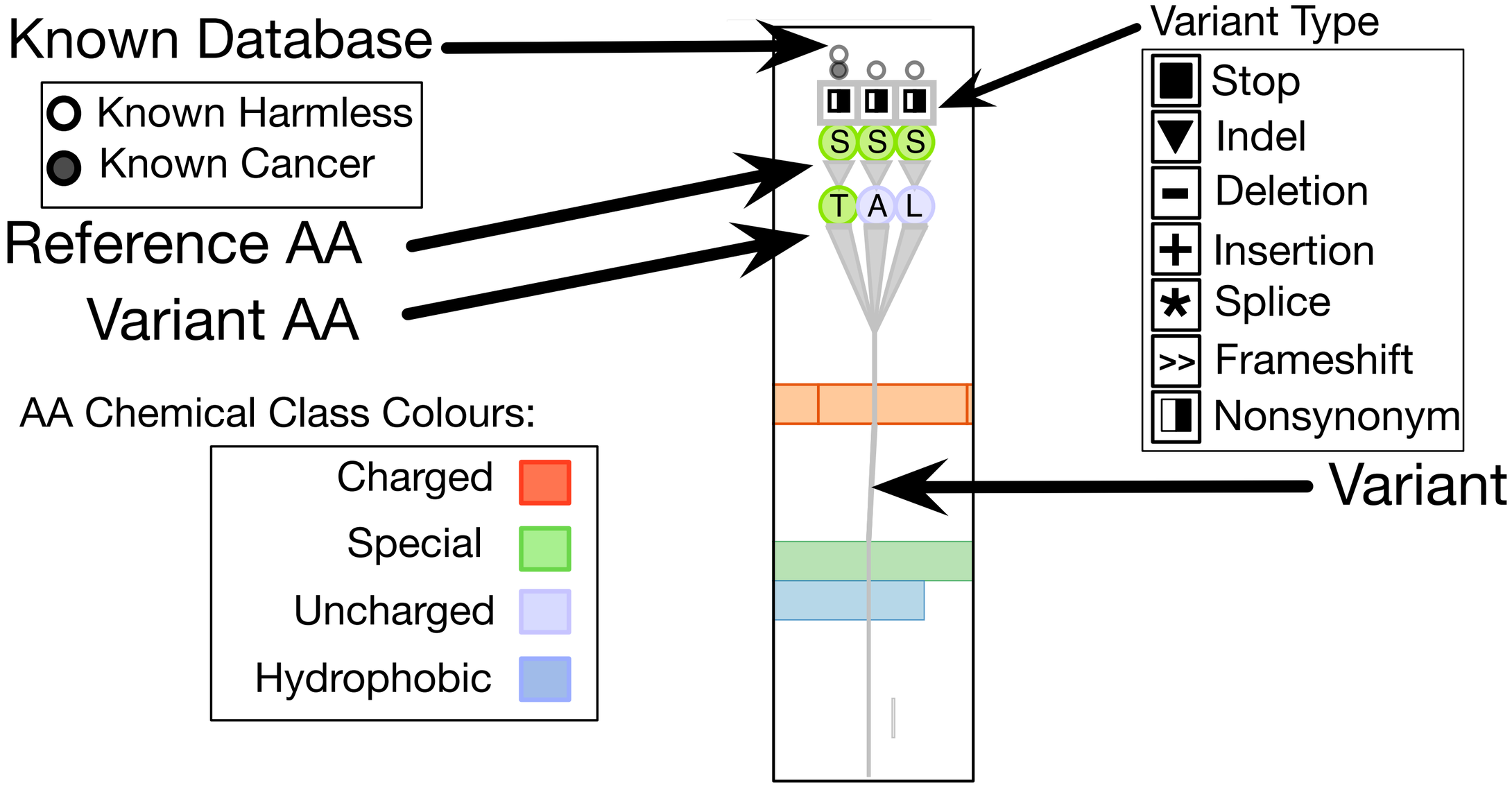

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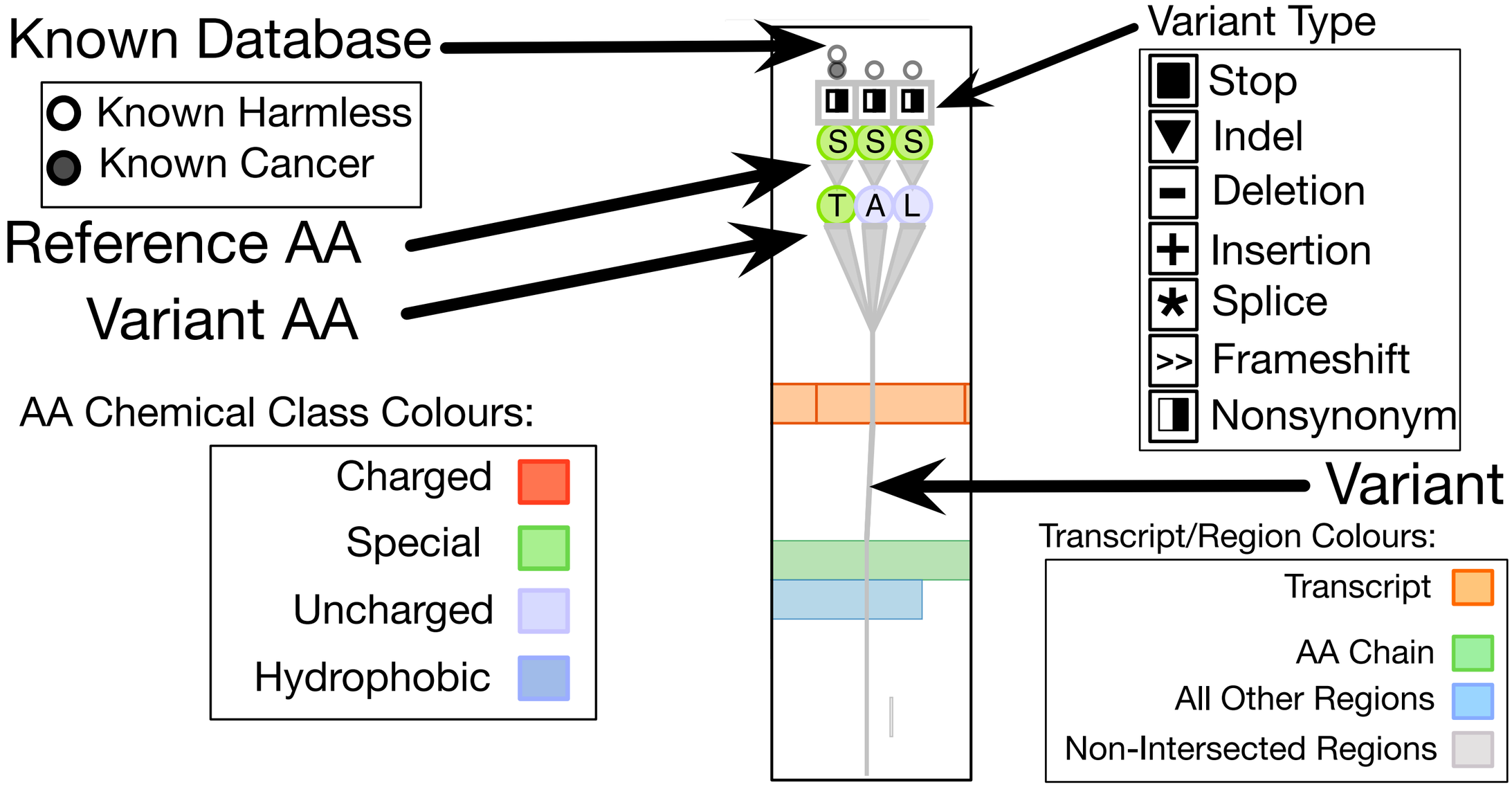
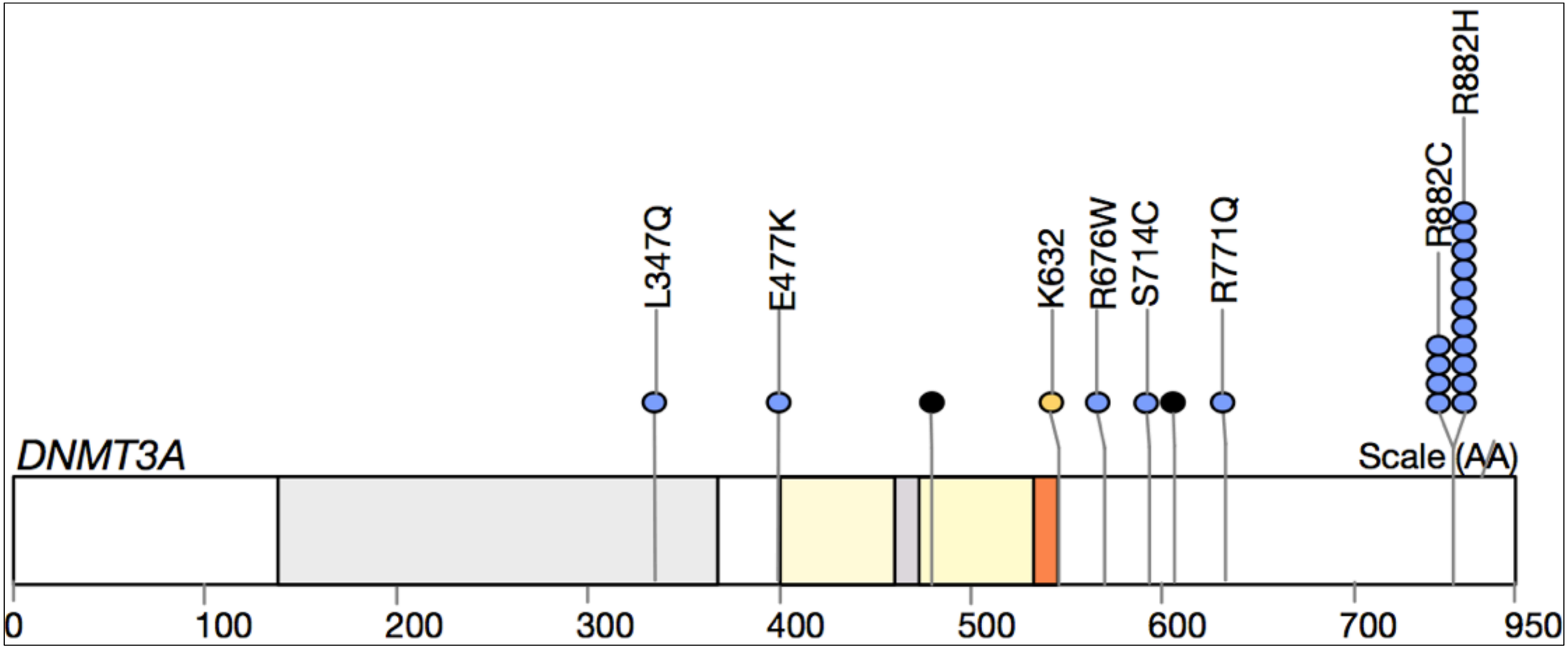


Previous work targeted at variant analysis: MuSiC



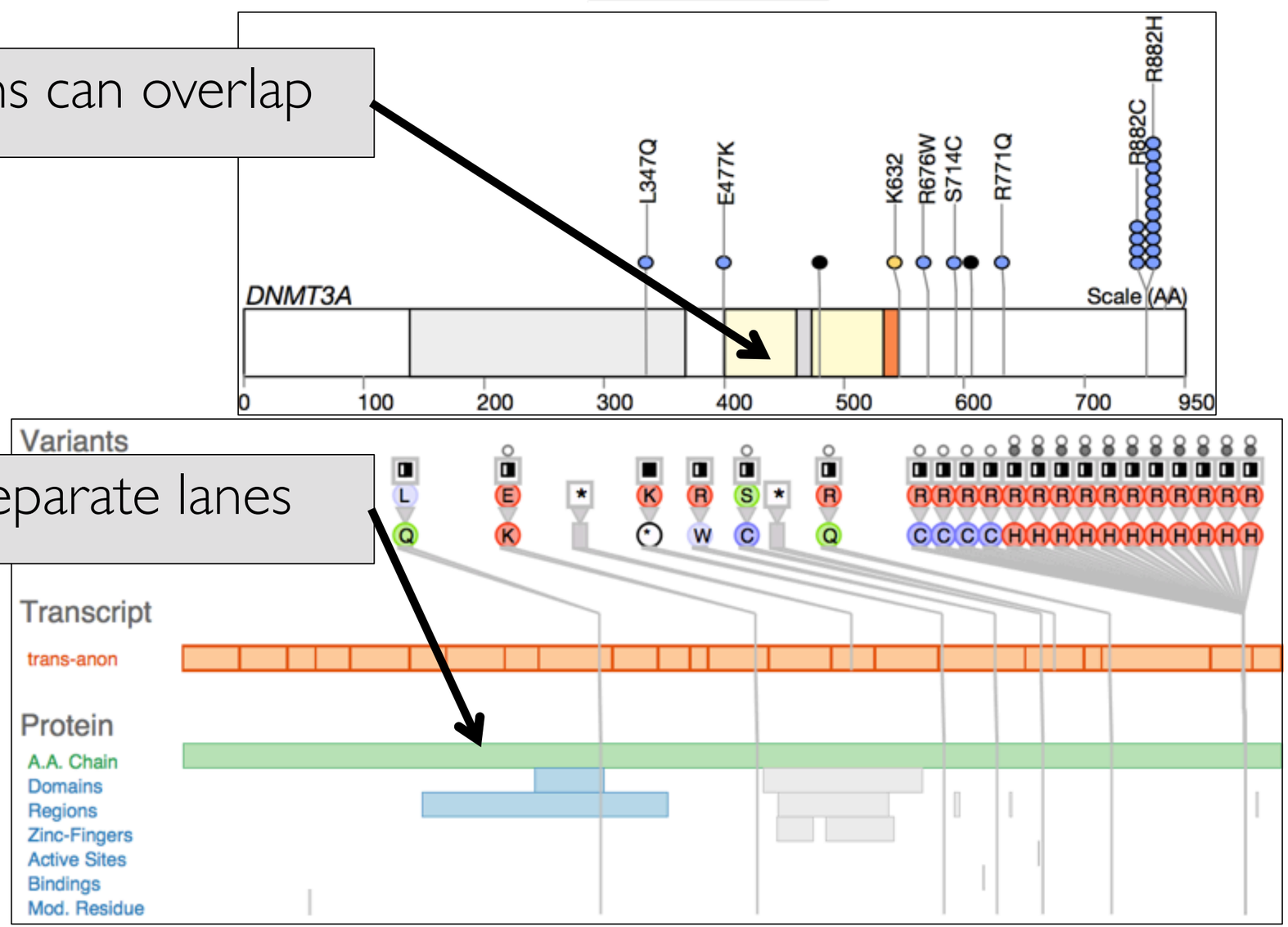
MuSiC

[Dees et al., Genome Research 2012]

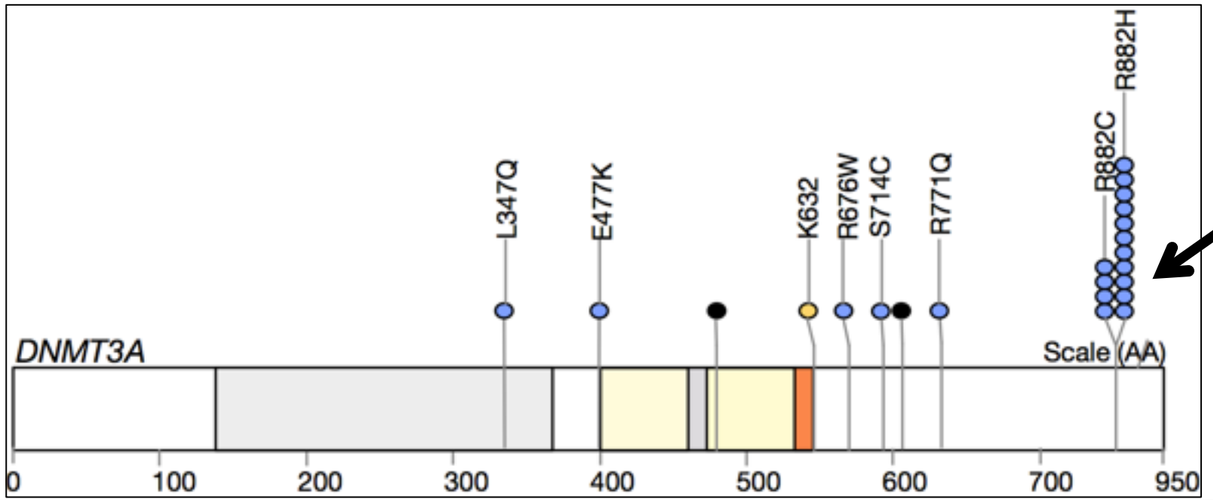
Side-by-side comparison: MuSiC vs Variant View

Protein regions can overlap

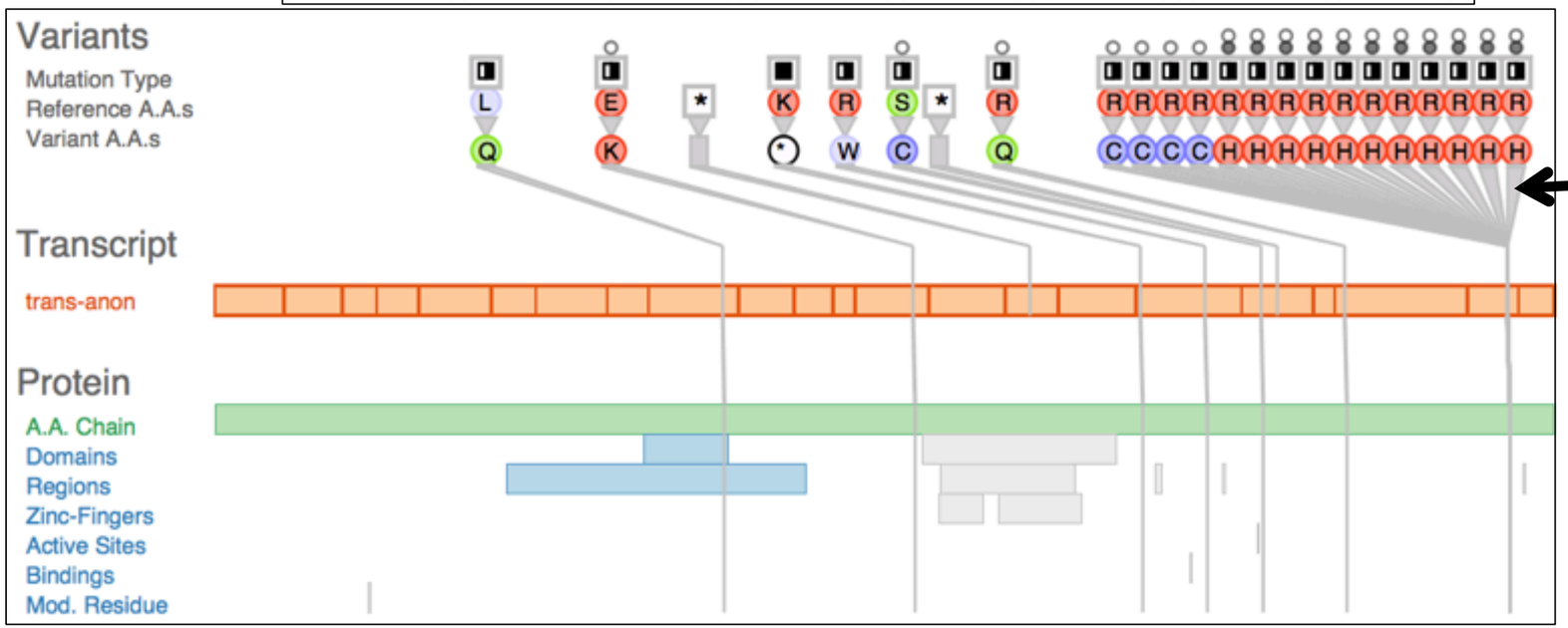
Regions get separate lanes



Side-by-side comparison: MuSiC vs Variant View



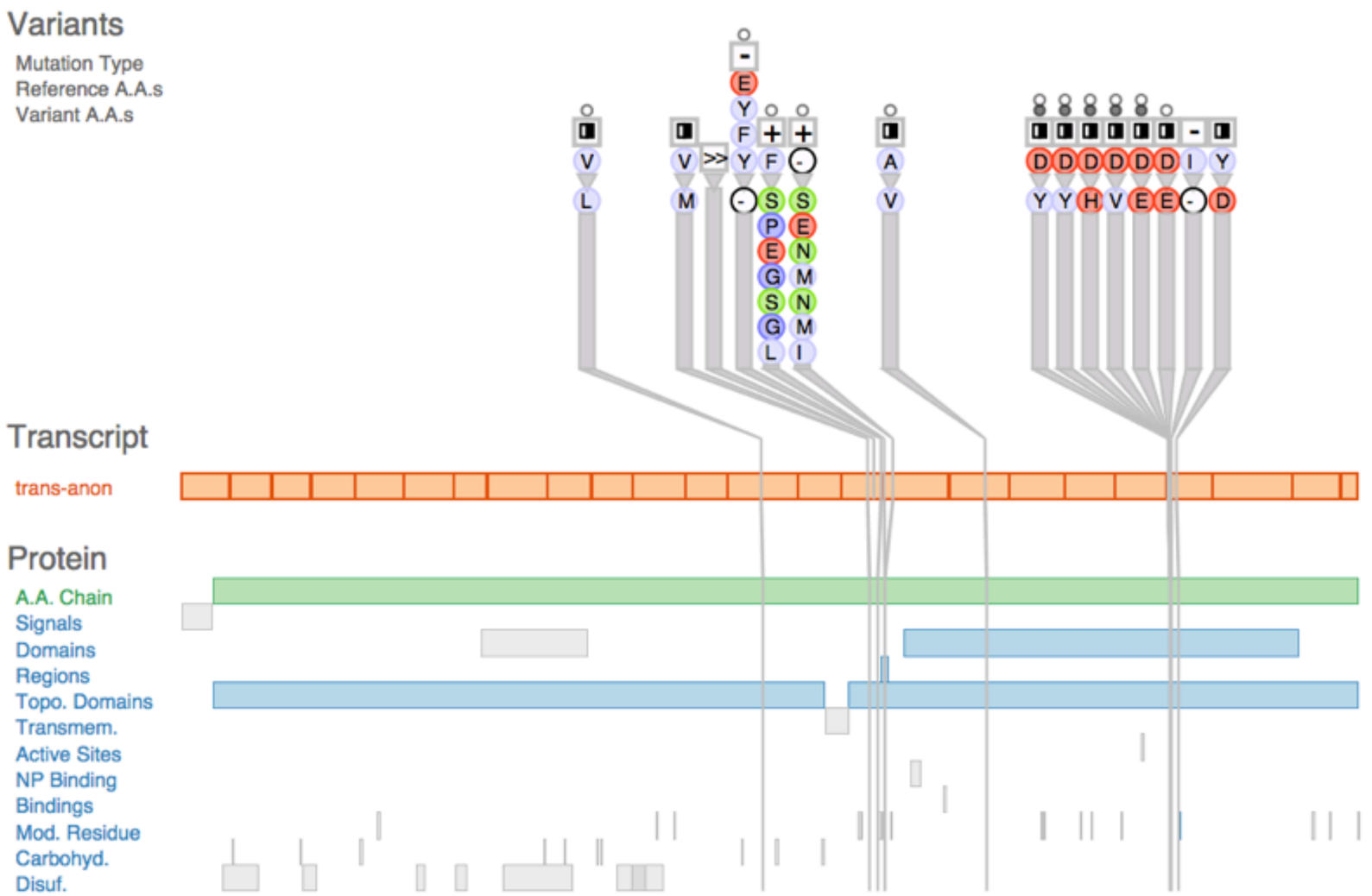
Many collocated variants



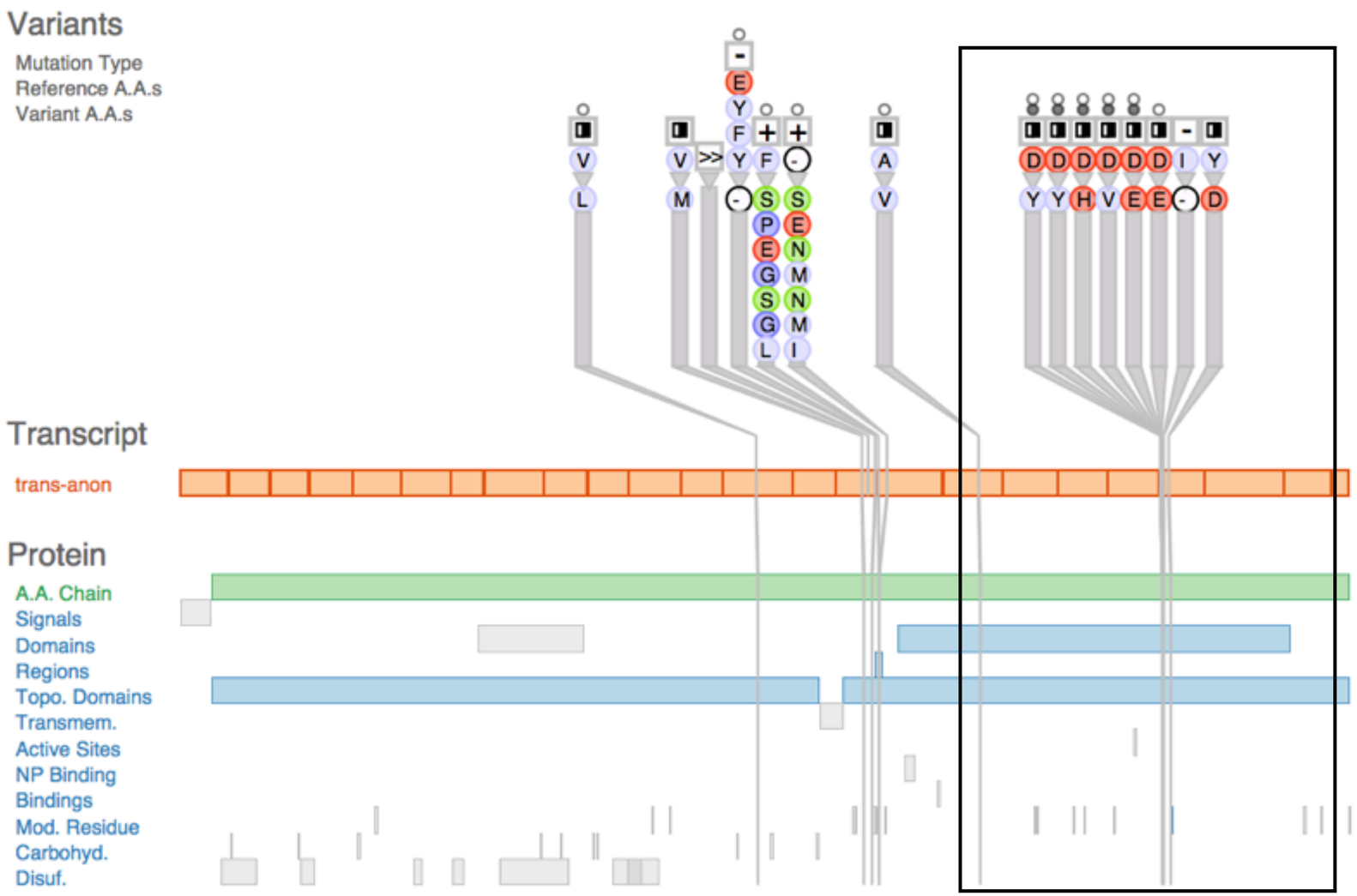
Large bloom of repeated elements: more salient

Results

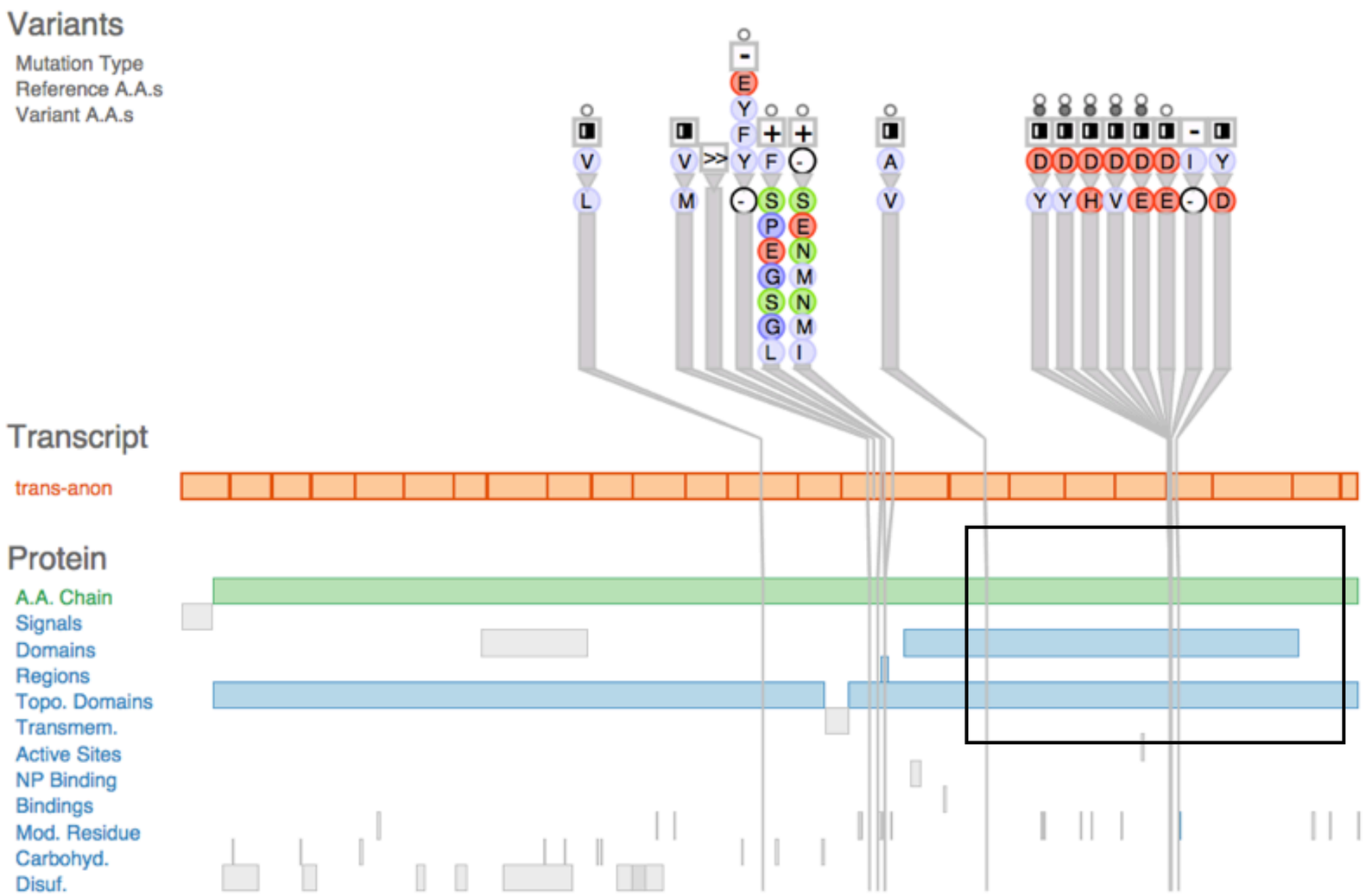
Verify known leukemia gene: Highly scored by sorting metric



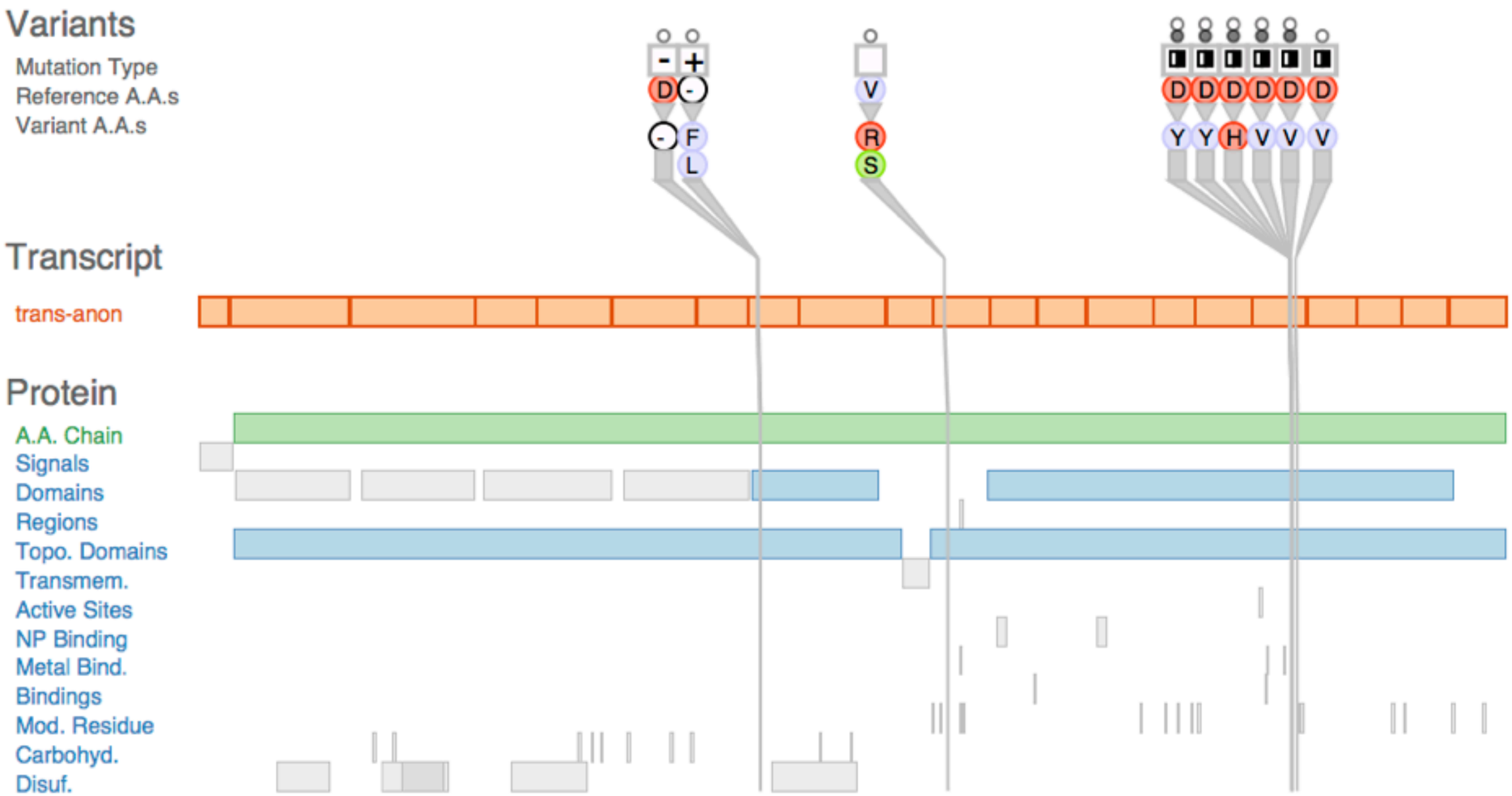
Visual inspection reveals collocation of variants



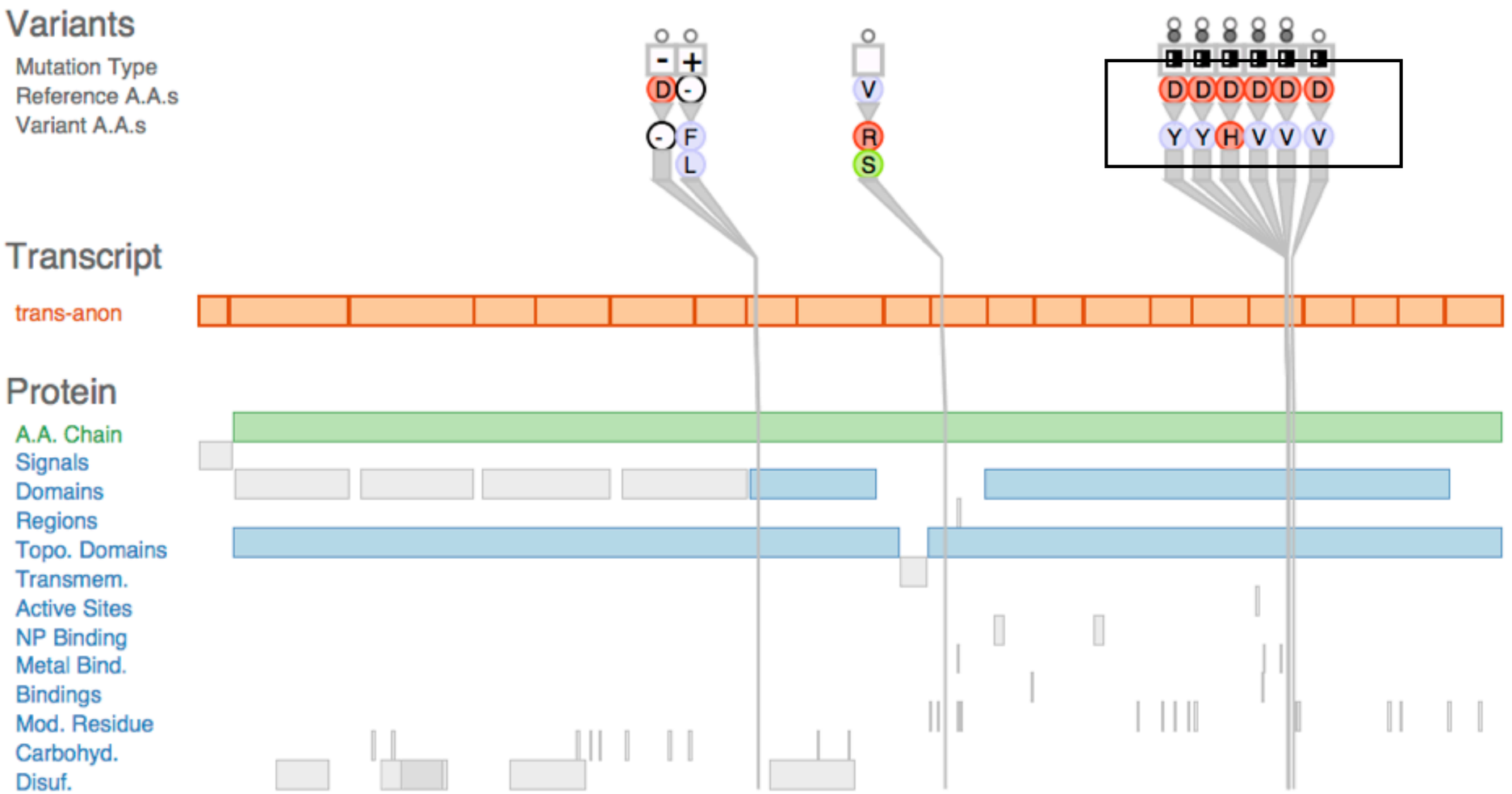
Several functional protein regions affected



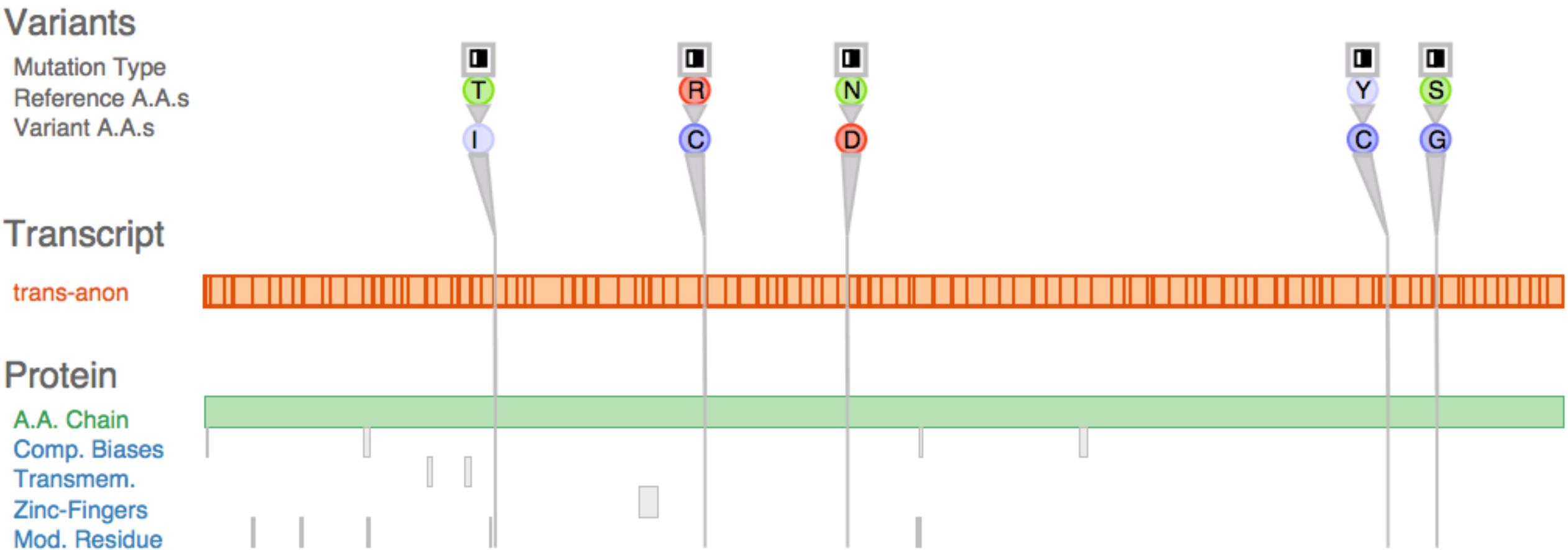
Highly scored by metric: not previously known, good candidate



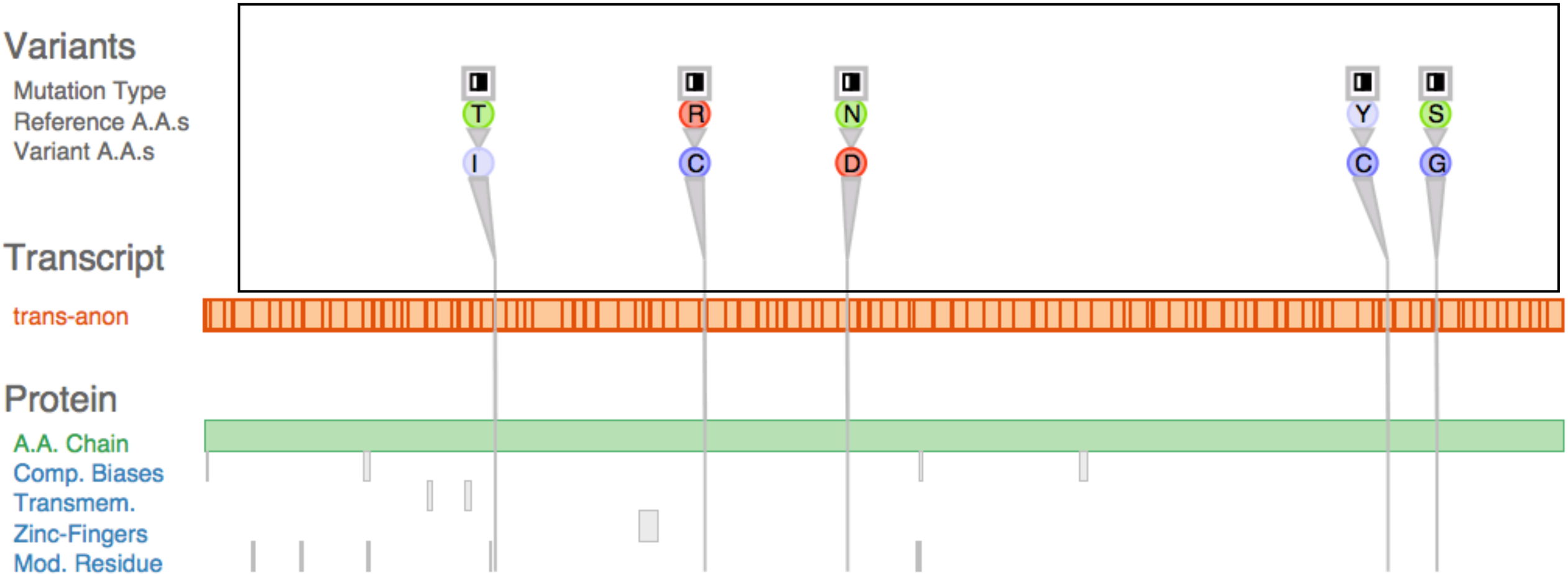
Protein chemical class change evident



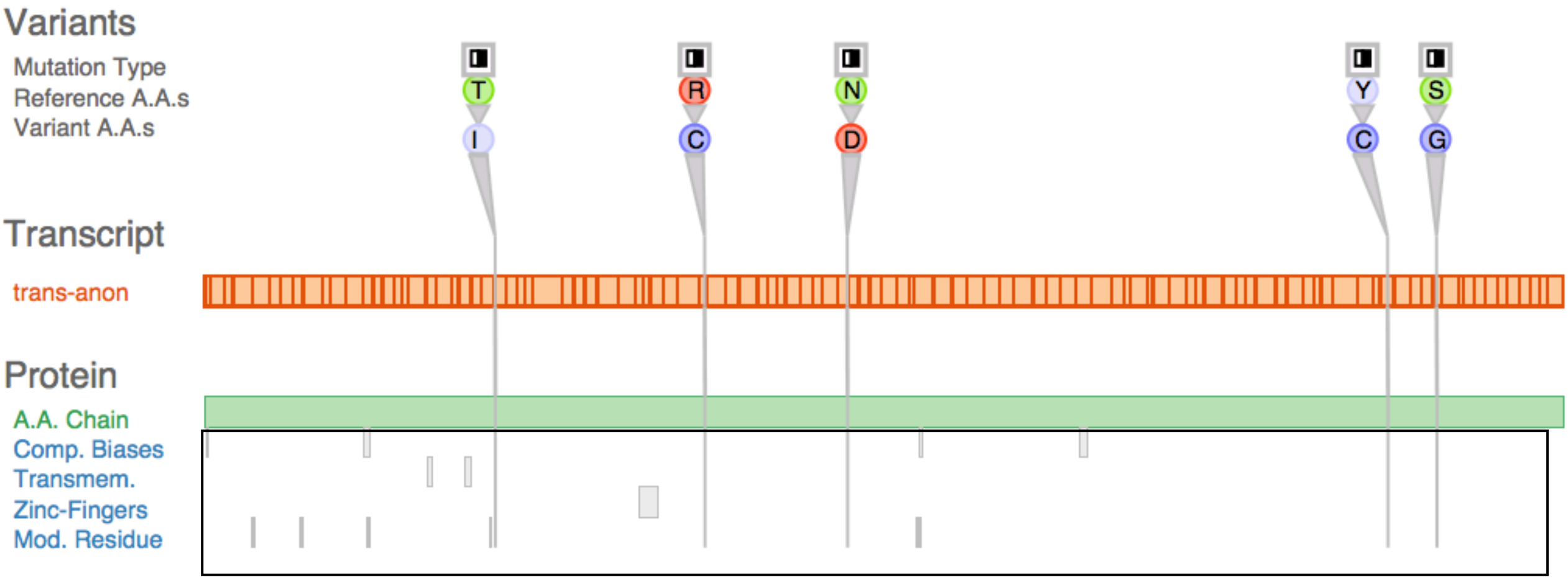
In contrast, low scoring gene



No collocation of variants



Mostly unaffected protein regions



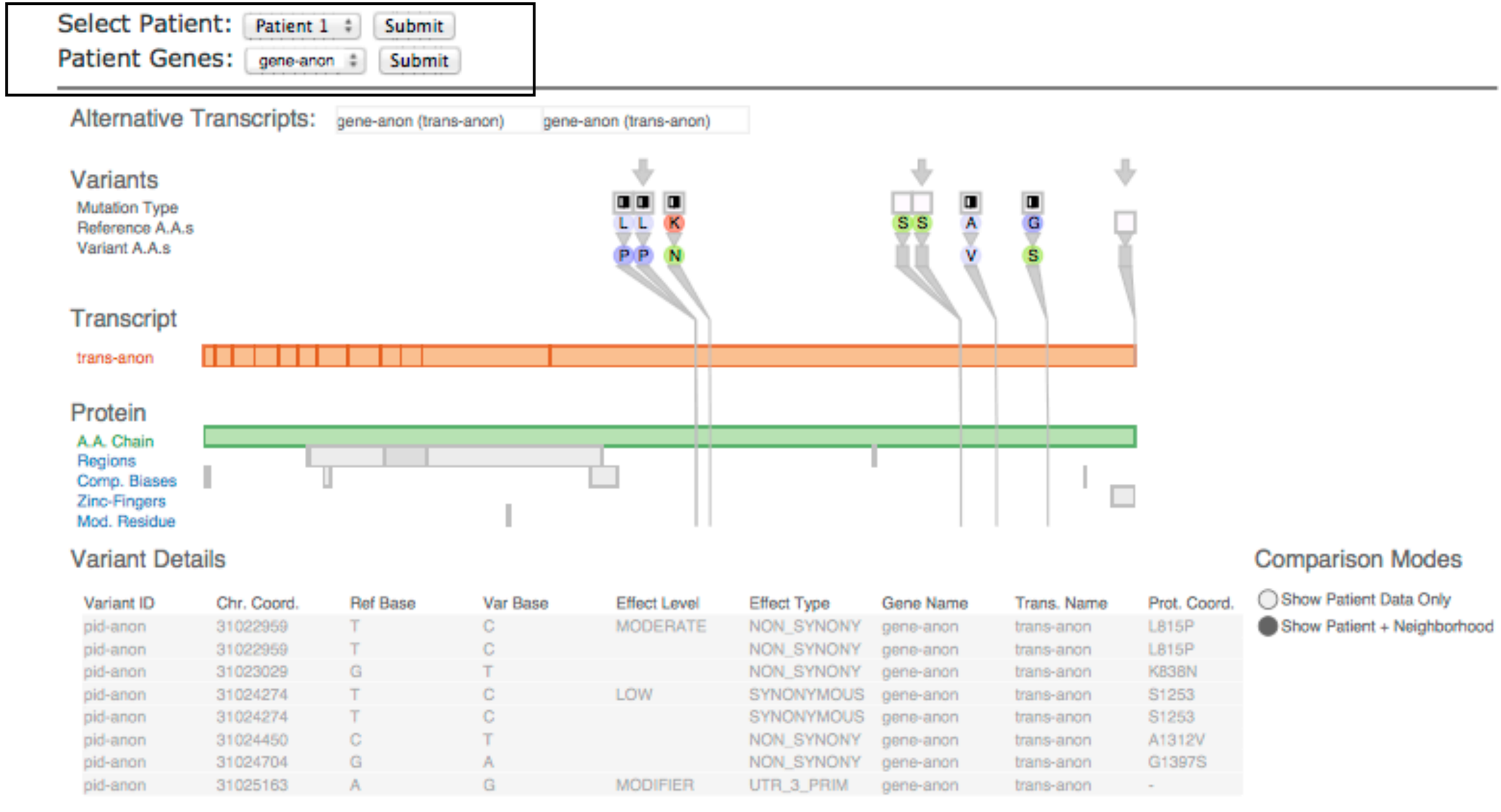
Additional tasks

- task 2: compare patients
  - clinical setting application
  - compare patient data to known harmful variants
  - challenge
    - similarity is loosely understood rather than fully characterized
    - visual inspection for what constitutes a match

Adapted Variant View with minimal changes

Variant ID	Chr. Coord.	Ref Base	Var Base	Effect Level	Effect Type	Gene Name	Trans. Name	Prot. Coord.
pid-anon	31022959	T	C	MODERATE	NON_SYNONY	gene-anon	trans-anon	L815P
pid-anon	31022959	T	C		NON_SYNONY	gene-anon	trans-anon	L815P
pid-anon	31023029	G	T		NON_SYNONY	gene-anon	trans-anon	K838N
pid-anon	31024274	T	C	LOW	SYNONYMOUS	gene-anon	trans-anon	S1253
pid-anon	31024274	T	C		SYNONYMOUS	gene-anon	trans-anon	S1253
pid-anon	31024450	C	T		NON_SYNONY	gene-anon	trans-anon	A1312V
pid-anon	31024704	G	A		NON_SYNONY	gene-anon	trans-anon	G1397S
pid-anon	31025163	A	G	MODIFIER	UTR_3_PRIM	gene-anon	trans-anon	-

Navigate through patient data with list



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pid-anon	31023029	G	T		NON_SYNONY	gene-anon	trans-anon	K838N
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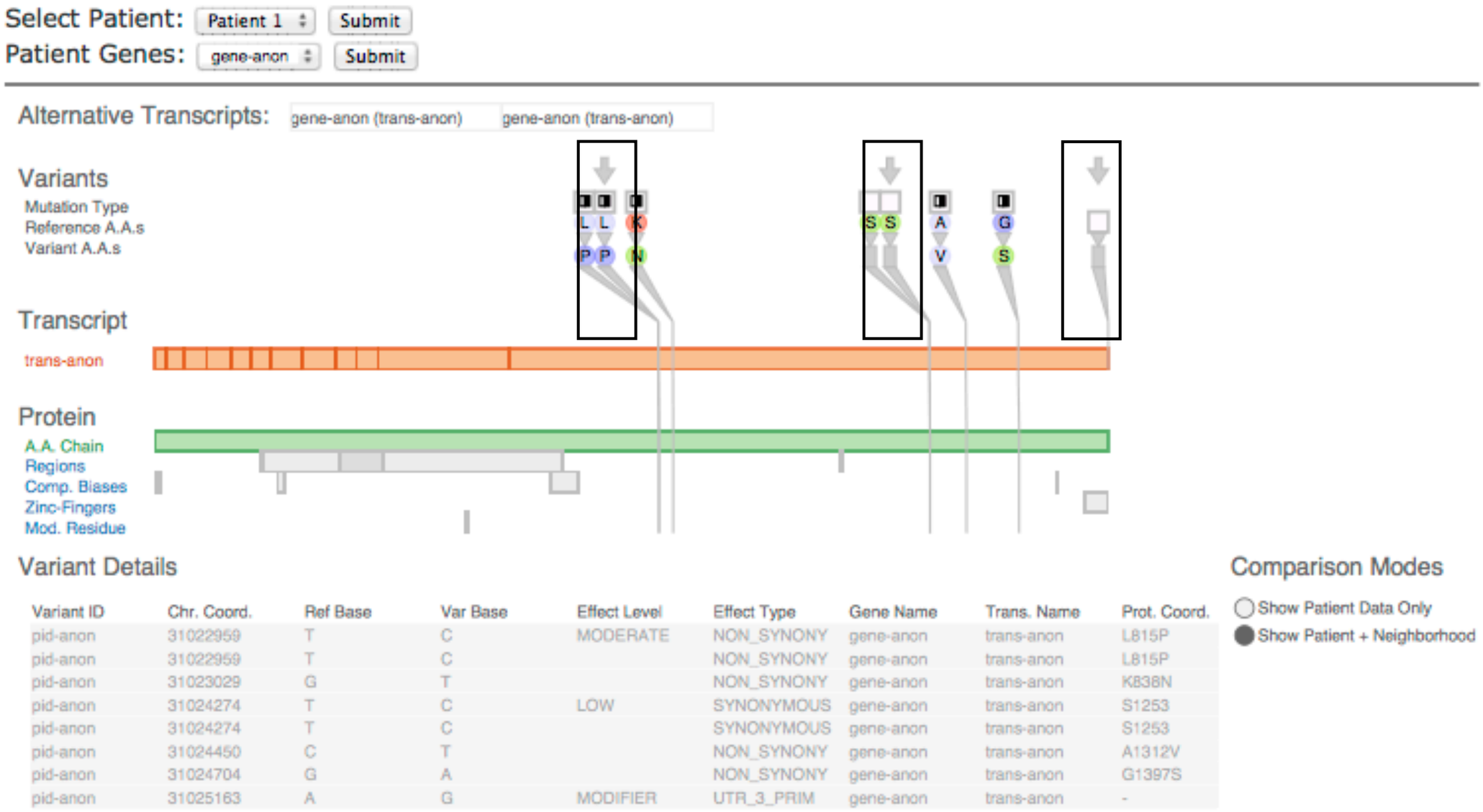
pid-anon	31024450	C	T		NON_SYNONY	gene-anon	trans-anon	A1312V
pid-anon	31024704	G	A		NON_SYNONY	gene-anon	trans-anon	G1397S
pid-anon	31025163	A	G	MODIFIER	UTR_3_PRIM	gene-anon	trans-anon	-

Patient data emphasized with arrows



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pid-anon	31023029	G	T		NON_SYNONY	gene-anon	trans-anon	K838N
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pid-anon	31025163	A	G	MODIFIER	UTR_3_PRIM	gene-anon	trans-anon	-

Patient has same harmful L to P mutation

Variant ID	Chr. Coord.	Ref Base	Var Base	Effect Level	Effect Type	Gene Name	Trans. Name	Prot. Coord.
pid-anon	31022959	T	C	MODERATE	NON_SYNONY	gene-anon	trans-anon	L815P
pid-anon	31022959	T	C		NON_SYNONY	gene-anon	trans-anon	L815P
pid-anon	31023029	G	T		NON_SYNONY	gene-anon	trans-anon	K838N
pid-anon	31024274	T	C	LOW	SYNONYMOUS	gene-anon	trans-anon	S1253
pid-anon	31024274	T	C		SYNONYMOUS	gene-anon	trans-anon	S1253
pid-anon	31024450	C	T		NON_SYNONY	gene-anon	trans-anon	A1312V
pid-anon	31024704	G	A		NON_SYNONY	gene-anon	trans-anon	G1397S
pid-anon	31025163	A	G	MODIFIER	UTR_3_PRIM	gene-anon	trans-anon	-

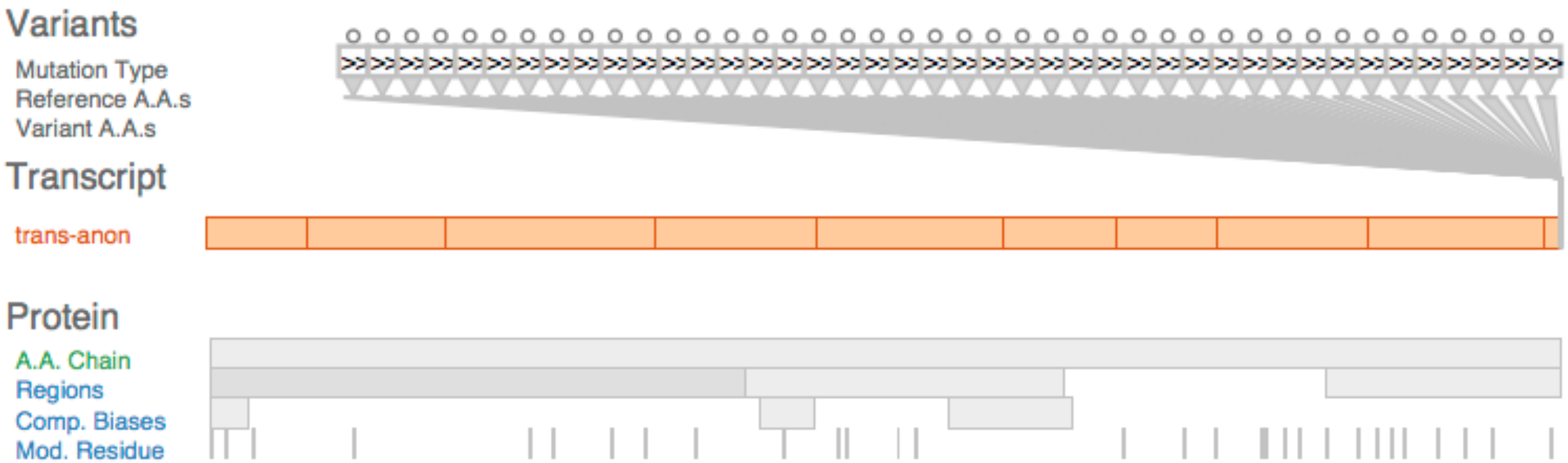
Nonmatching variants

Variant ID	Chr. Coord.	Ref Base	Var Base	Effect Level	Effect Type	Gene Name	Trans. Name	Prot. Coord.
pid-anon	31022959	T	C	MODERATE	NON_SYNONY	gene-anon	trans-anon	L815P
pid-anon	31022959	T	C		NON_SYNONY	gene-anon	trans-anon	L815P
pid-anon	31023029	G	T		NON_SYNONY	gene-anon	trans-anon	K838N
pid-anon	31024274	T	C	LOW	SYNONYMOUS	gene-anon	trans-anon	S1253
pid-anon	31024274	T	C		SYNONYMOUS	gene-anon	trans-anon	S1253
pid-anon	31024450	C	T		NON_SYNONY	gene-anon	trans-anon	A1312V
pid-anon	31024704	G	A		NON_SYNONY	gene-anon	trans-anon	G1397S
pid-anon	31025163	A	G	MODIFIER	UTR_3_PRIM	gene-anon	trans-anon	-

Additional tasks

- task 3: debug pipeline
  - data cleansing before analysis
  - analysts originally thought pipeline fully debugged
    - no perceived need for vis support

Tool revealed errors in the data



The tool exposed artifacts in the data that slid past at least two rounds of quality metric filtering … this type of problem would not have been caught by our previous, automated methods.

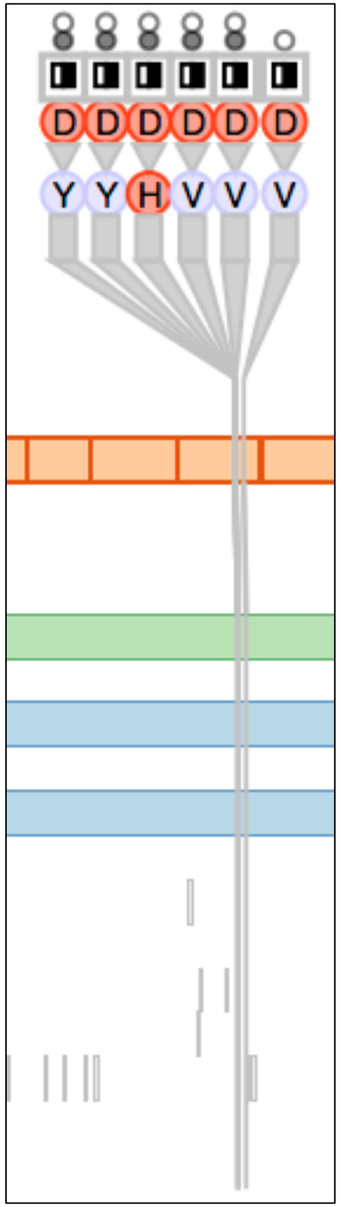
- Analyst 3

Reflections: vis design guidelines

- transferrable to other domains
  - specialize first, generalize later
    - good for domains where with complex, multi-scale data
    - difficult to judge a priori which design elements will generalize
  - high-level considerations
    - identifying scales of interest
    - what to visually encode directly vs what to support through interaction
    - when (and how) to eliminate navigation

Conclusions

- visual variant impact assessment
  - designed, implemented, and deployed tool for
- originally designed for Discover Genes task
  - adapted to two others with minimal changes
- features
  - navigation-free main overview at gene level
  - reveal genes of interest through sorting by new derived metrics
- major considerations
  - what to show
    - filtering data scope
  - how to show it
    - carefully selected visual encodings



Further Information

- paper page
  - **http://www.cs.ubc.ca/labs/imager/tr/2012/VariantView/**
- open source software download
  - http://www.cs.ubc.ca/labs/imager/tr/2013/VariantView/VariantViewSoftware/
- further info
  - http://www.cs.ubc.ca/~tmm/talks.html#bioit14 (this talk, and many others)
  - http://www.cs.ubc.ca/group/infovis (papers, software, videos)
- acknowledgements
  - funding: Vancouver Institute for Visual Analytics (VIVA), Aeroinfo/Boeing, Mitacs
  - collaborators at the GSC
    - Dr. Aly Karsan
    - Rod Docking
    - Dr. Linda Chang
    - Dr. Gerben Duns
    - Simon Chang