Variant View

Genomics, Big Data, and Patient Privacy Implications

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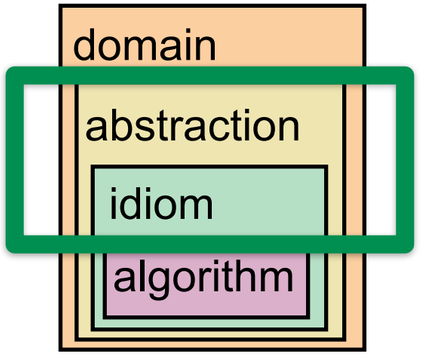
THINK Conference
6 Nov 2015, Santa Cruz CA

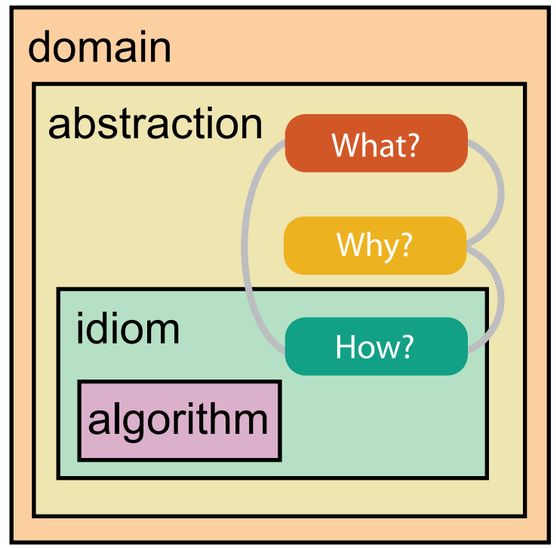
http://www.cs.ubc.ca/~tmm/talks.html#think15 **@tamaramunzner**

Visualization analysis framework: Four levels, three questions

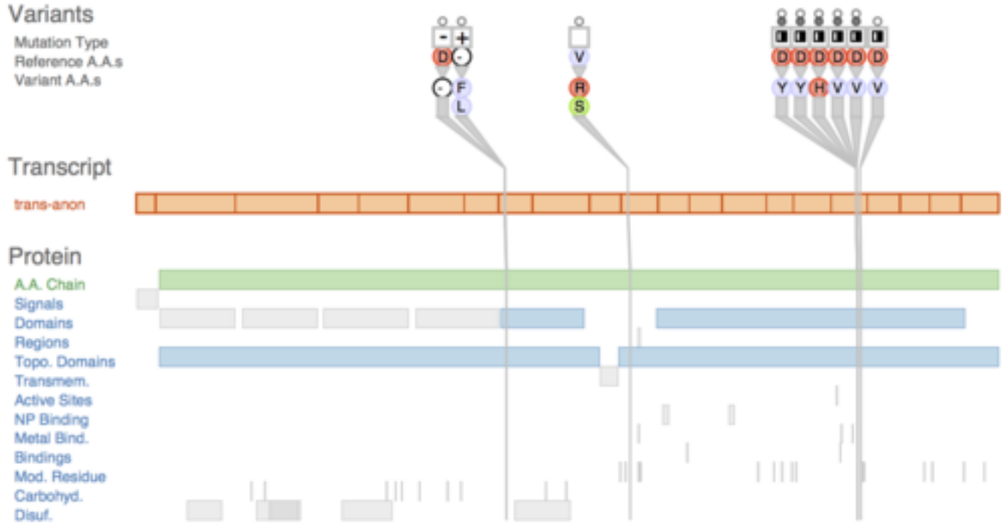
- *domain* situation
  - who are the target users?
- *abstraction*
  - translate from specifics of domain to vocabulary of vis
  - **what** is shown? **data abstraction**
    - often don't just draw what you're given: transform to new form
  - **why** is the user looking at it? **task abstraction**
- *idiom*
  - **how** is it shown?
    - **visual encoding idiom**: how to draw
    - **interaction idiom**: how to manipulate
- *algorithm*
  - efficient computation



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



[A Multi-Level Typology of Abstract Visualization Tasks
Brehmer and Munzner. IEEE TVCG 19(12):2376-2385, 2013 (Proc. InfoVis 2013).]



Variant View

Visualizing Sequence Variants in their Gene Context

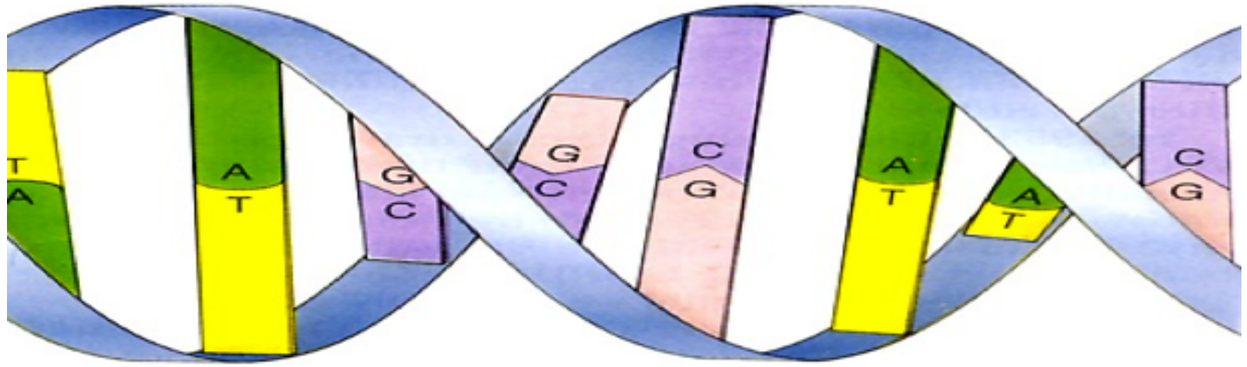
joint work with:
Joel Ferstay, Cydney Nielsen

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 person's 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?

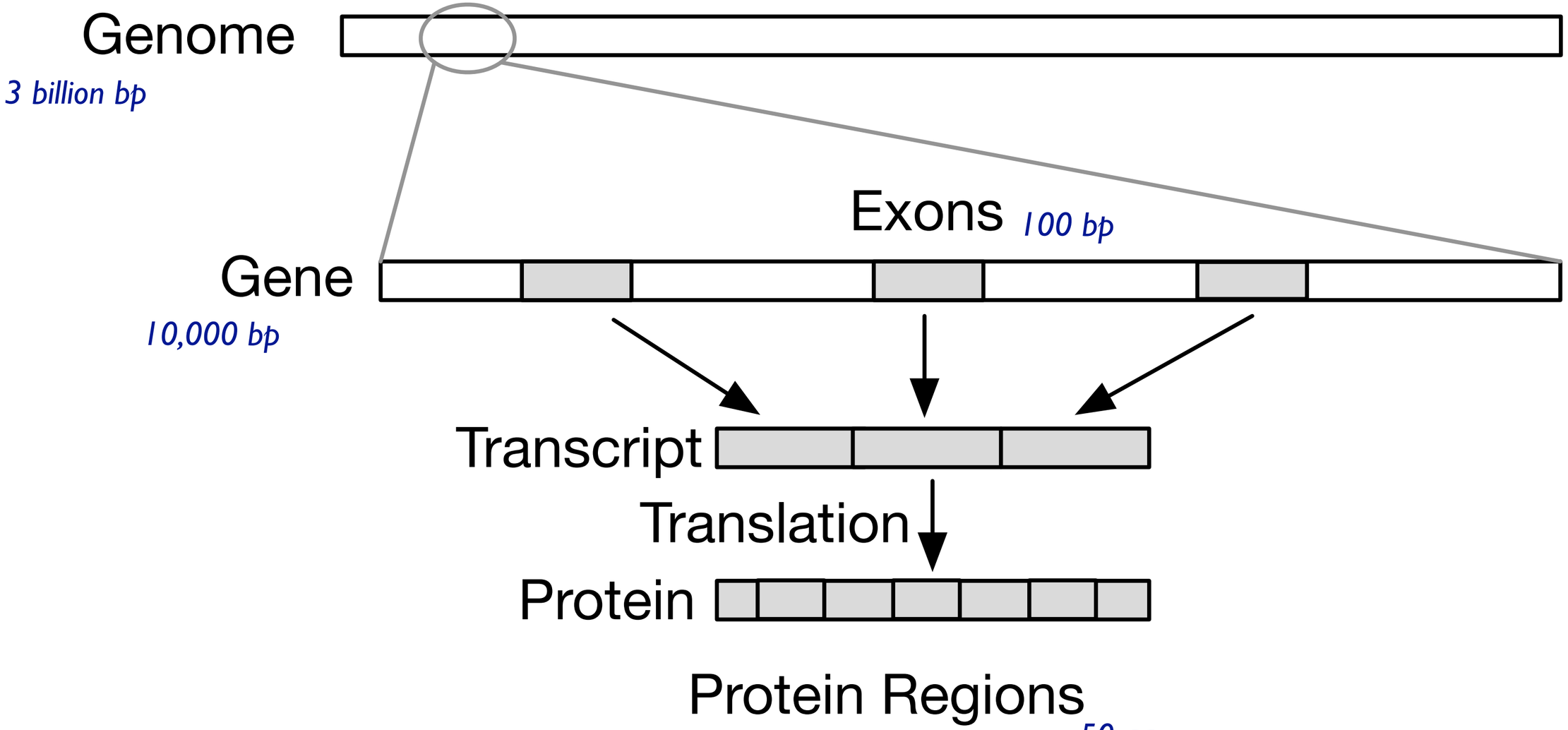
Harmless?

Cancer Research

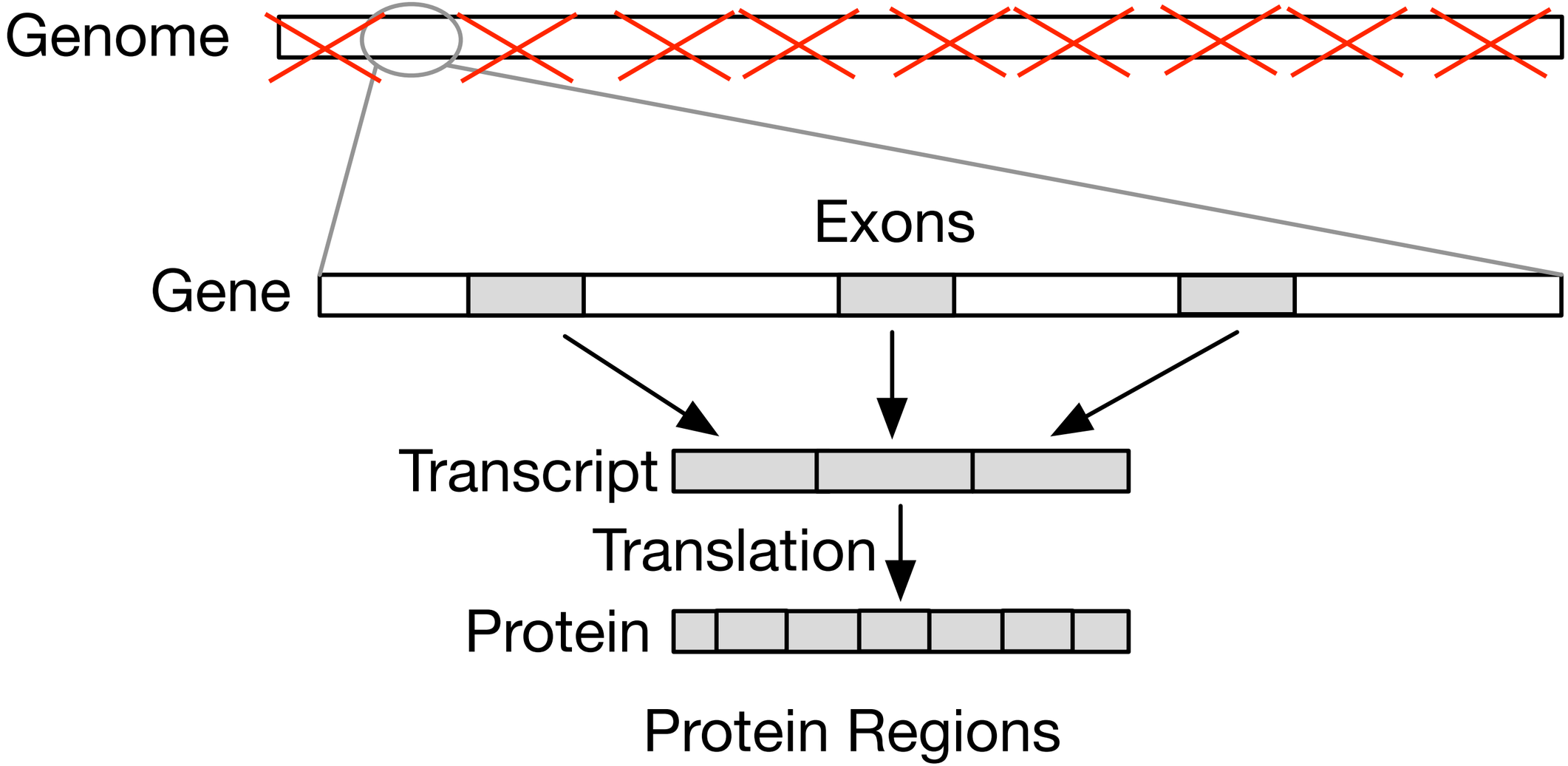
- collaboration with analysts at BC Genome Sciences Center
  - studying genetic basis of leukemia
- driving task
  - discover new candidate genes with harmful variants
- two big questions
  - what to show
    - data abstraction
    - challenge: enormous range of scales in the data
  - how to show it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

Abstractions

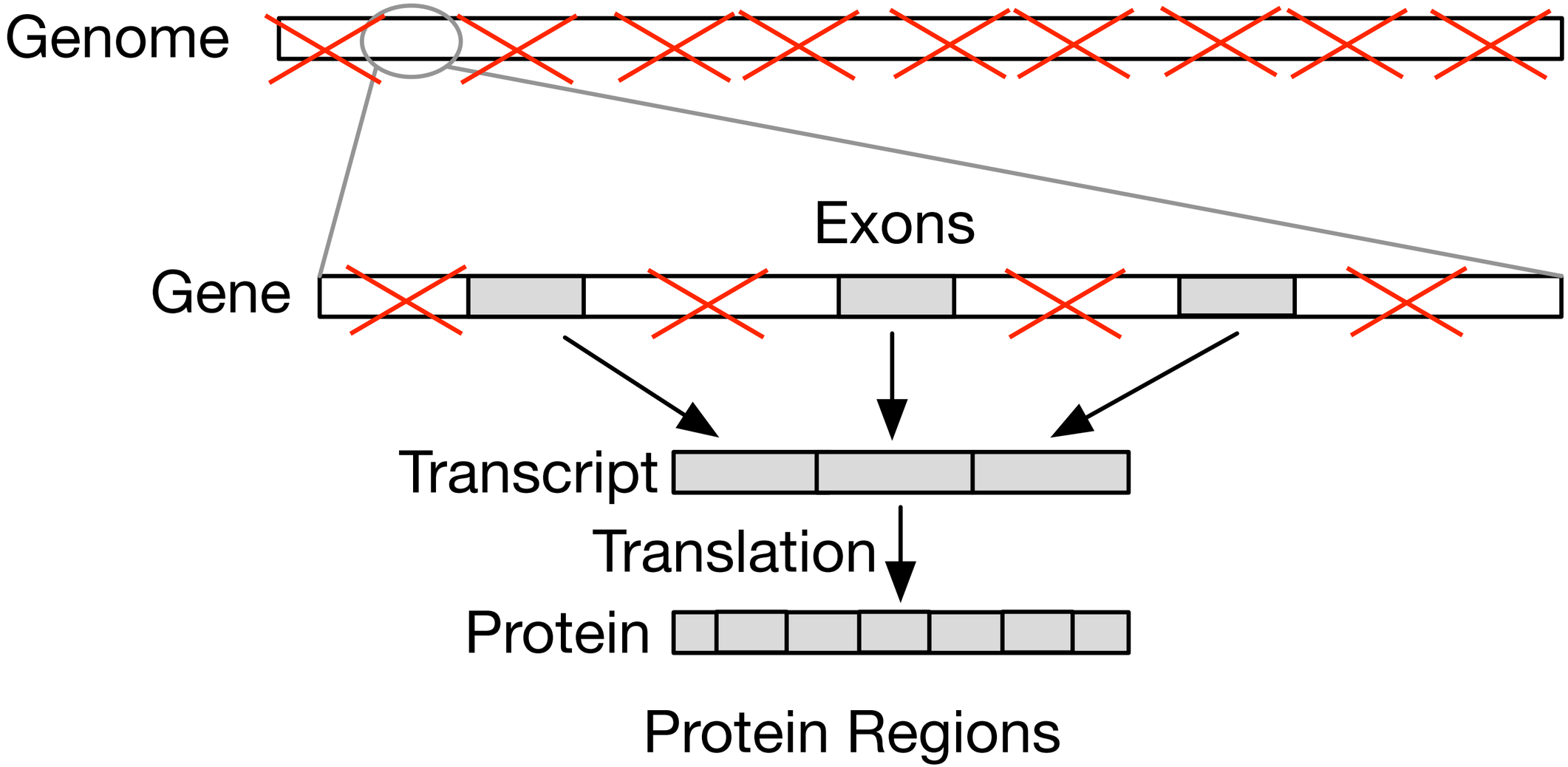
Data: Filtering to relevant biological levels and scales



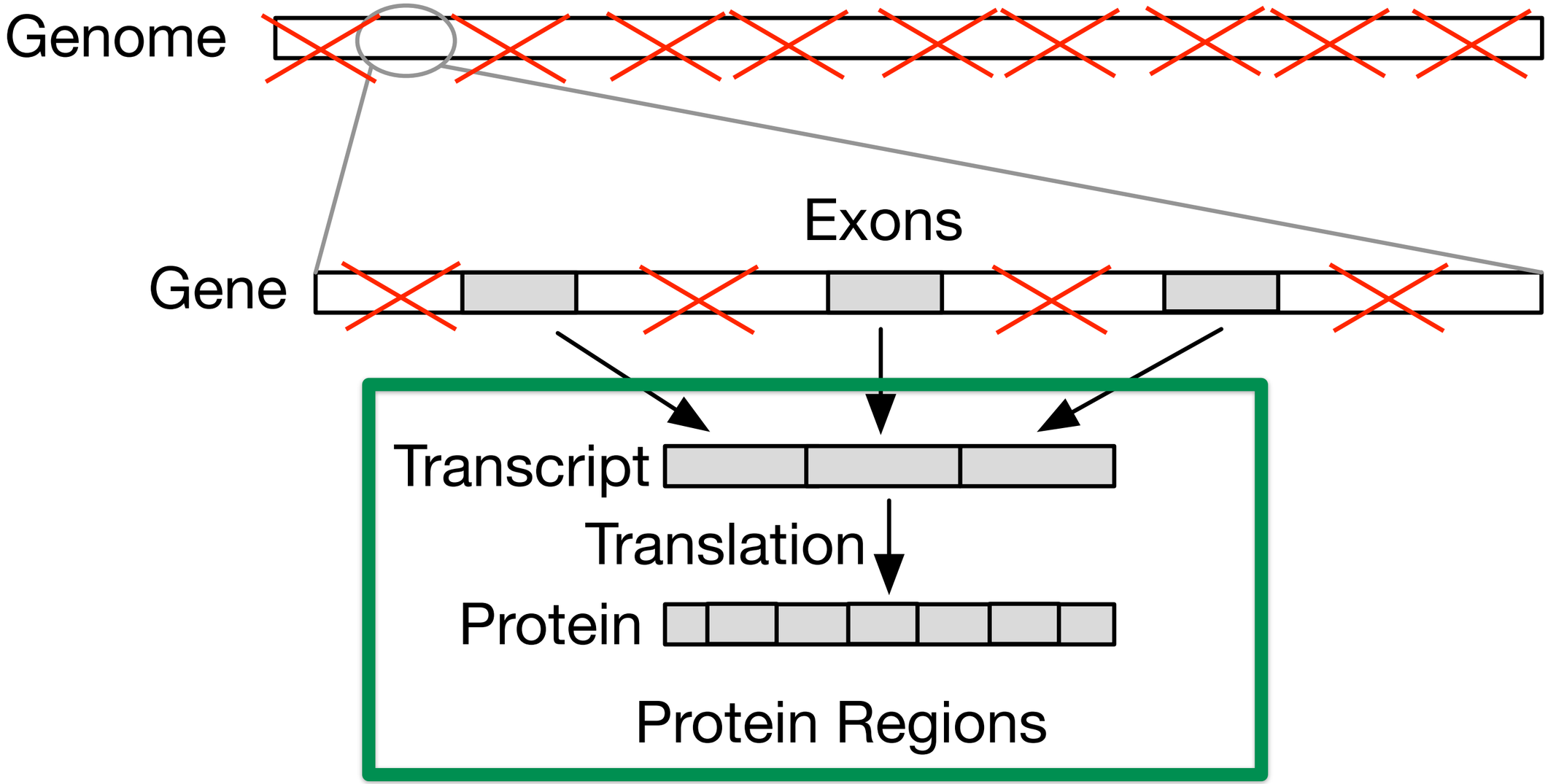
Filter out whole genome; keep genes



Filter out non-exon regions

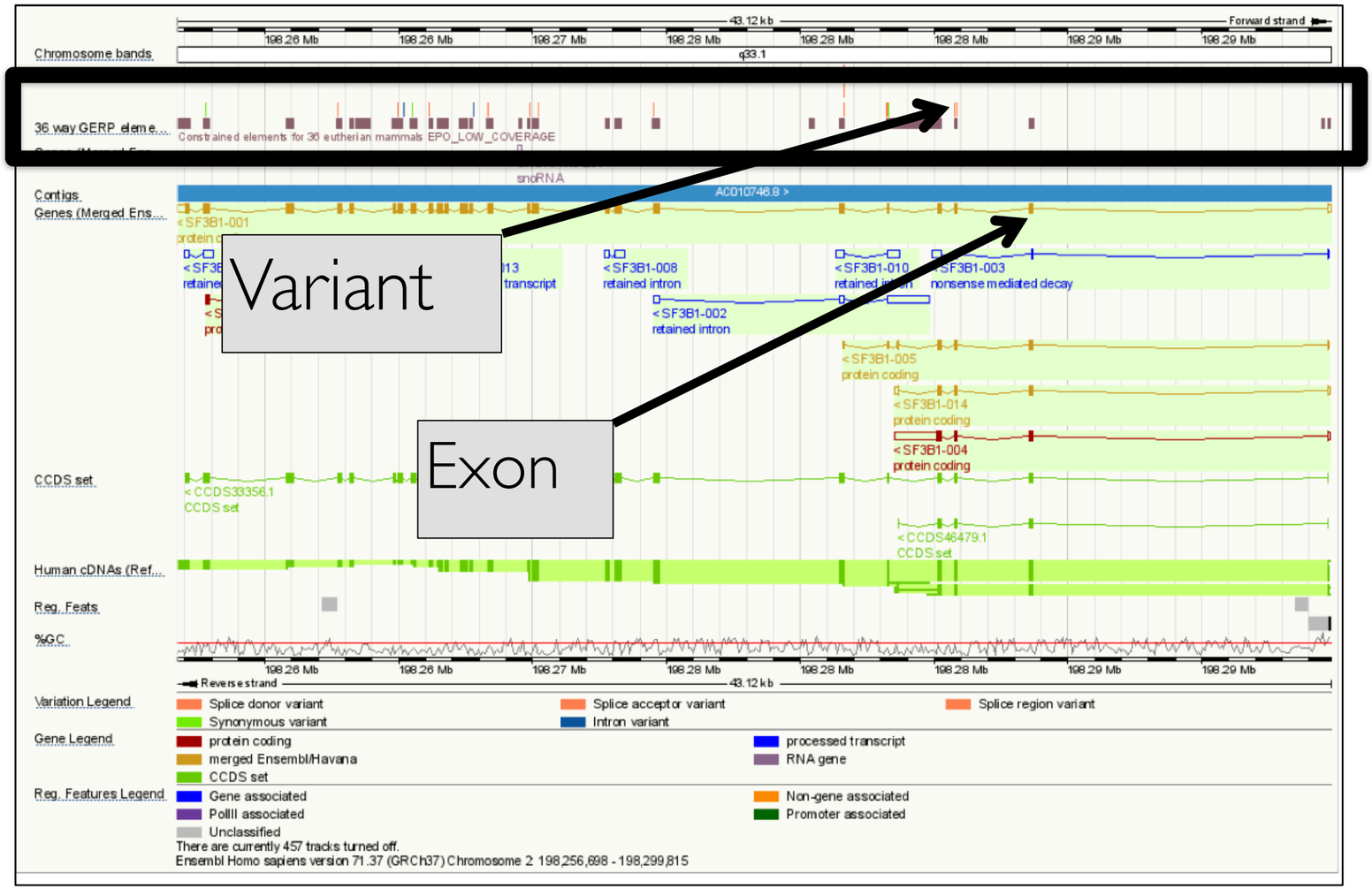


Data abstraction: highly filtered scope



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

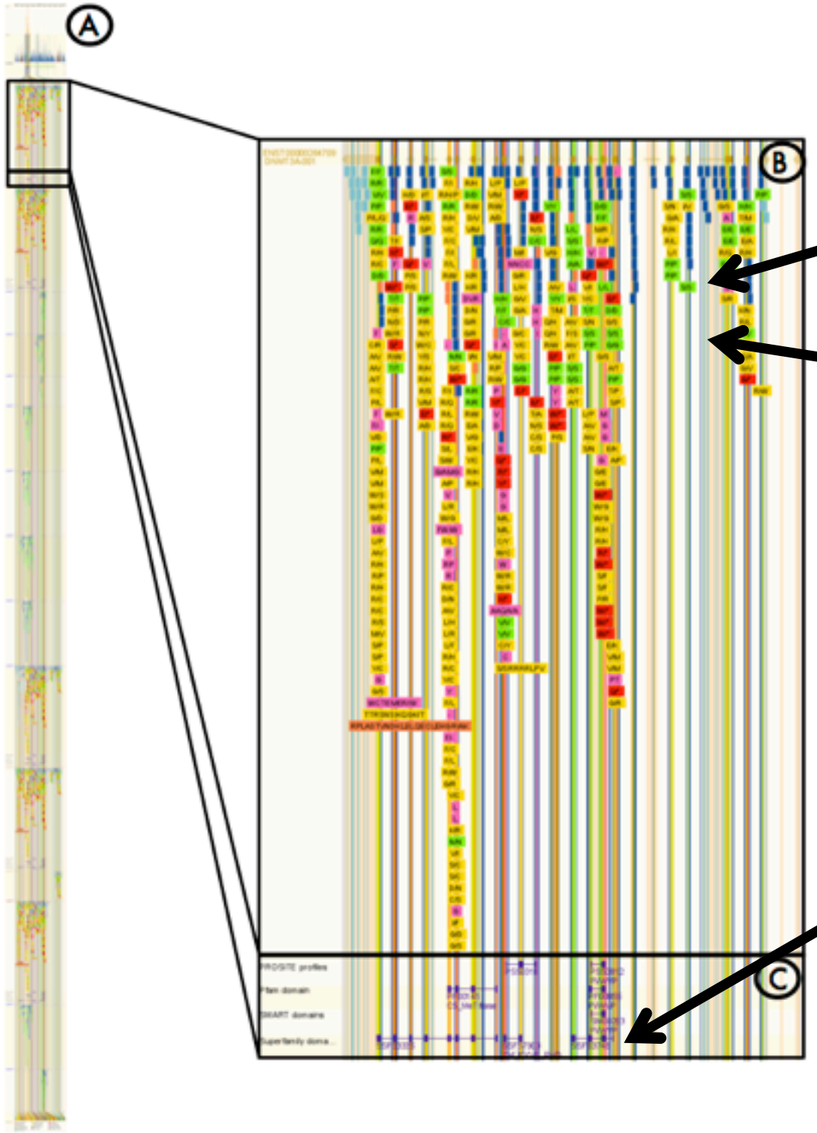


representative example: Ensembl

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

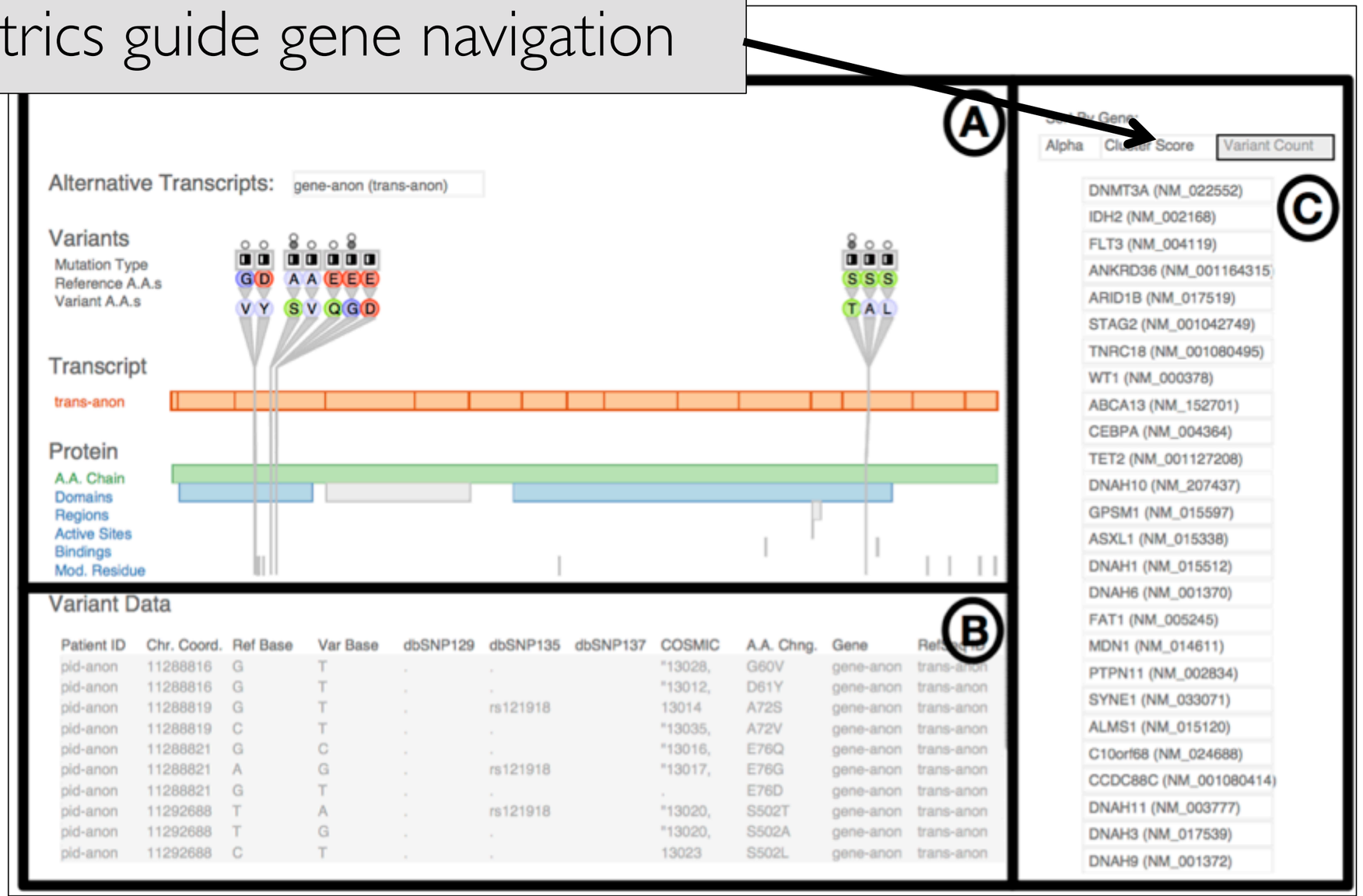
Previous: Table, one row per variant

Information-dense single gene view

Variant View

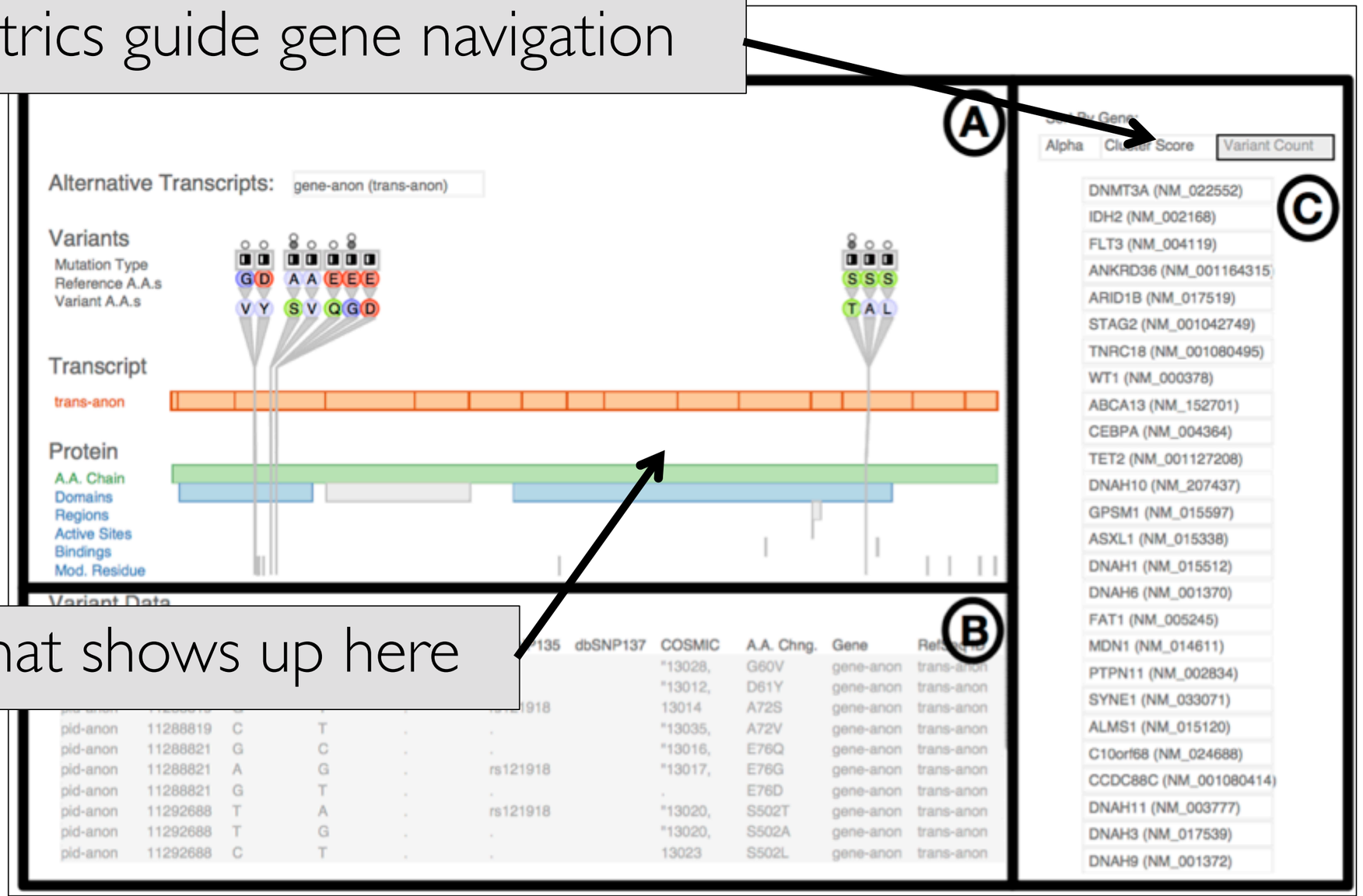
Variant View

Sorting metrics guide gene navigation



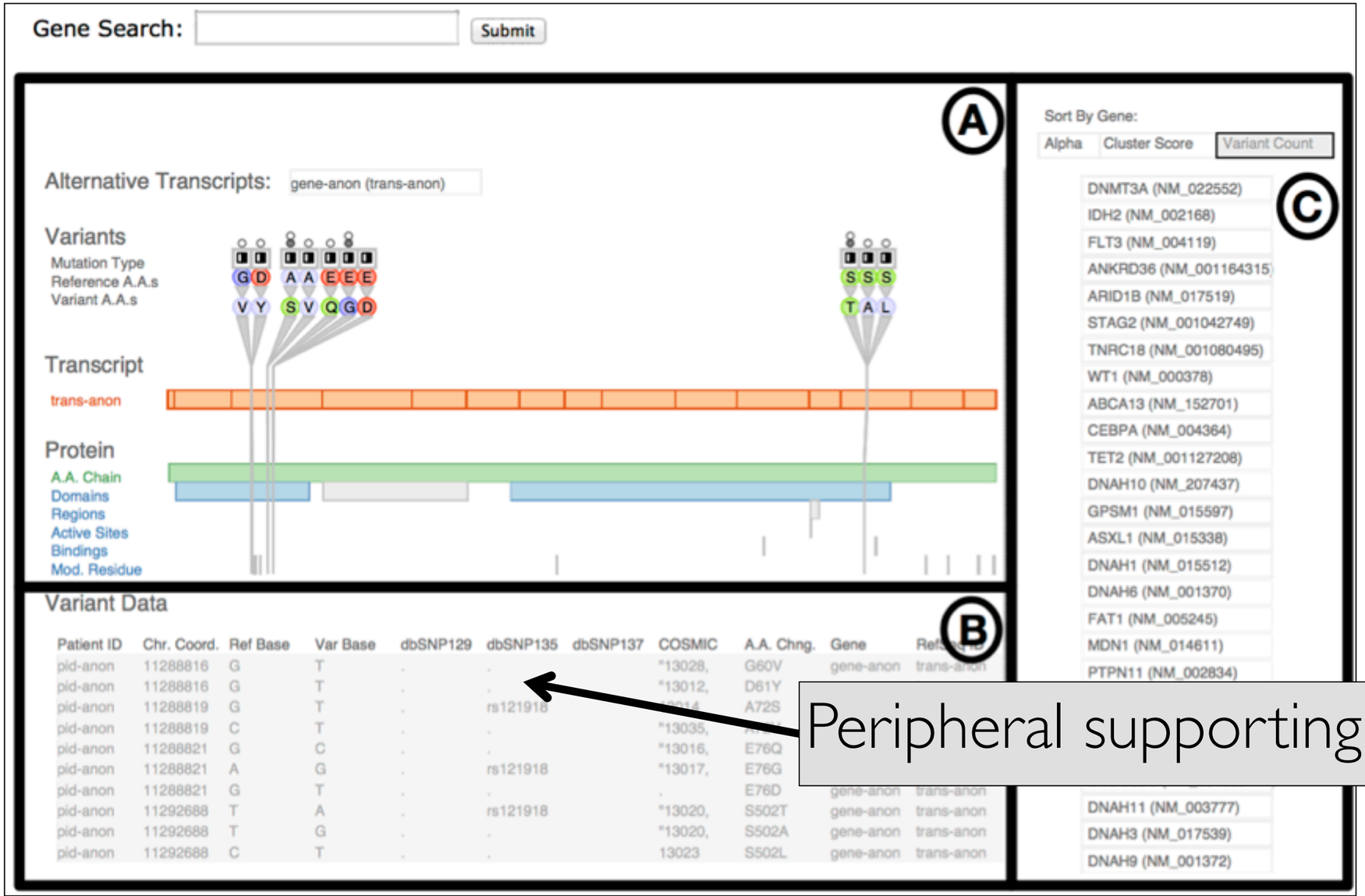
Variant View

Sorting metrics guide gene navigation



Control what shows up here

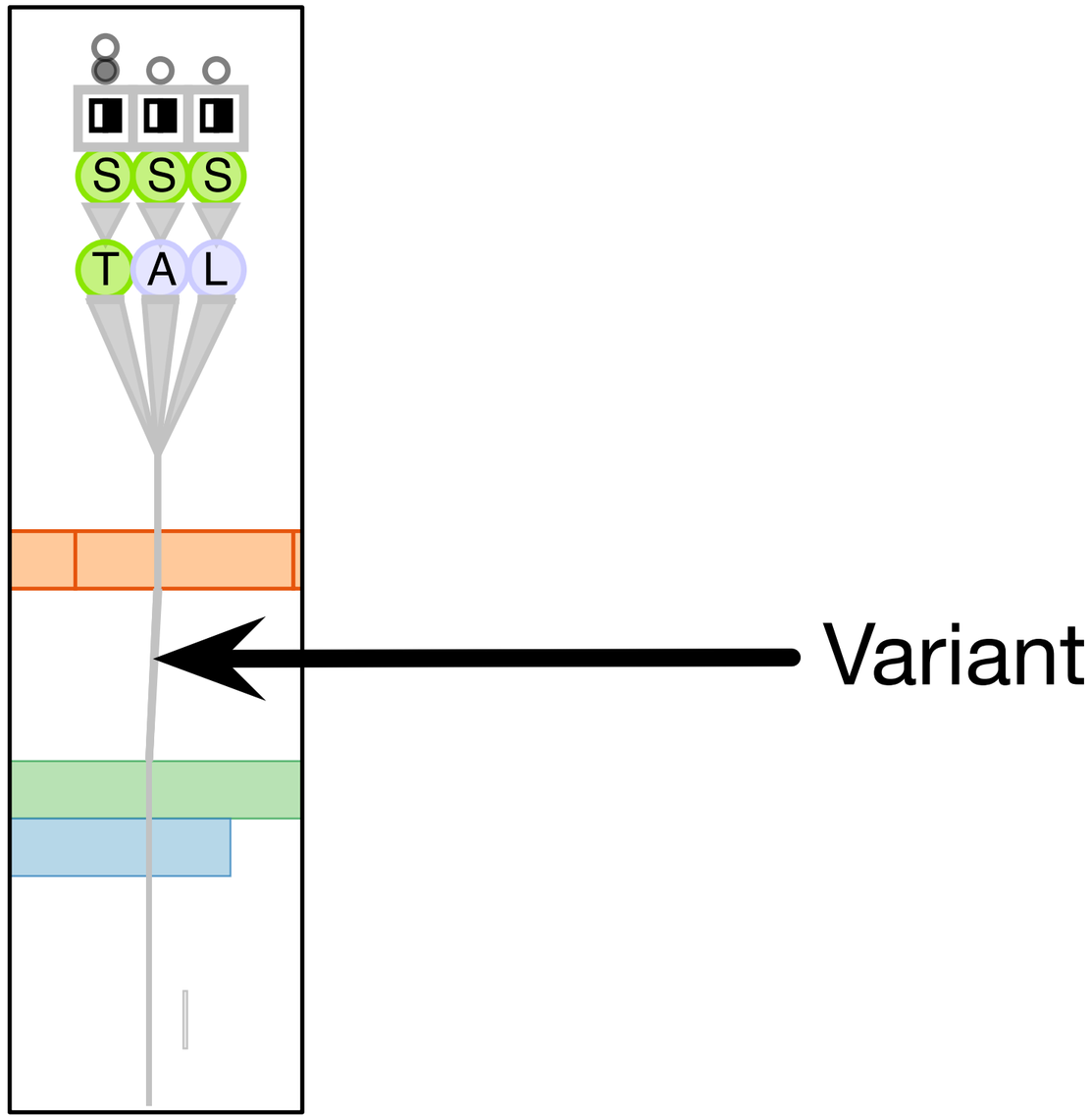
Variant View



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



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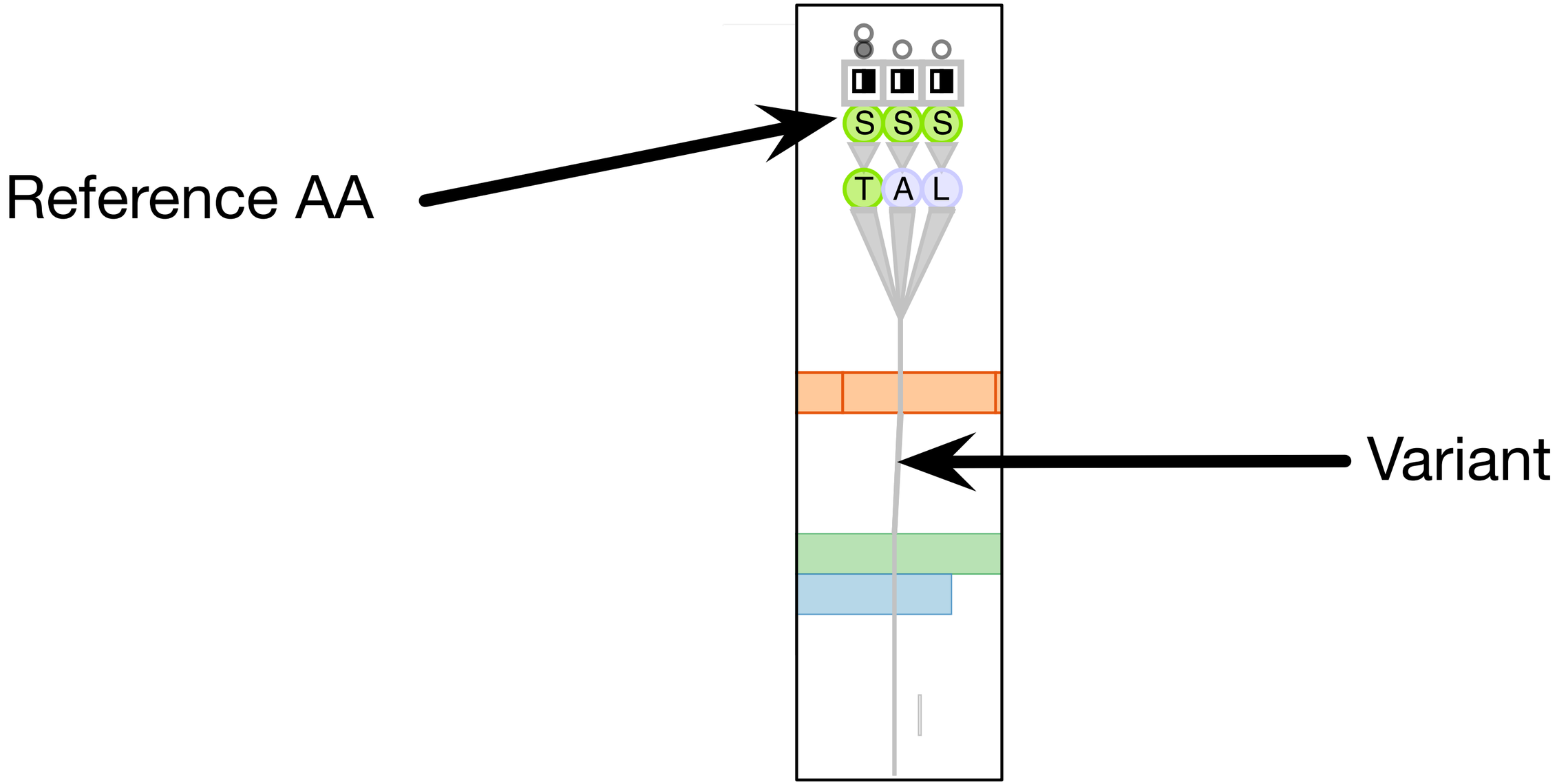

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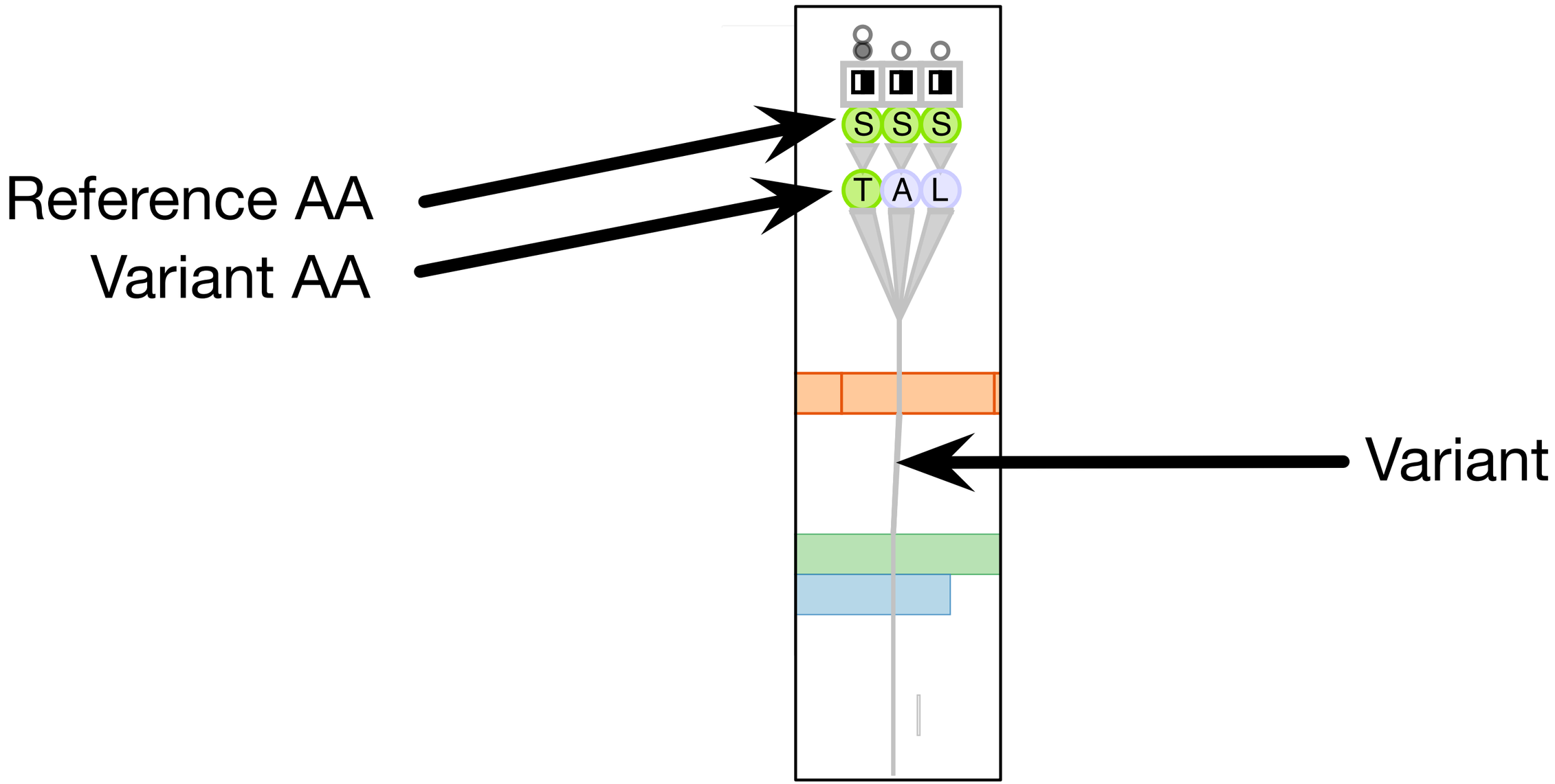

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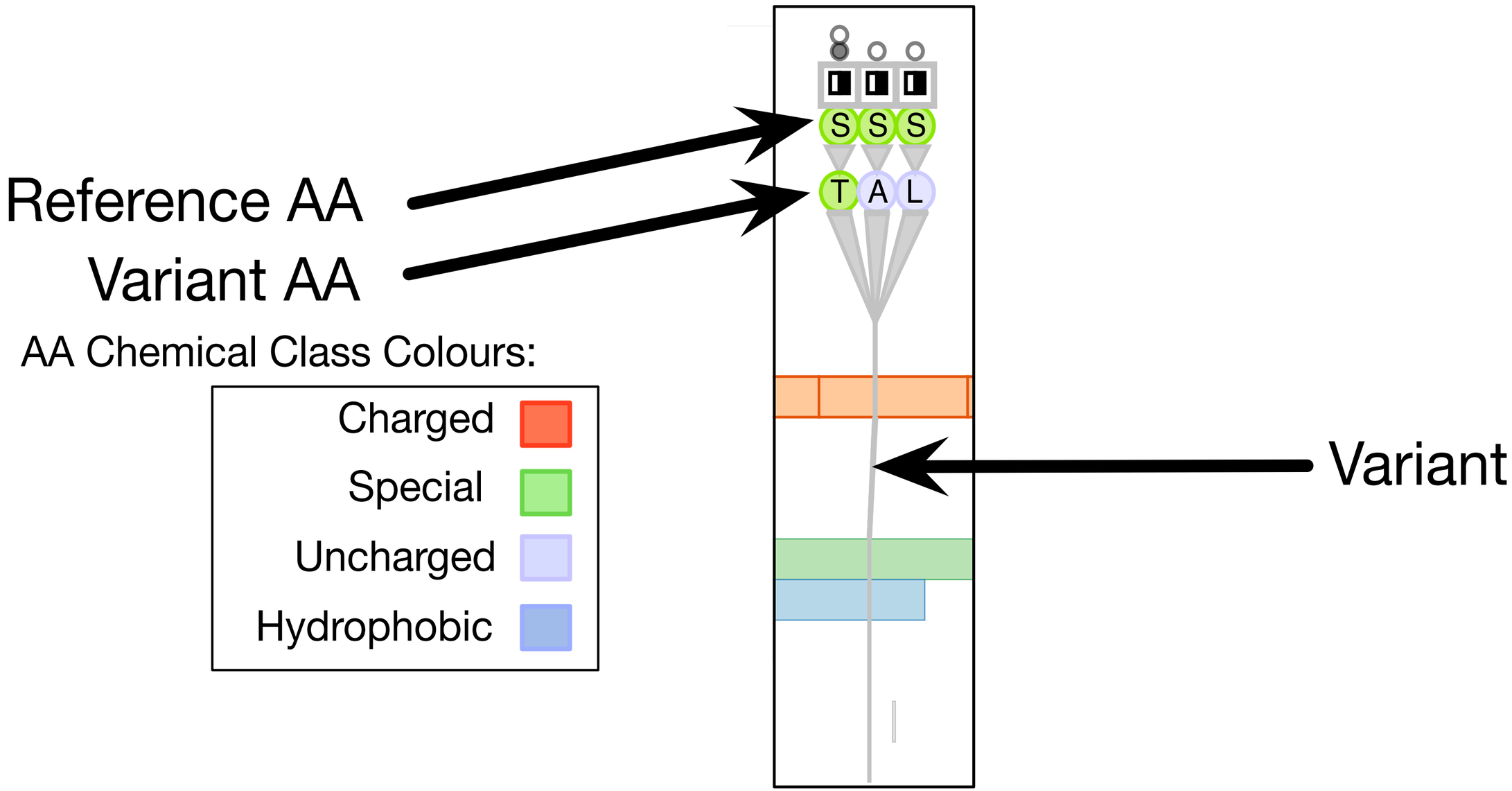

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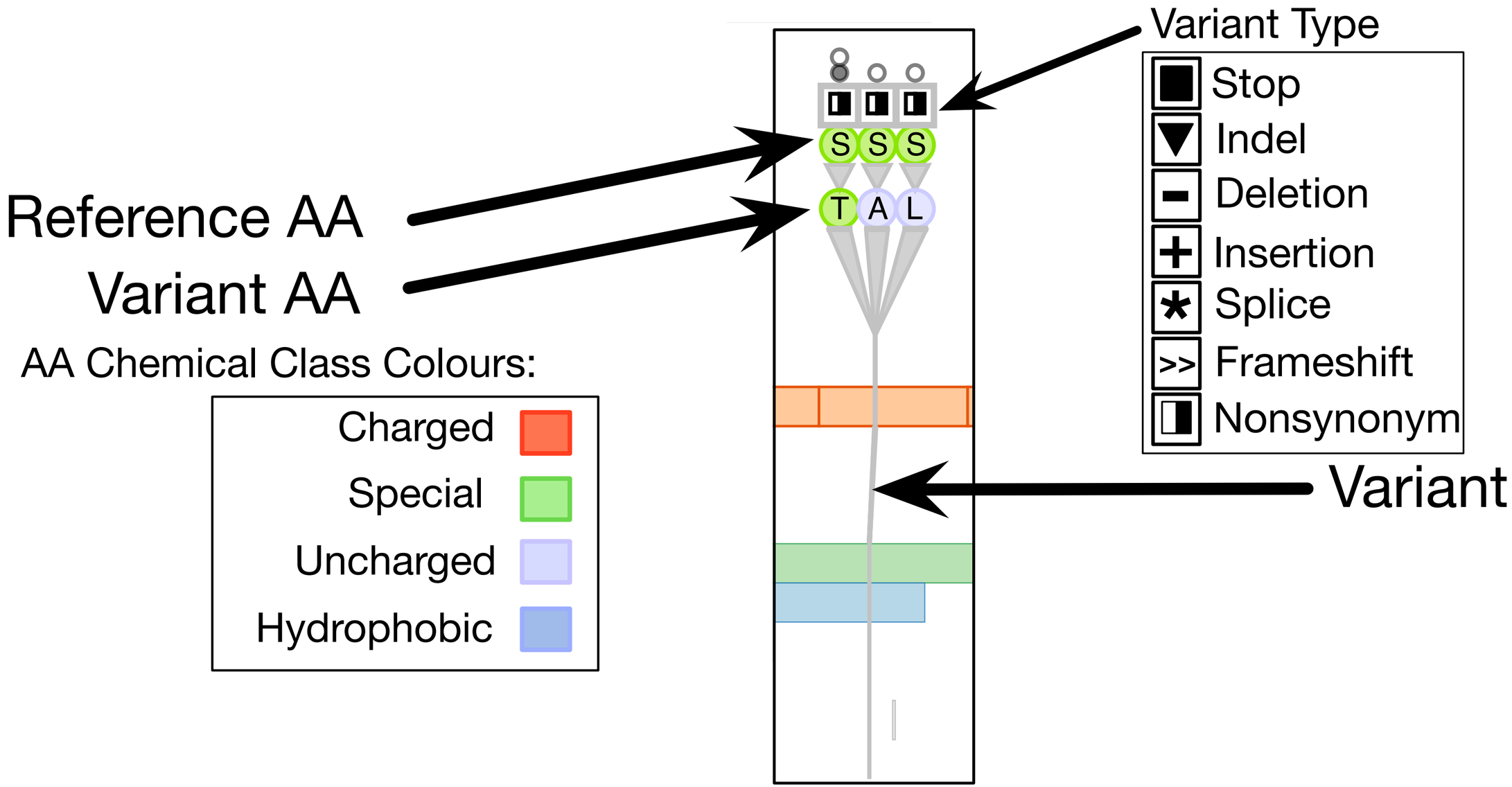

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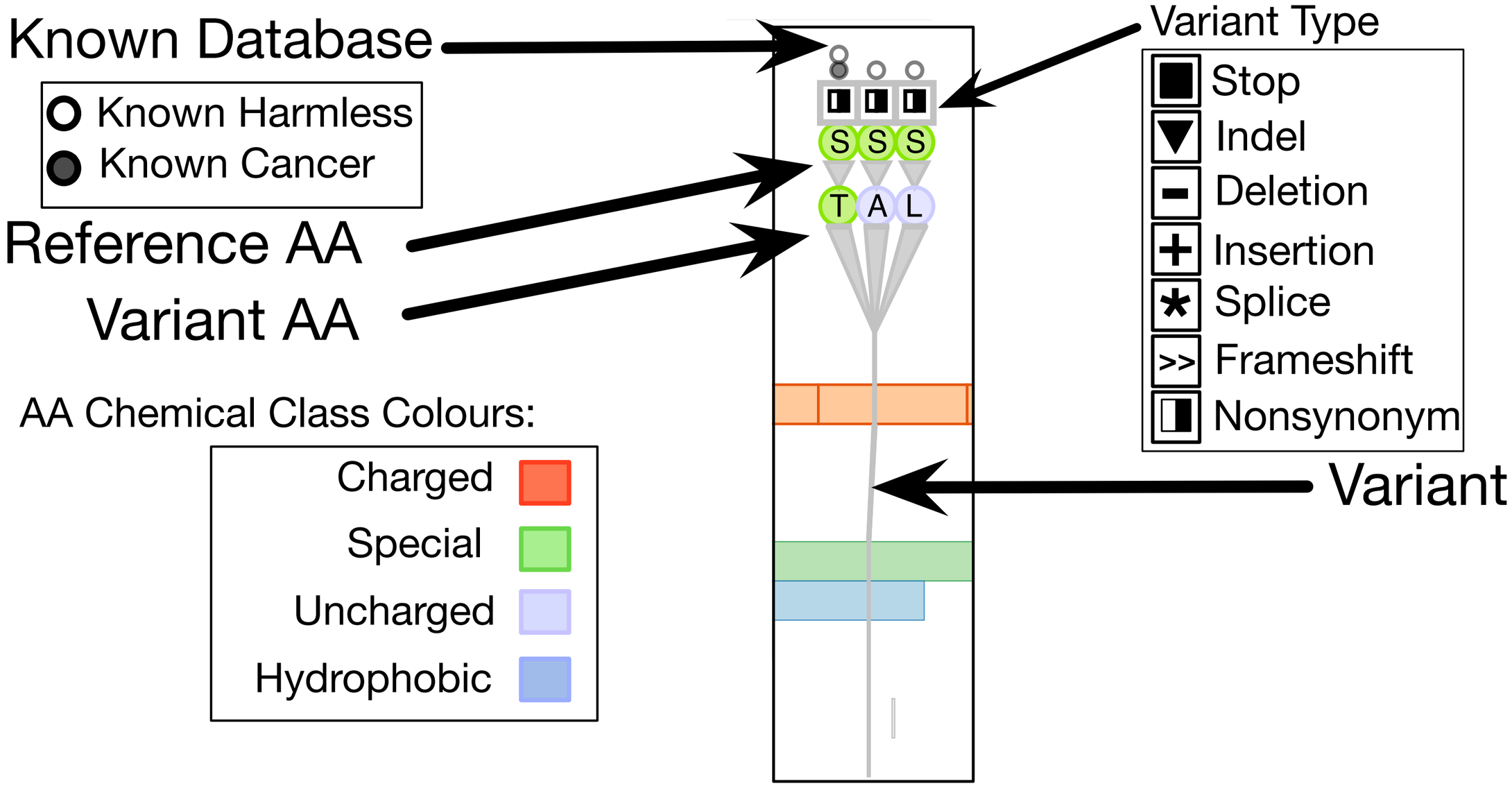

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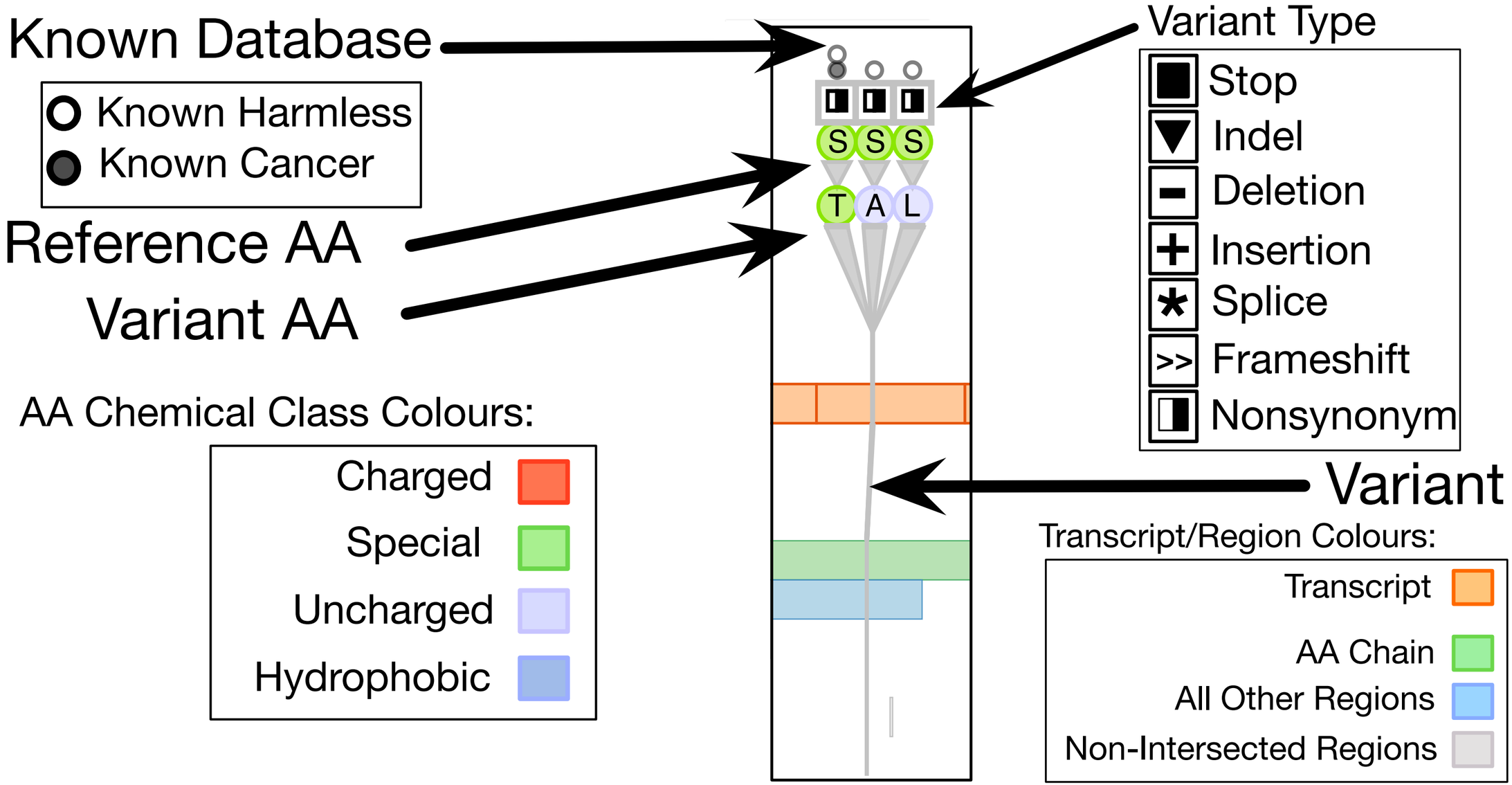
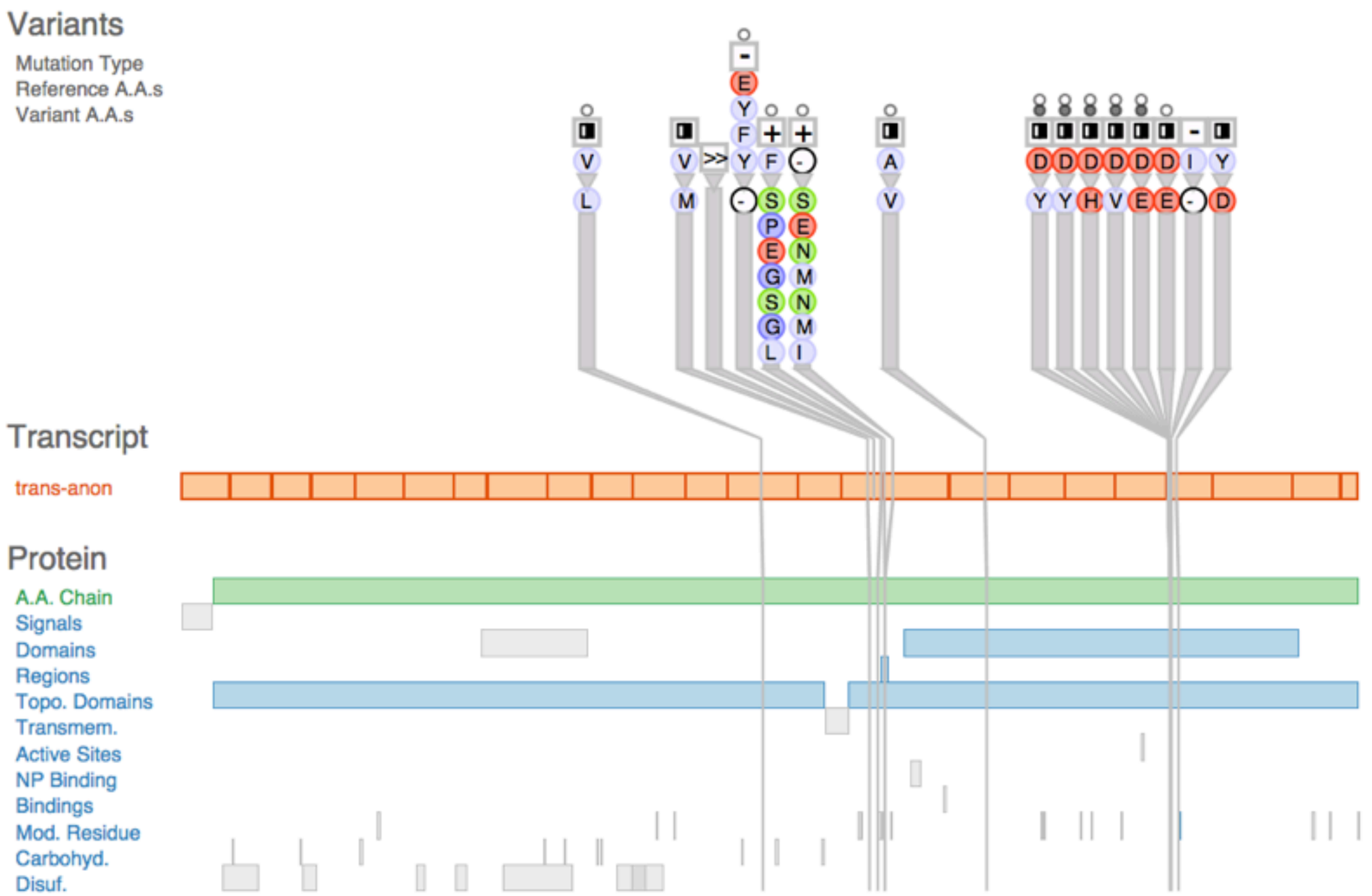
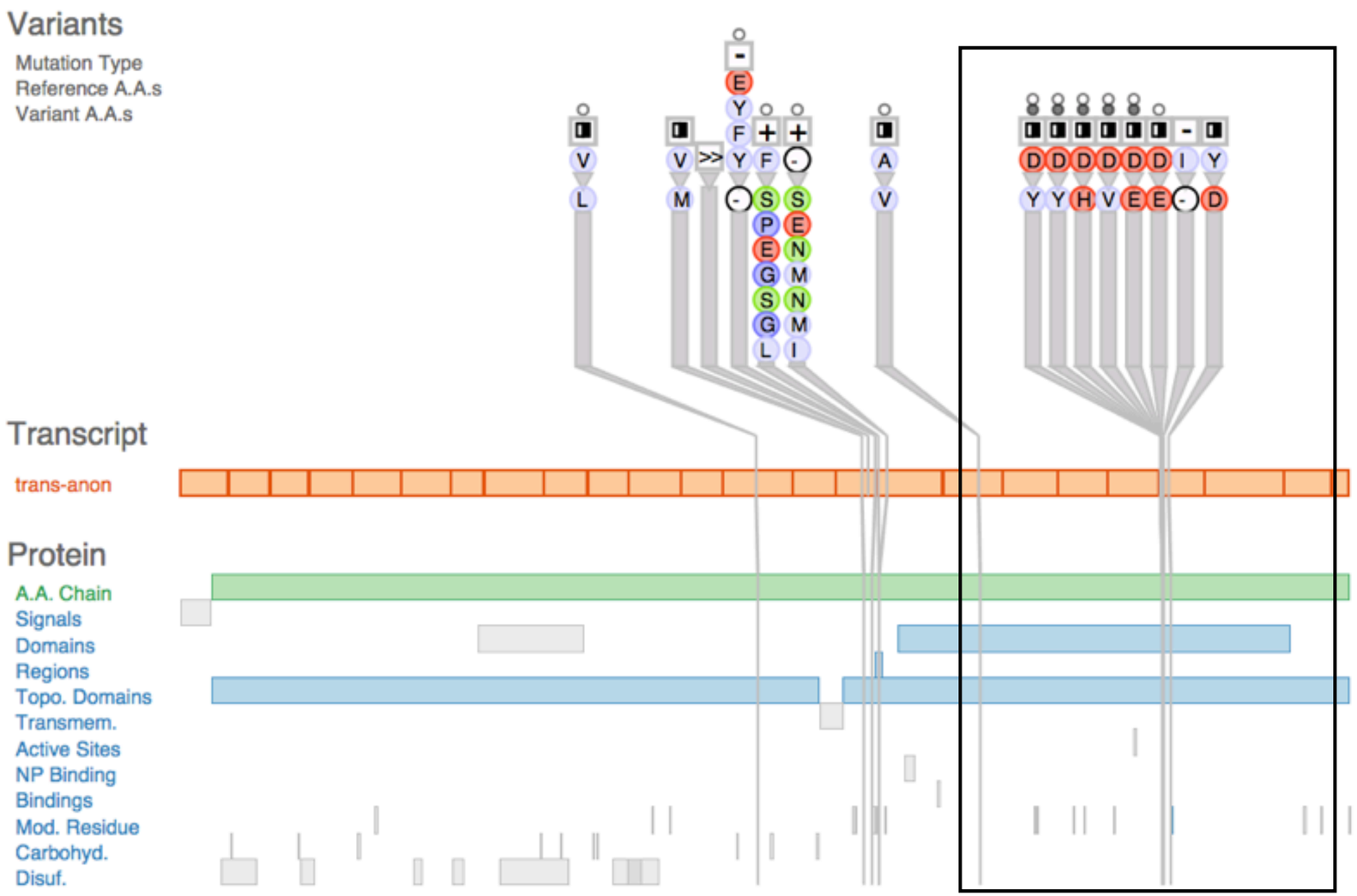


Results

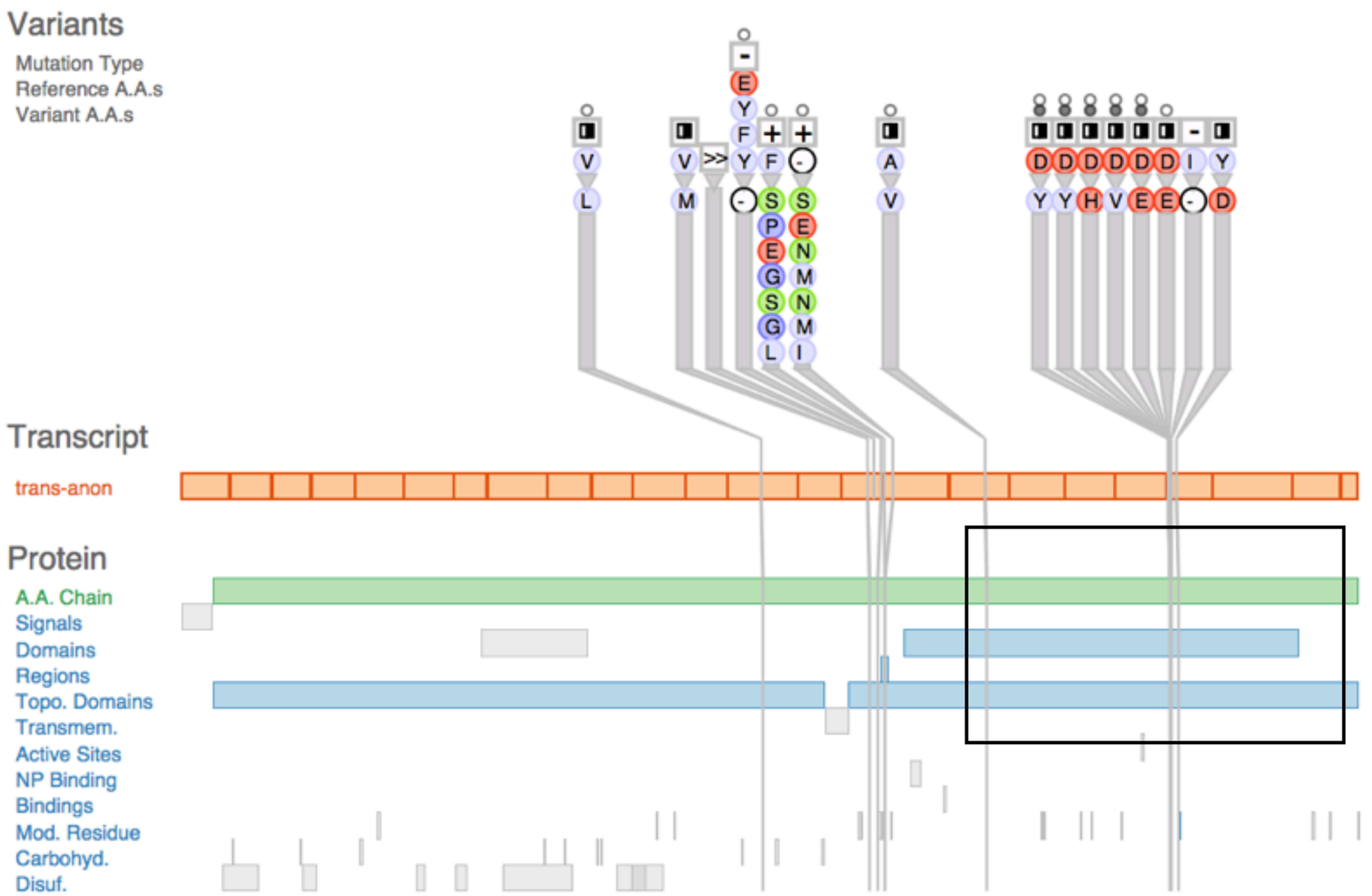
Verify known leukemia gene: Highly scored by sorting metric



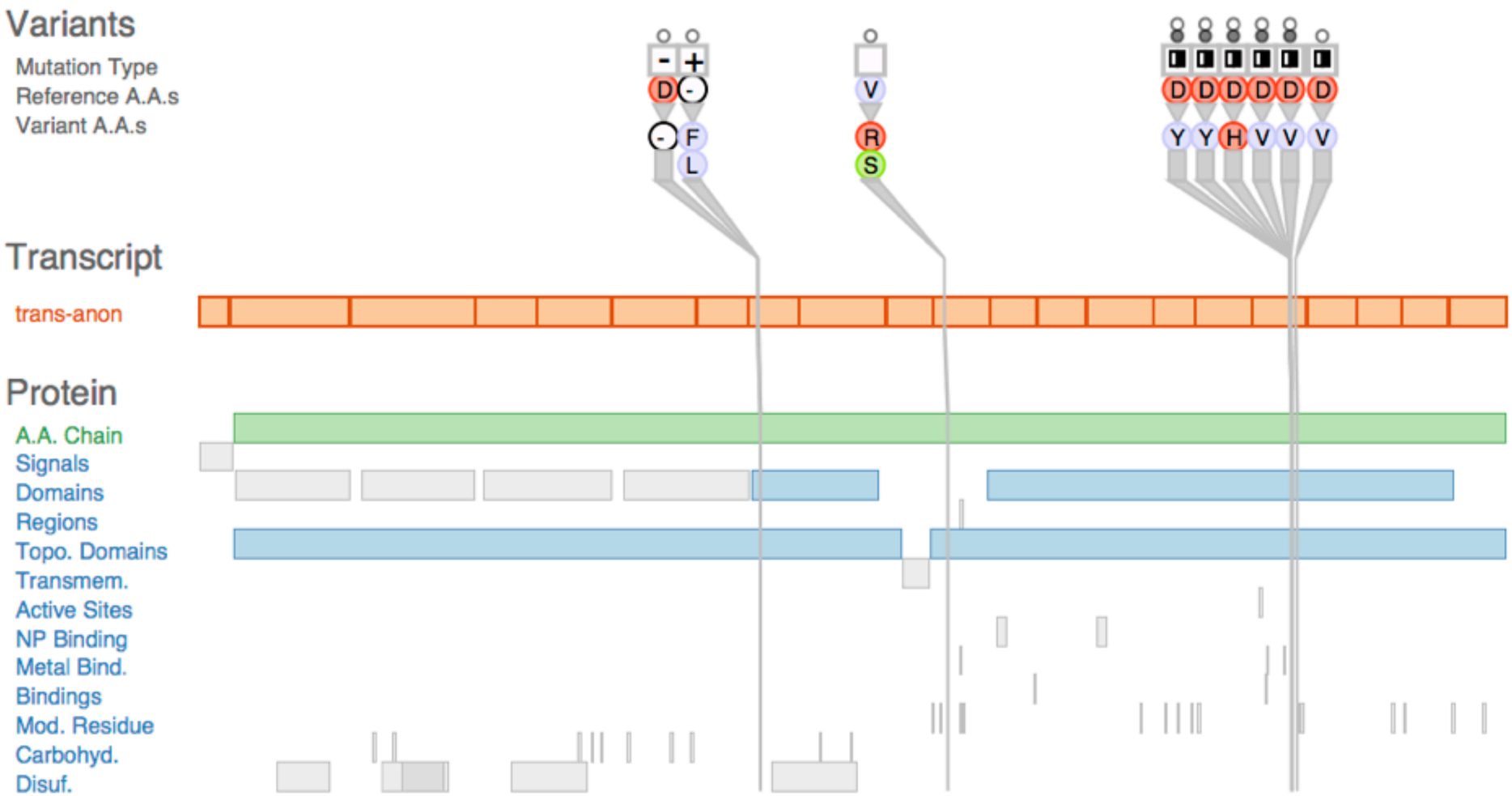
Visual inspection reveals collocation of variants



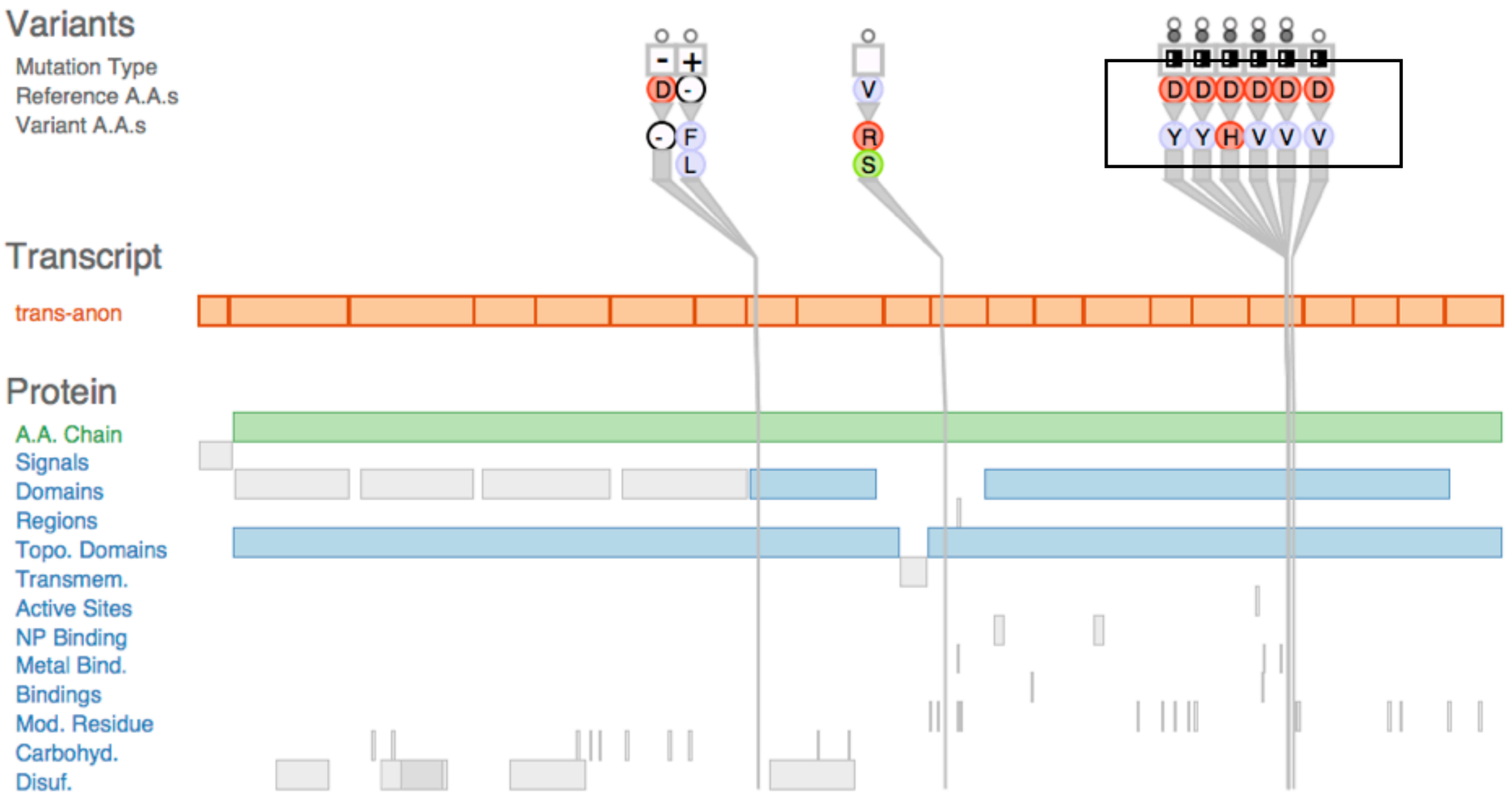
Several functional protein regions affected



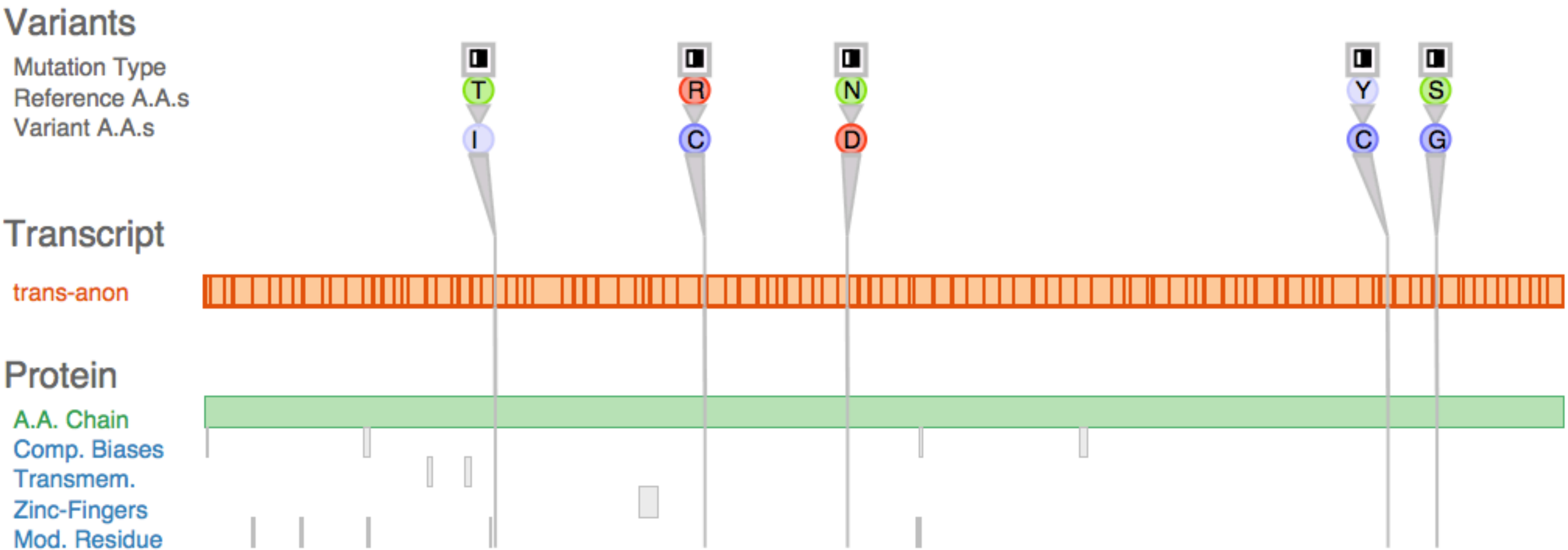
Highly scored by metric: not previously known, good candidate



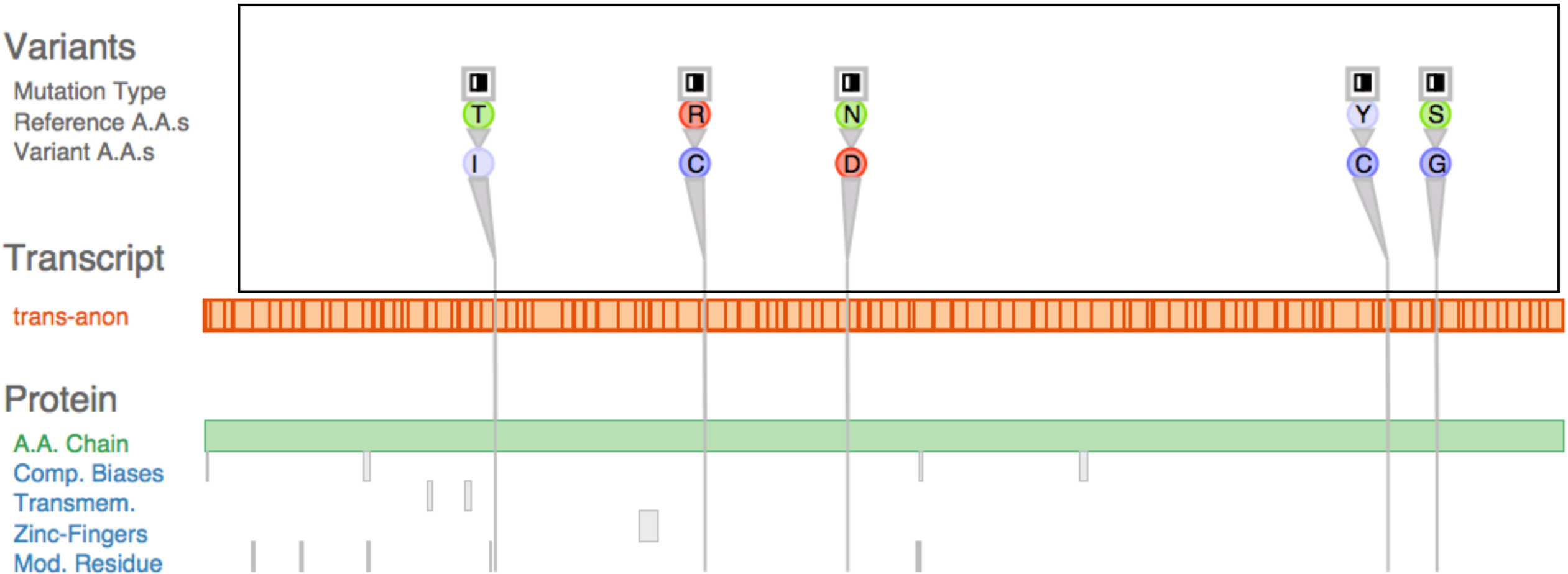
Protein chemical class change evident



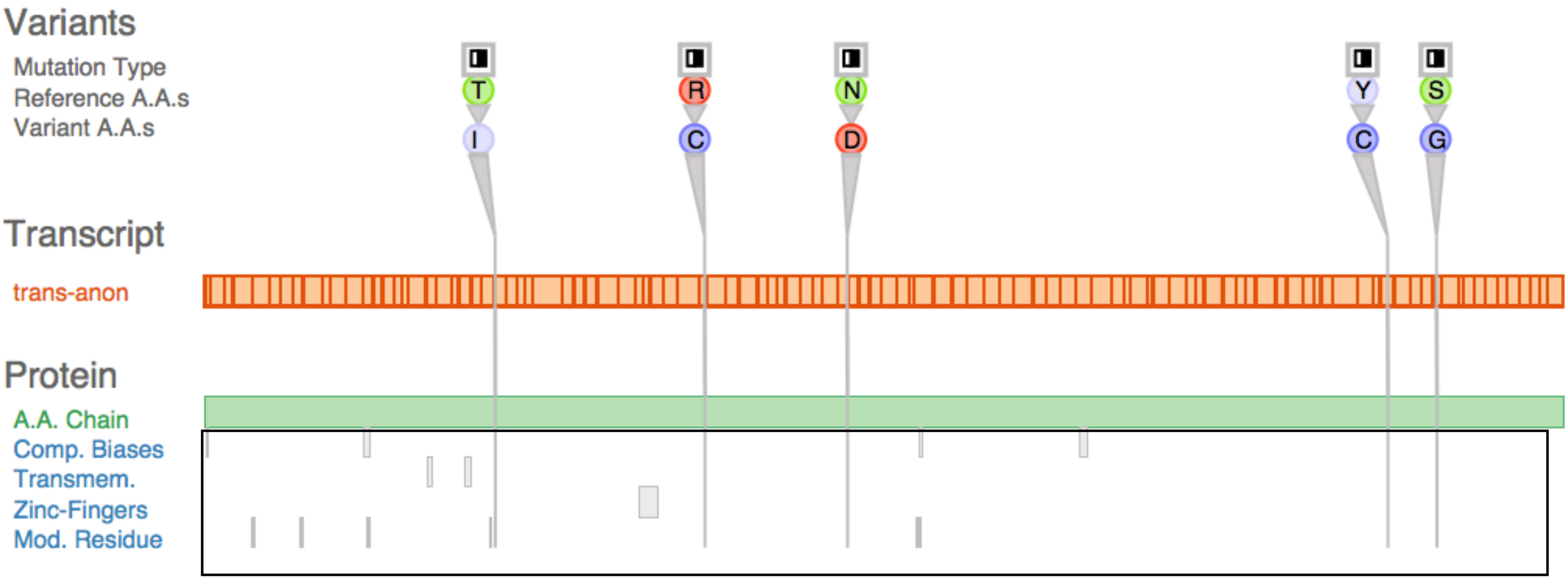
In contrast, low scoring gene



No collocation of variants



Mostly unaffected protein regions



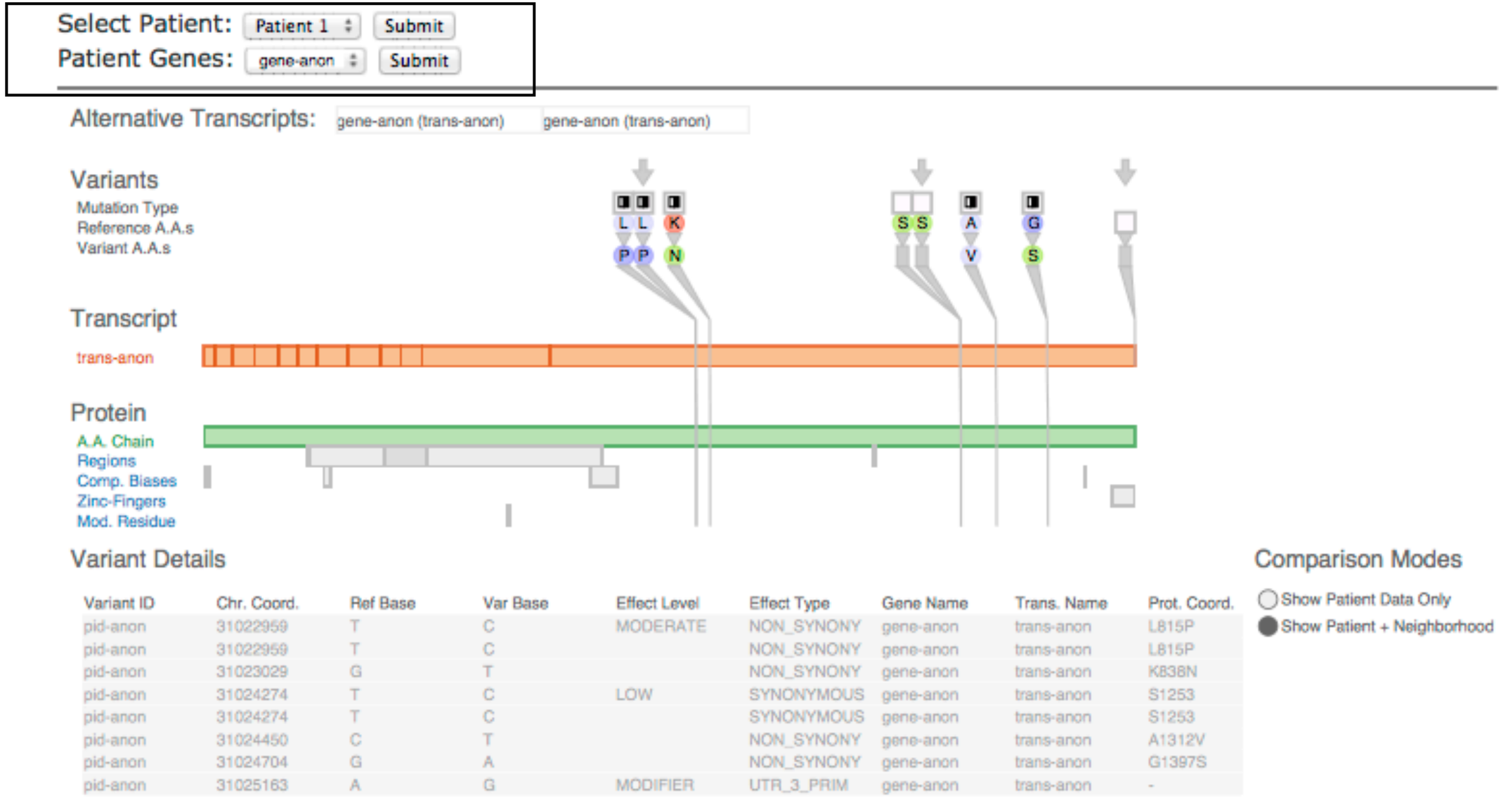
Additional tasks

- 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	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

Variant ID	Chr. Coord.	Ref Base	Var Base	Effect Level	Effect Type	Gene Name	Trans. Name	Prot. Coord.
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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

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pid-anon	31022959	T	C		NON_SYNONY	gene-anon	trans-anon	L815P
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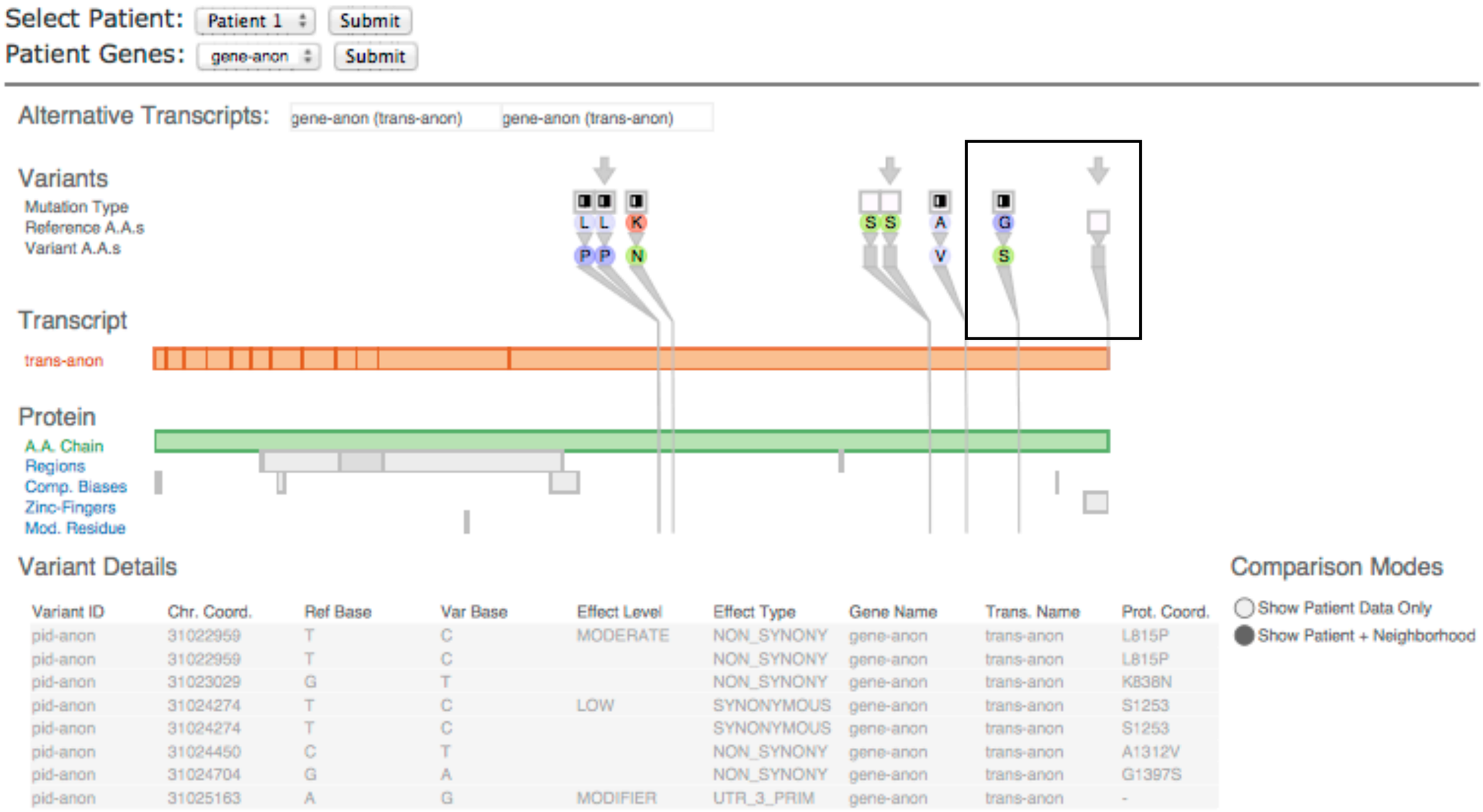
pid-anon	31024704	G	A		NON_SYNONY	gene-anon	trans-anon	G1397S
pid-anon	31025163	A	G	MODIFIER	UTR_3_PRIM	gene-anon	trans-anon	-

Nonmatching variants



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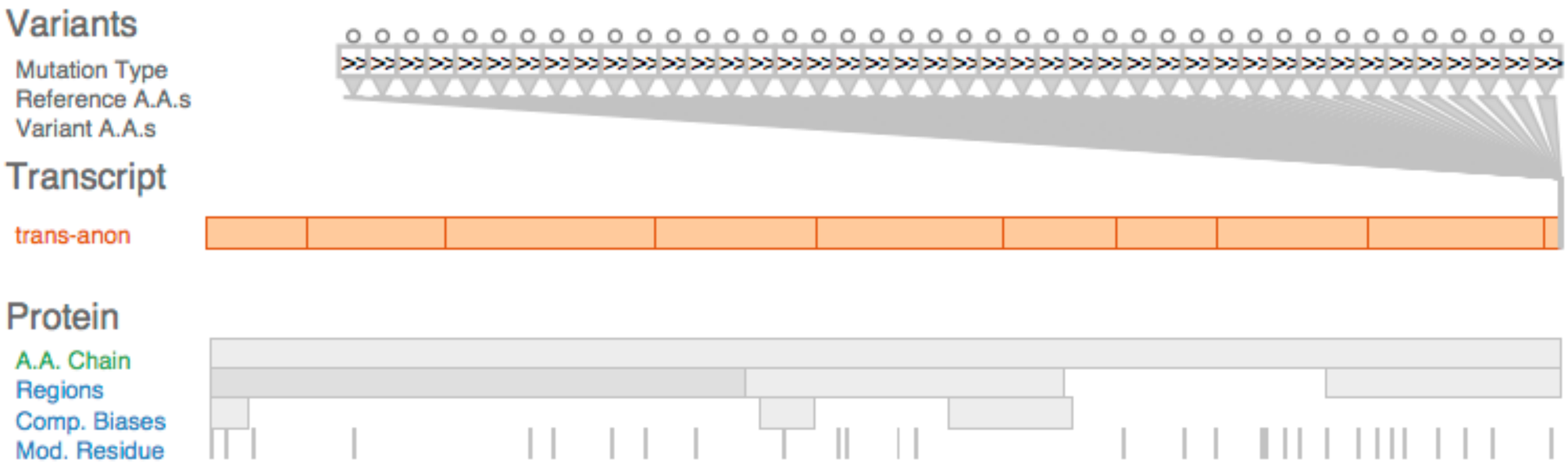
pid-anon	31025163	A	G	MODIFIER	UTR_3_PRIM	gene-anon	trans-anon	-

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

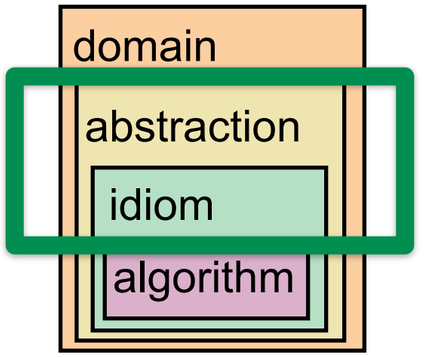


The tool exposed artifacts in the data that slid past at least two rounds of quality metric filtering … this type of problem would not have been caught by our previous, automated methods.

- Analyst 3

Reduce from big data to manageable data

- at abstraction level, not algorithm level
  - filter away huge amounts of detail
  - transform from variant centric to gene centric



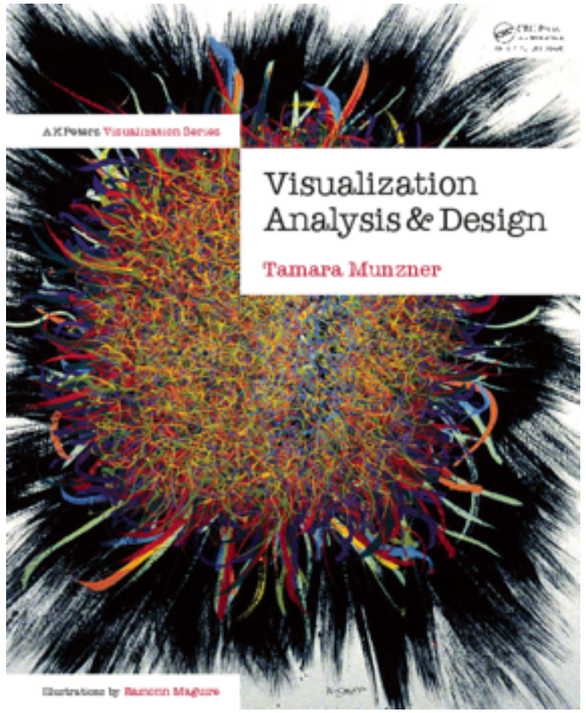
[A Nested Model of Visualization Design and Validation.
Munzner. IEEE TVCG 15(6):921-928, 2009 (Proc. InfoVis 2009).]

Privacy implications

- anonymizing
  - protect patients: strip/change patient names
  - protect researchers: strip/change gene names
  - deanonymization threats: minor in this case
- future projects
  - genomics meets clinical meets administrative meets demographic
    - enable data re-use: link individuals across datasets to create research study cohorts
    - health research opportunity: major
    - deanonymization threat: major
  - ferociously privacy-protected data silos/vaults
    - can't see data without permission; what to ask for?
    - upcoming project: privacy preserving visual metadata browsing

More Information

- paper & open source download
  http://www.cs.ubc.ca/labs/imager/tr/2013/VariantView/
- this talk
  http://www.cs.ubc.ca/~tmm/talks.html#think15
- papers, videos, software, talks, courses
  http://www.cs.ubc.ca/group/infovis
  http://www.cs.ubc.ca/~tmm
- book: Visualization Analysis and Design. CRC Press 2014.
  http://www.cs.ubc.ca/~tmm/vadbook
  - 20% promo code for book+ebook combo: HVN17
  - http://www.crcpress.com/product/isbn/9781466508910



- acknowledgements
  - funding: VIVA, Aeroinfo/Boeing, MITACS

@tamaramunzner