Technical evaluation of Alamut - a decision-support software application for molecular genetics

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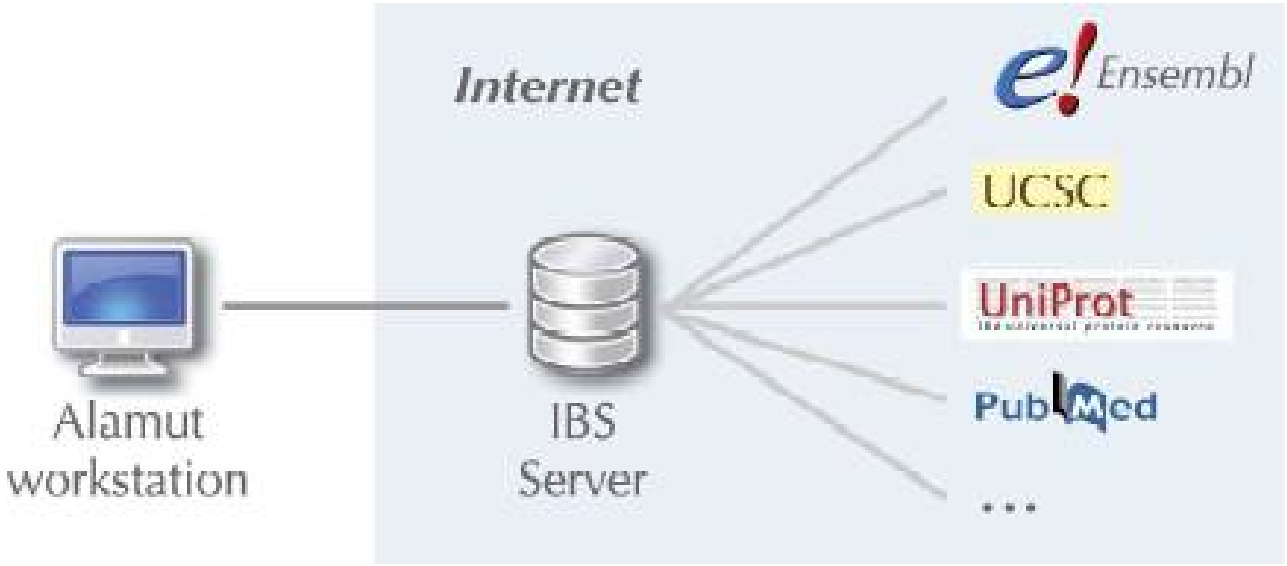
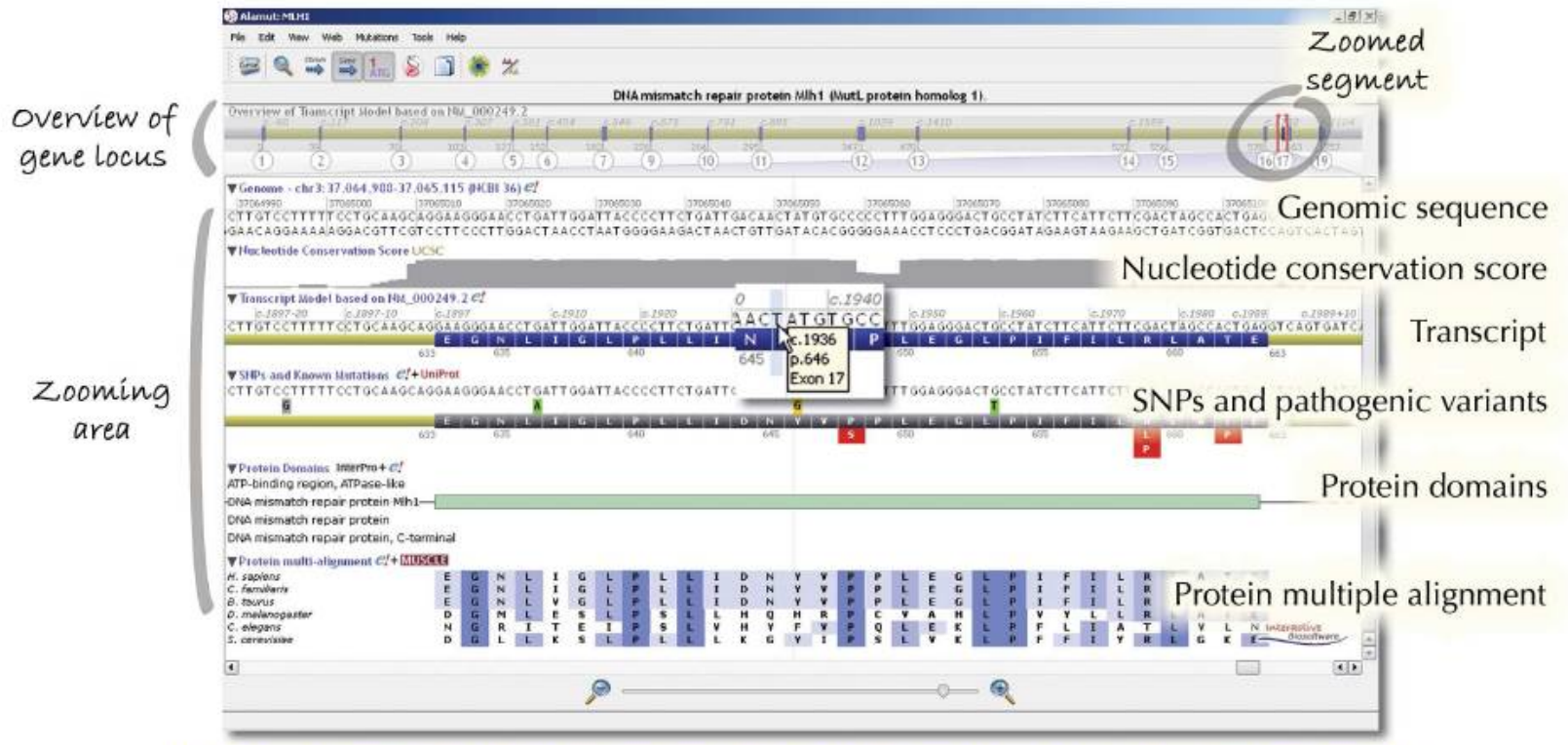
Alamut

- A decision support application developed by Interactive Biosoftware
- Aimed at molecular genetics laboratories
- Supports location and naming of variants using HGVS nomenclature
- Supports interpretation of variant pathogenicity
- It does this by bring together data from many sources

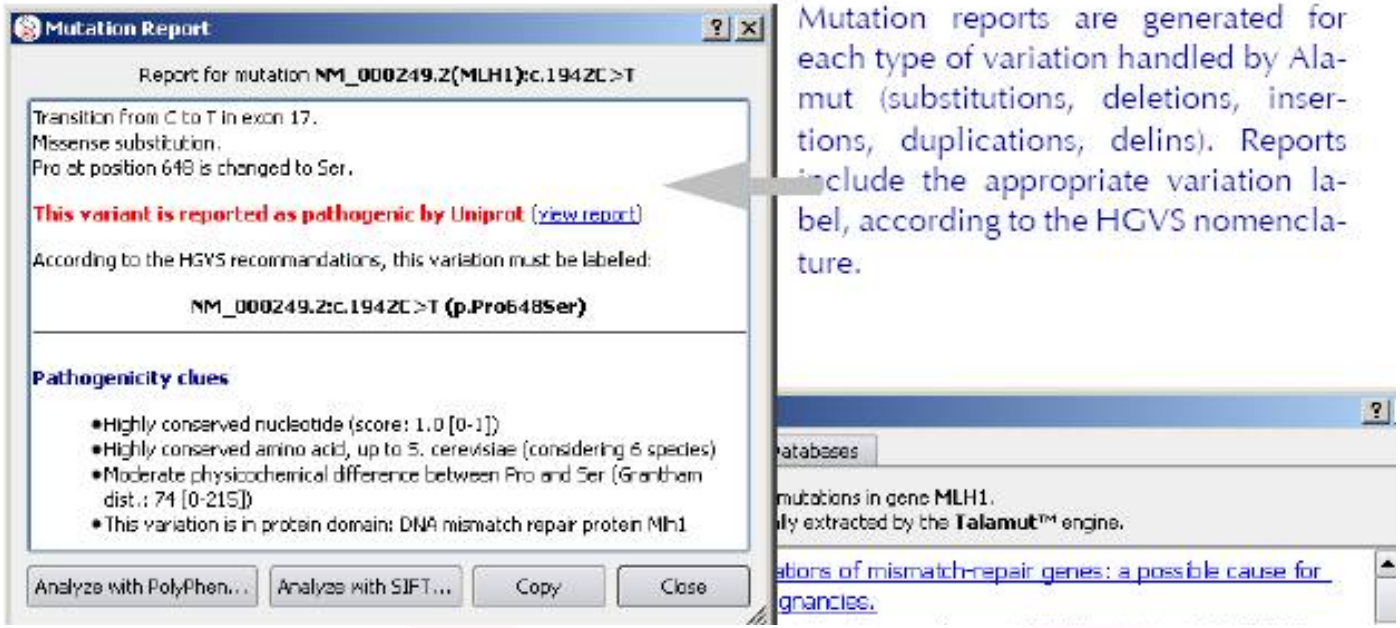
A client/server application



Location


Overview of gene locus
Zooming area
Zoomed segment
DNA mismatch repair protein Mlh1 (MutL protein homolog 1).
Genomic sequence
Nucleotide conservation score
Transcript
SNPs and pathogenic variants
Protein domains
Protein multiple alignment
c.1936
p.646
Exon 17

Nomenclature and interpretation



Our evaluation

- Aimed to test the suitability of the software for diagnostic molecular genetic testing, not to test how good the design is
- Assessed four areas:
  - User interface and usability
  - Suitability of data sources
  - Applicability to diagnostic testing
  - Validity and accuracy

Centres and genes tested

- London - Guy's and St Thomas': 193 variants in 6 genes
- Leiden – LUMC-LDGA: 182 variants in 7 genes
- Prague – CF centre: 34 variants in CF
- Manchester – NGRL: 38 variants in CF

Usability

- Few problems with installation – hospital firewalls can be an issue which may need support at first
- Intuitive and easy to use, no training required

Data sources

- Well known and trusted data sources are used
- Information about sources may be needed – interpretation of dbSNP data needs support as presence ≠ polymorphism
- Important not to interpret data from other sources – point users to the source

Application to diagnostic testing

- Addresses a frequent task and makes it easier
- This saved time even for well trained staff
- It addresses many of the tasks covered in the UV guidelines published by CMGS in 2007
- Therefore well suited to diagnostic labs

Validity and accuracy

- Few issues with nomenclature – some were higher quality and mistakes were found
- Issues only affected protein nomenclature and concern splicing effects
- No problems were found with variant or gene coordinates

Mutation reports

- Only issues are with data from other sources
- For BRCA some data from SwissProt were reported wrongly
- Data from dbSNP are reported as polymorphisms, which is not always true

Conclusions

- Alamut is easy to use, saves time and is potentially an asset to the diagnostic laboratory
- Alamut provided accurate and higher quality nomenclature than manual efforts
- Users need to be aware of that problems can occur with complex predictions
- Users need to inspect interpretation data at its source and use usual professional care

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