Tutorial Genomic variant interpretation & prioritisation for clinical research

ISMB/ECCB 2025

20 July 2025
Liverpool, UK

PDBe Protein Data Bank in Europe

Open Targets

wellcome sanger institute

DECIPHER GRCh38

G2P

UniProt

e!Ensembl

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Learning outcomes

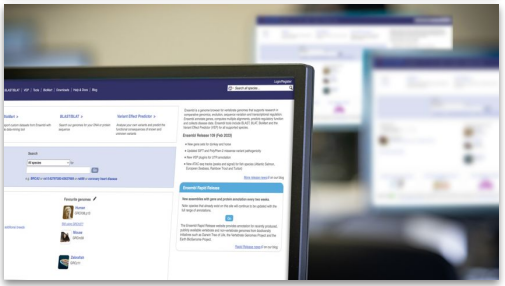
By the end of the tutorial, we expect you will be able to:

- **Explore human variation types** in commonly used bioinformatics file formats
- **Compare experimental methods** for variant effect analysis and understand the specific strengths of each
- **Navigate bioinformatics knowledge bases** to explore information about genetic variants and to contrast different approaches to see how they can be combined for interpretation
- **Evaluate evidence** from multiple sources supporting variant effect and impact in the context of research and study design
- **Investigate the impact** of variant interpretation on clinical diagnostics and drug tractability

Workshop structure

- Lectures and hands-on activities on key themes
  - Genome annotation & variation
  - Variant effects on proteins
  - Experimental methods
  - Clinical applications & resources
- Group projects & presentations
- Lunch and refreshment breaks

Full info:
https://www.iscb.org/ismbeccb2025/programme-agenda/tutorials#ip3



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Materials for this tutorial

- EBI training page: https://trainingcontent.embl.org/genomic-variant-interpretation-prioritisation-clinical-research
  - TODO: QR code
  - TODO: bit.ly link
-

Agenda for today TO ADD

Meet your trainers

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Introduction The challenge of variant interpretation

ISMB/ECCB 2025

Mallory Freeberg

Human Genomics Team Lead

20 July 2025 - Liverpool, UK

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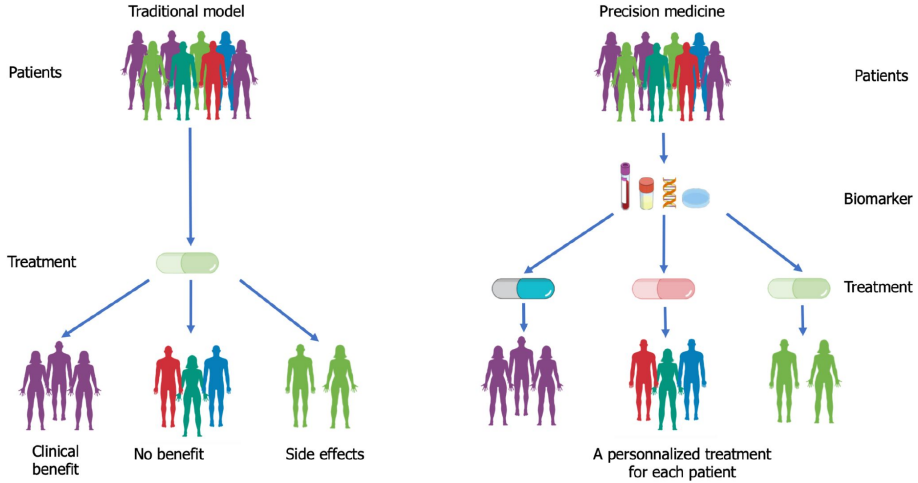
Variant interpretation is crucial for understanding health

- Genetic variation underpins both health and disease
- Interpreting variants is critical for:
  - Faster diagnosis
  - Understanding disease progression
  - Identifying drug targets
  - Personalising treatments

→ Improved health outcomes and societal and clinical benefits



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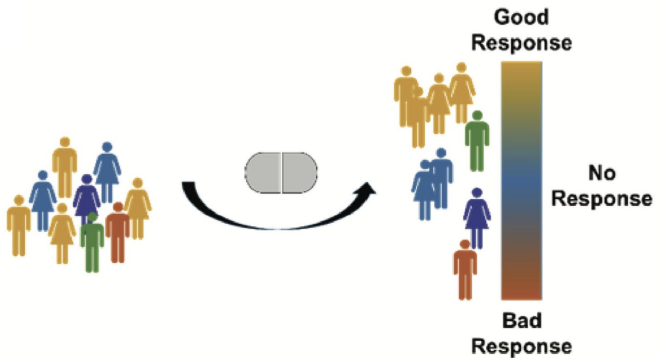
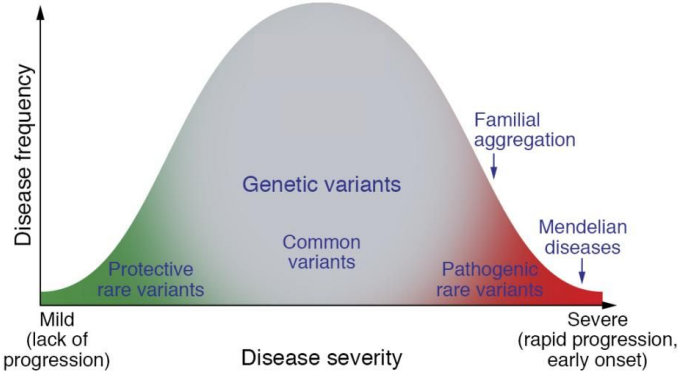
Variant interpretation is crucial for understanding health

Modulating drug response



Dictating disease prognosis



http://dx.doi.org/10.1093/bioinformatics/btz023; https://doi.org/10.1172/JCI93556

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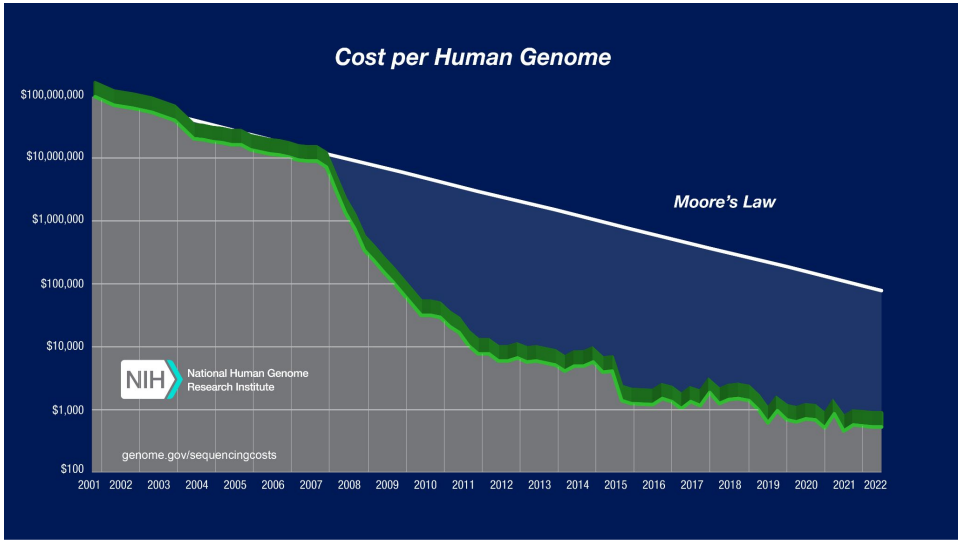
Genomic data explosion brings benefits and challenges

- Sequencing is faster and cheaper
- Genome sequencing part of healthcare in some countries
- Millions of variants per genome → interpretation remains a bottleneck



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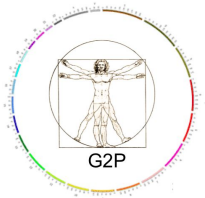
Variant interpretation is challenging in many aspects

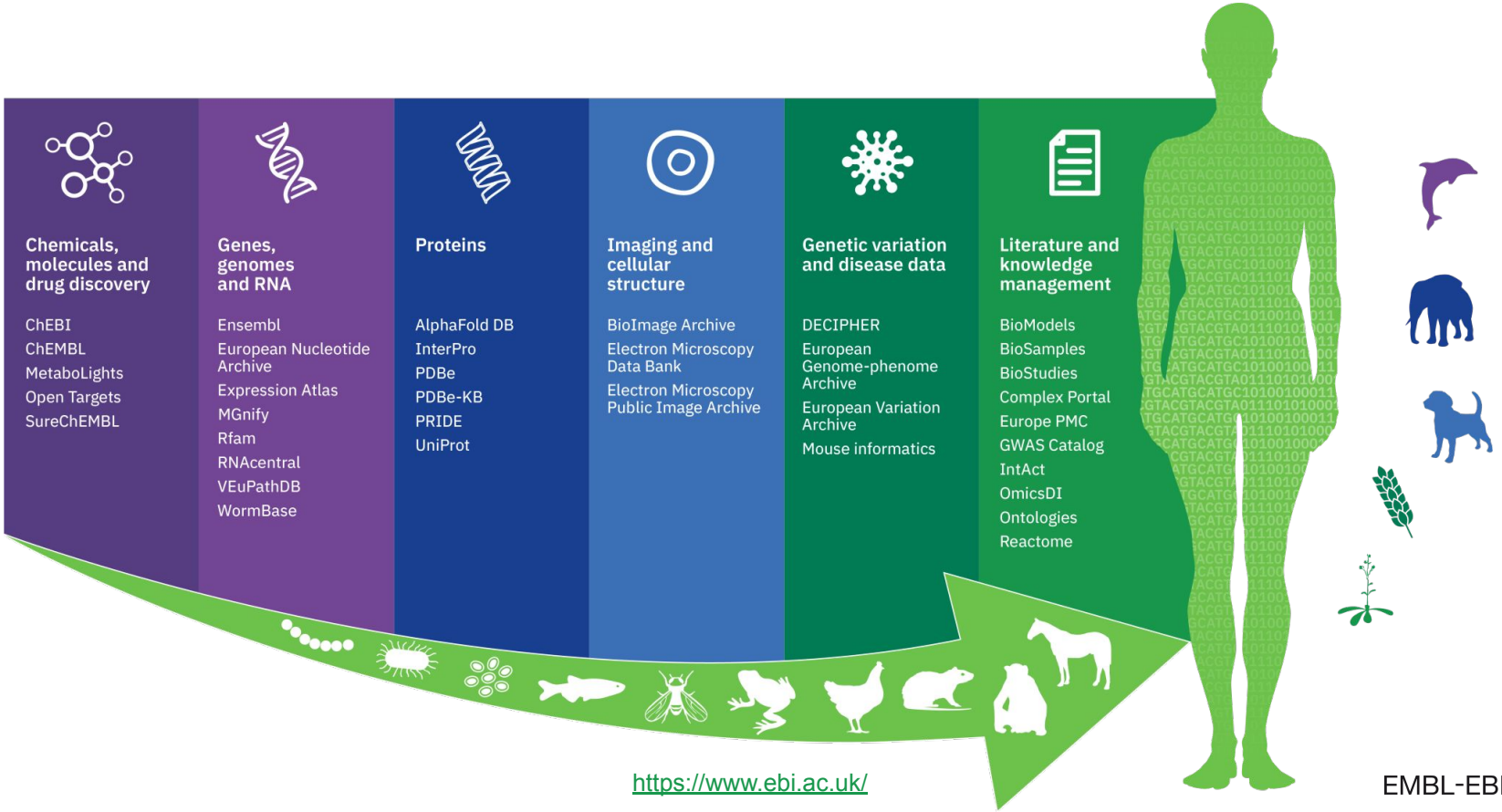
- Variants are diverse
  - Rare vs common
  - Coding vs non-coding
  - Single vs structural vs complex
- Functional effects can be population-specific and context-dependent
- *Diversity in mechanisms of action at gene and protein levels → not always obvious what is causing observations!*
- Information can be missing, incomplete, conflicting

Many resources available to tackle these challenges

- Data, annotations, and tools can help us understand variant effects
  - Bioinformatics tools & pipelines
  - Experimental assays
  - Genomic & proteomic data resources
  - Clinical databases



EMBL European Bioinformatics Institute (EMBL-EBI)



https://www.ebi.ac.uk/

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Agenda for today TO ADD

Questions?

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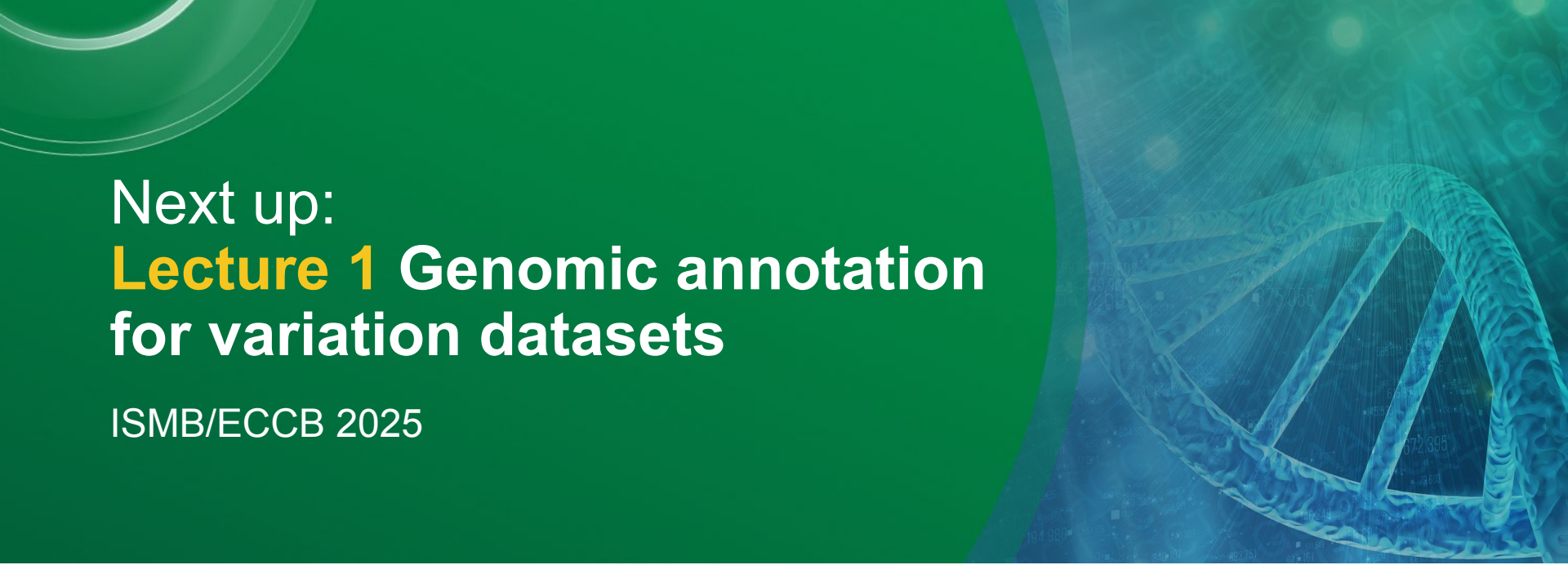

Next up:
Lecture 1 Genomic annotation for variation datasets

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Share your Feedback!

Scan the QR code to let us know your thoughts on this tutorial. Thank you!

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EMBL-EBI resources

https://www.ebi.ac.uk/services/data-resources-and-tools

The European Molecular Biology Laboratory

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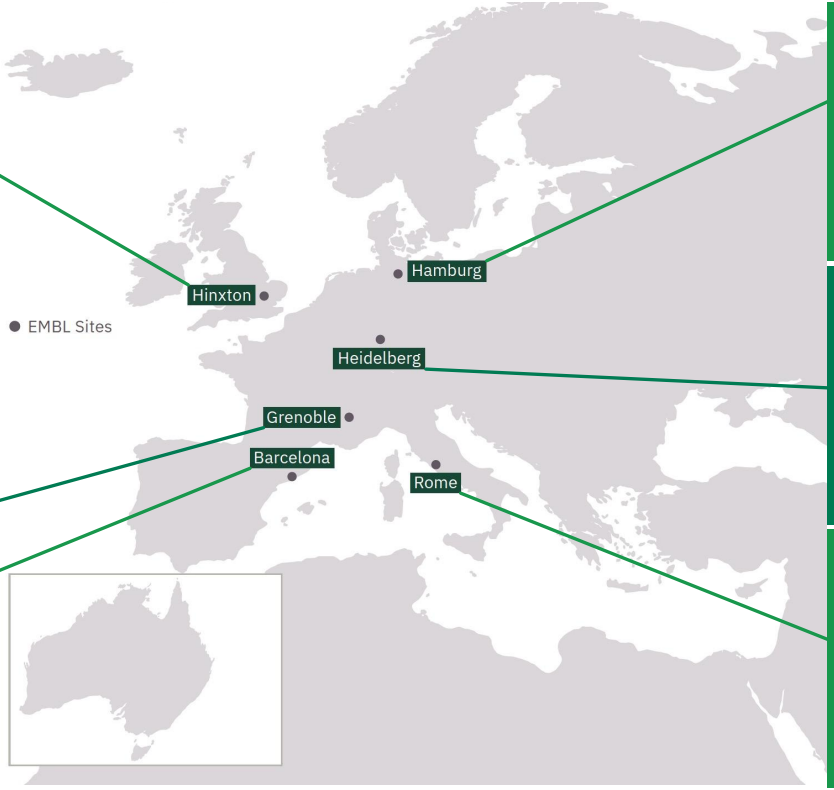
Bioinformatics

Grenoble

Structural biology

Barcelona

Tissue biology and disease modelling

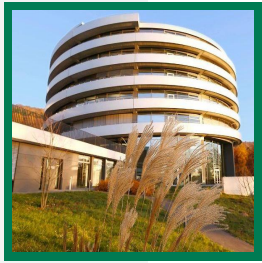


Hamburg

Structural biology

Heidelberg

Life sciences



Rome

Epigenetics and neurobiology

https://www.embl.org/

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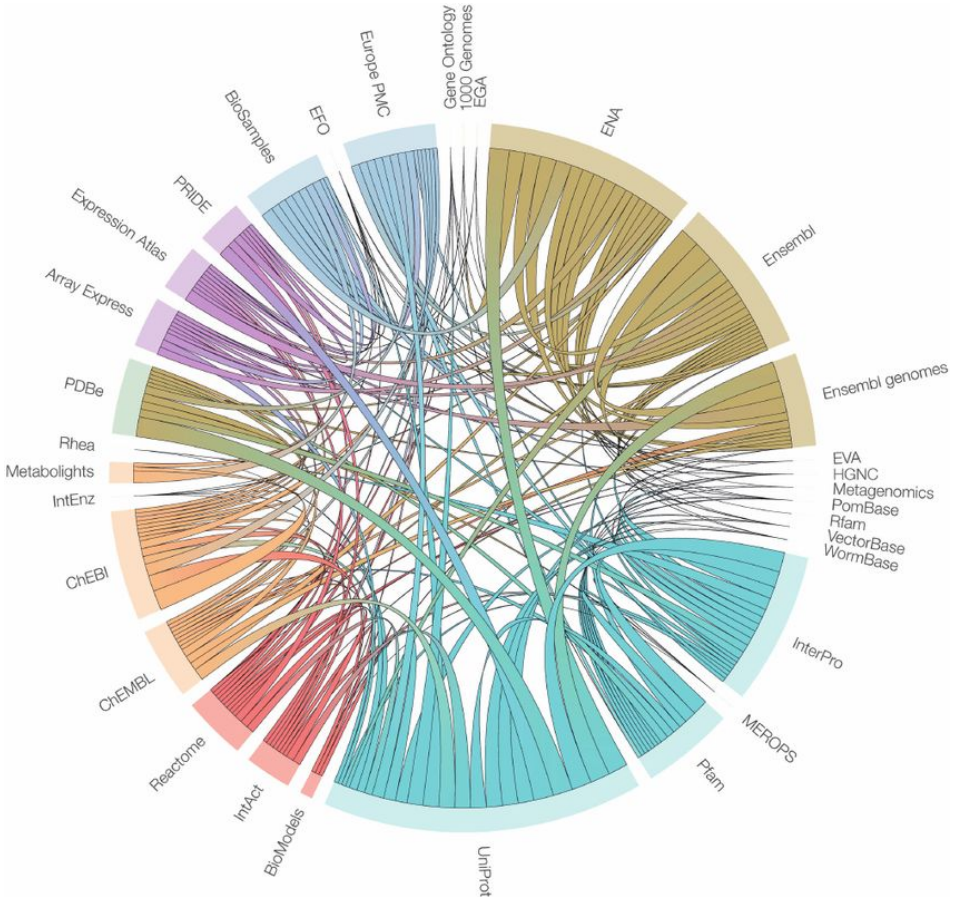
EMBL-EBI services and resources share data



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