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Bioinformatics Summer School

Long-reads Transcriptomics

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LongTREC - The Long-reads TRanscriptome European Consortium
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Course Contents

1. Functional Annotation
2. IsoAnnot & IsoAnnotLite

Section 1

Functional Annotation

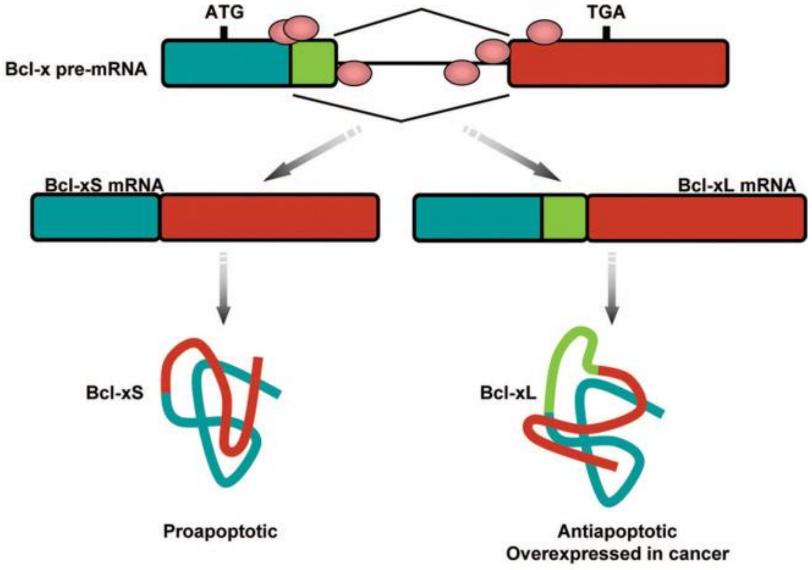
Understanding the functional impact of alternative splicing

Isoforms of the same gene can have different functions

So far, we have focused on **structural annotation.**
But how do novel transcripts differ from reference transcripts in their **biological functions**?

Isoforms from the same gene can have **different**, even opposite, **functions**.

We want to obtain **functional annotations** for transcript or protein sequences and investigate differences between isoforms.



Intervention opportunities

Detection:

- Overexpression of splicing regulatory factors
- mRNA from cancer-related splice isoforms
- Proteins from cancer-related splice isoforms
- Autoantibodies

Treatment:

- Drugs affecting the activity of splicing factors
- Antisense oligonucleotides (SMOs)
- Drugs against cancer-related isoforms
- Vaccines

Diagram:
BCL2L1 xS and xL isoforms
Pio, Ruben, and Luis M. Montuenga. "Alternative splicing in lung cancer." Journal of Thoracic Oncology 4.6 (2009): 674-678.

Many methods exist to add functional annotations to sequences

Blast2GO:
Links high-scoring BLAST hits to Gene Ontology terms for transcriptome/protein function inference.

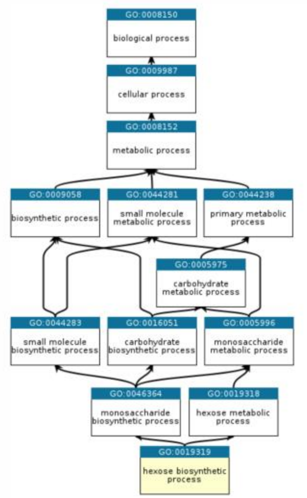
InterProScan:
Scans sequences through InterPro member databases, e.g. for conserved domains, motifs, and family signatures, and maps to GO terms.

eggNOG-mapper:
Assigns functional annotations via fast orthology mapping, leveraging precomputed orthologous groups from the eggNOG database.

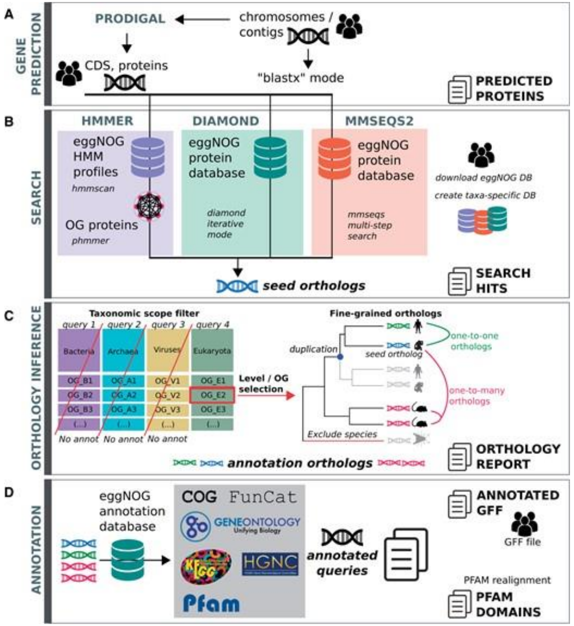
Deep Learning:
Emerging deep learning methods **(DeepGO, FANTASIA, etc.)** leverage deep neural networks to assign functions e.g. by prediction from sequence or inference from protein language model embeddings.

See:
[Gene Ontology Resource]
[About - InterPro]
[eggNOG-mapper]

Gene Ontology (GO)



eggNOG-mapper



Section 2

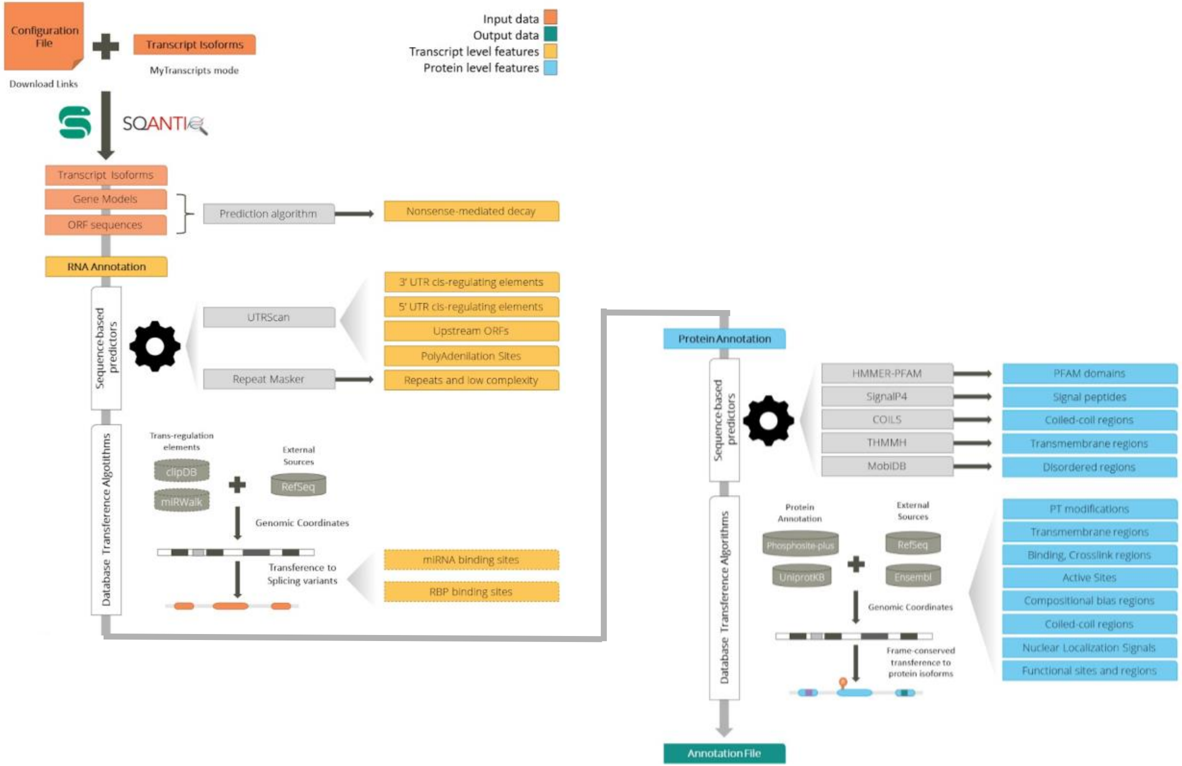
IsoAnnot & IsoAnnotLite

Understanding how to annotate functions to custom transcriptomes

IsoAnnot brings a wide variety of annotations to the isoform level

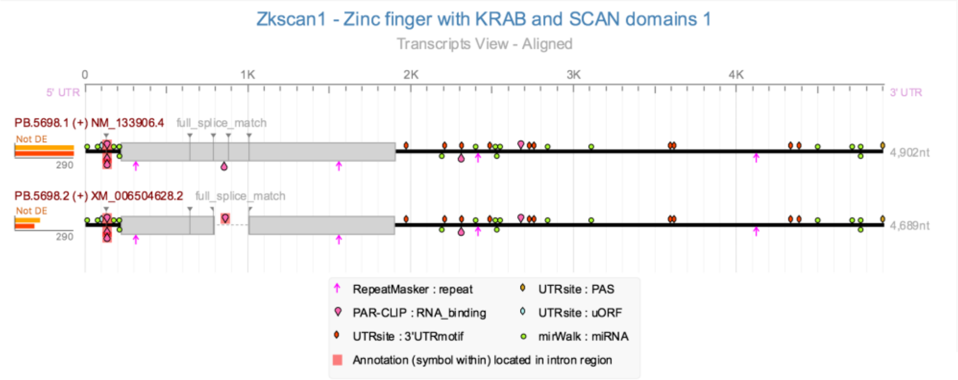
IsoAnnot combines a variety of databases and predictive algorithms to obtain **isoform-resolved functional annotations.**

Currently, it is challenging to use. **IsoAnnotLite** offers easily usable transference of functional annotations from pre-computed and manually curated gff3 files.

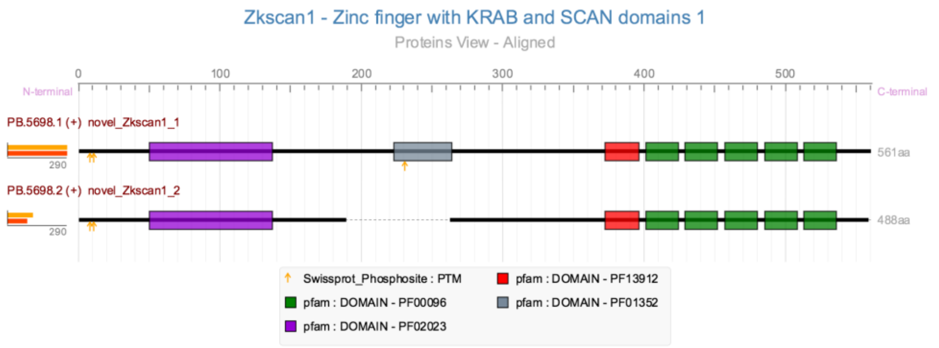


tappAS visualizes functional annotations at isoform resolution … and more

Transcript annotations

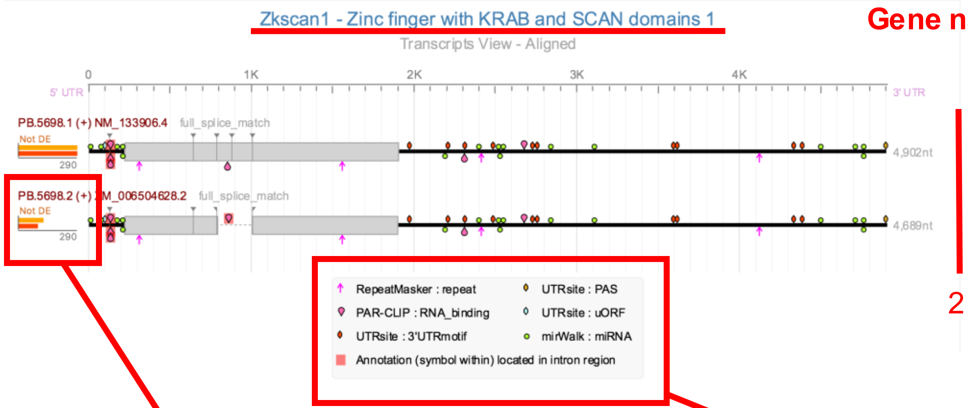


Protein annotations



tappAS visualizes functional annotations at isoform resolution … and more

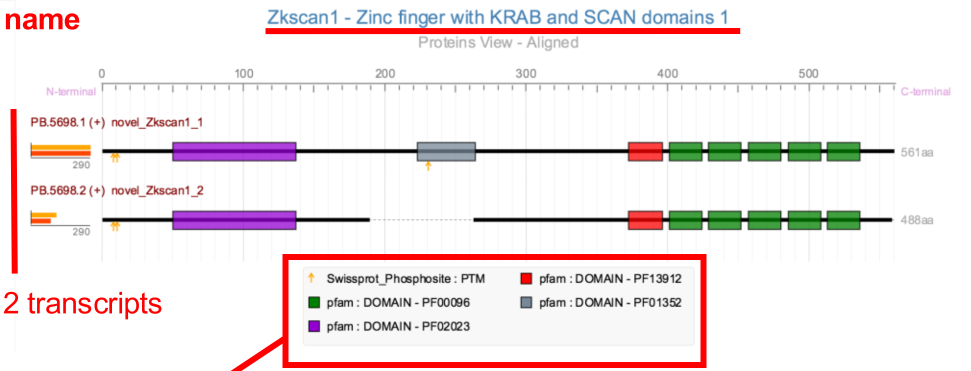
Transcript annotations



Protein annotations

Gene name

2 transcripts



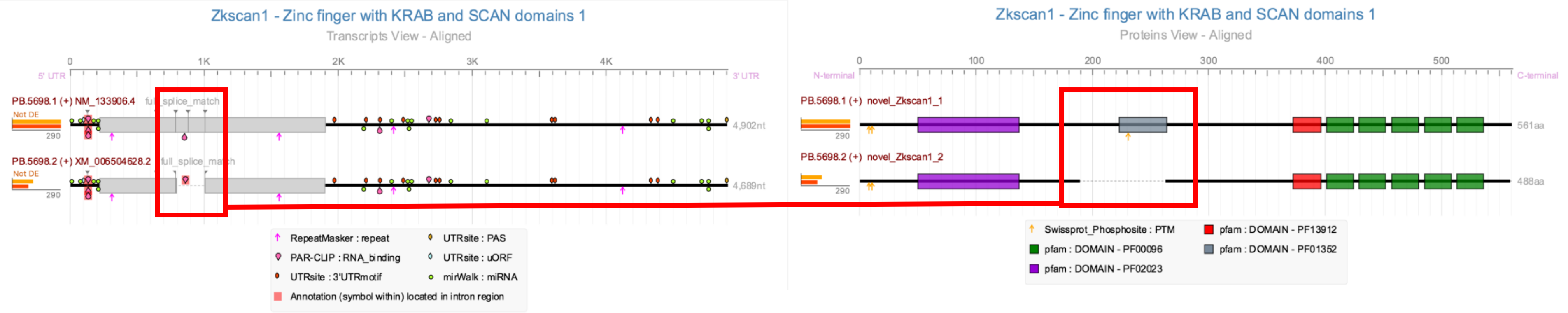
Expression in 2 conditions and whether there is differential expression.

Present transcript / protein annotations and their sources.

tappAS visualizes functional annotations at isoform resolution … and more

Transcript annotations

Protein annotations



Missing exon caused loss of PFAM domain PF01352 which included a post-translational modification (phosphorylation site).

Reflection

- Why is functional annotation at isoform-resolution useful?
- Which types of functional annotations provided by IsoAnnot(Lite) can you remember?

Thank You!

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For more information about the LongTREC Summer School:

https://longtrec.eu