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Single Day Event

Clinical Trials in the Era of Precision Medicine: Innovative Approaches and Best Practices

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Abstract

Precision Medicine and Data Quality Analysis: Innovative Approaches and Best Practices
With an ever-growing need for developing therapeutic technologies for more than 7,000 rare diseases and continuous efforts in making existing therapies better, precision medicine is revolutionizing healthcare by tailoring treatments to cohorts/individual patients based on genetic, environmental and lifestyle factors. The success of this approach heavily relies on the quality and analysis of the data. High-quality data ensures accurate diagnosis, effective treatment plans and improved patient outcomes. Innovative approaches in data quality involve advanced data collection methods, integration of diverse data sources, and robust validation techniques. Analysis techniques leverage AI/ML to uncover patterns and insights from vast datasets. Best practices include establishing standardized protocols for data management, ensuring data privacy and security, and fostering interdisciplinary collaboration among healthcare professionals, data scientists and researchers.

This presentation will underscore the critical role of data quality and analysis in advancing precision medicine, highlighting innovative strategies and best practices that drive this transformative field.

About me

- **PhD in Cell & Molecular Biology**
  Drexel University
- **Postdoctoral Research**
  Drexel University College of Medicine
  The Wistar Institute
- **Senior Research Scientist**
  Cell & Gene Therapy Division, Intas Pharmaceuticals
- **Technology Solutions for Life Sciences & Healthcare**
  Cognizant
  Hexaware Technologies

Research Areas

- **Immunology**
- **Oncology**
- **Infectious Diseases**
- **Cell & Gene Therapy**
- **Virology**

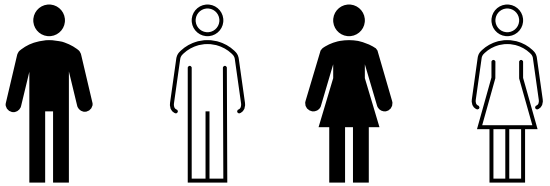
Agenda

1. Traditional Medicine vs. Precision Medicine
2. Clinical Trial Design in Precision Medicine
3. Challenges in Genomics and Precision Medicine
4. Clinical Data Management: Innovative Approaches and Best Practices
5. Summary, Q & A

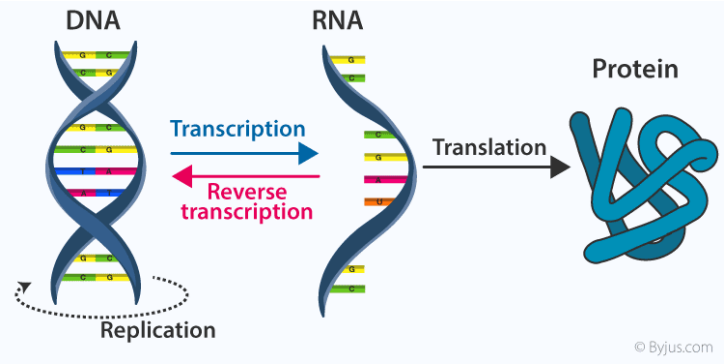
Traditional Medicine has been <u>One Size Fits All</u>

Understanding Human Genome

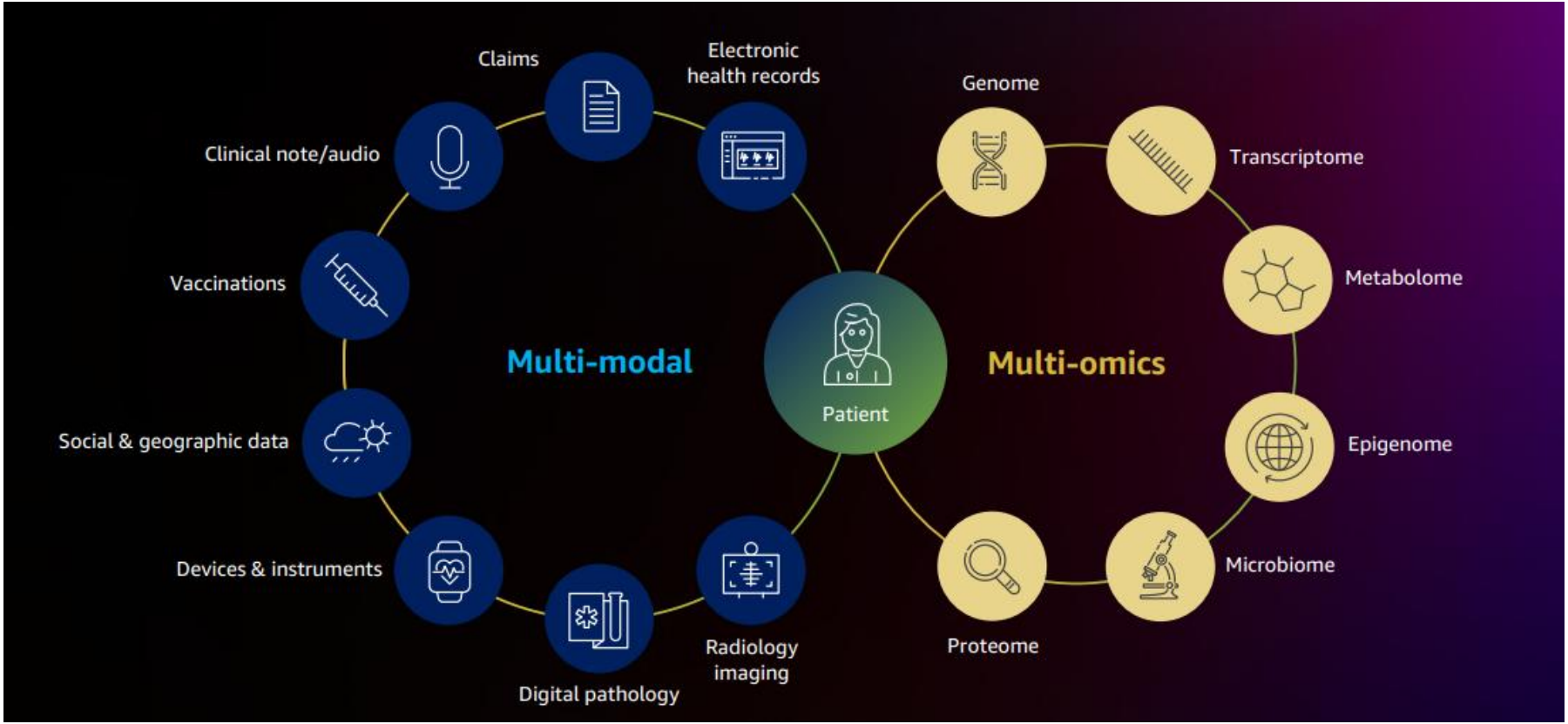
Human Genome is 3 Billion Base Pairs of DNA in a single cell



Humans are 99.9% genetically identical, which means that out of 3 billion base pairs, 0.1% i.e., 3 million pairs are unique



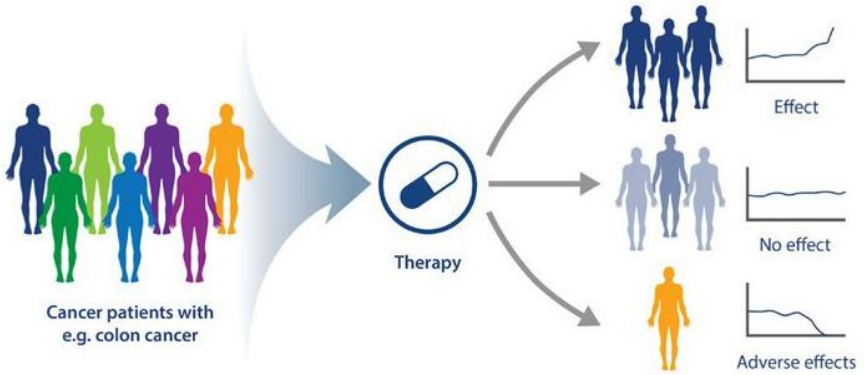
Creating a more holistic view of the patient



Medicine should not be “One Size Fits All”

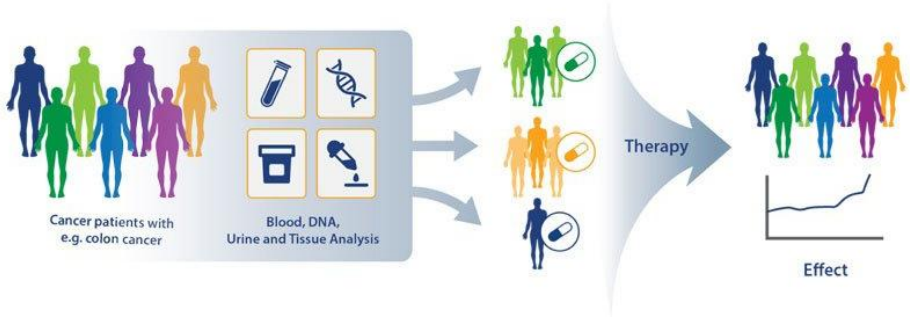
Traditional Medicine

One Size Fits All

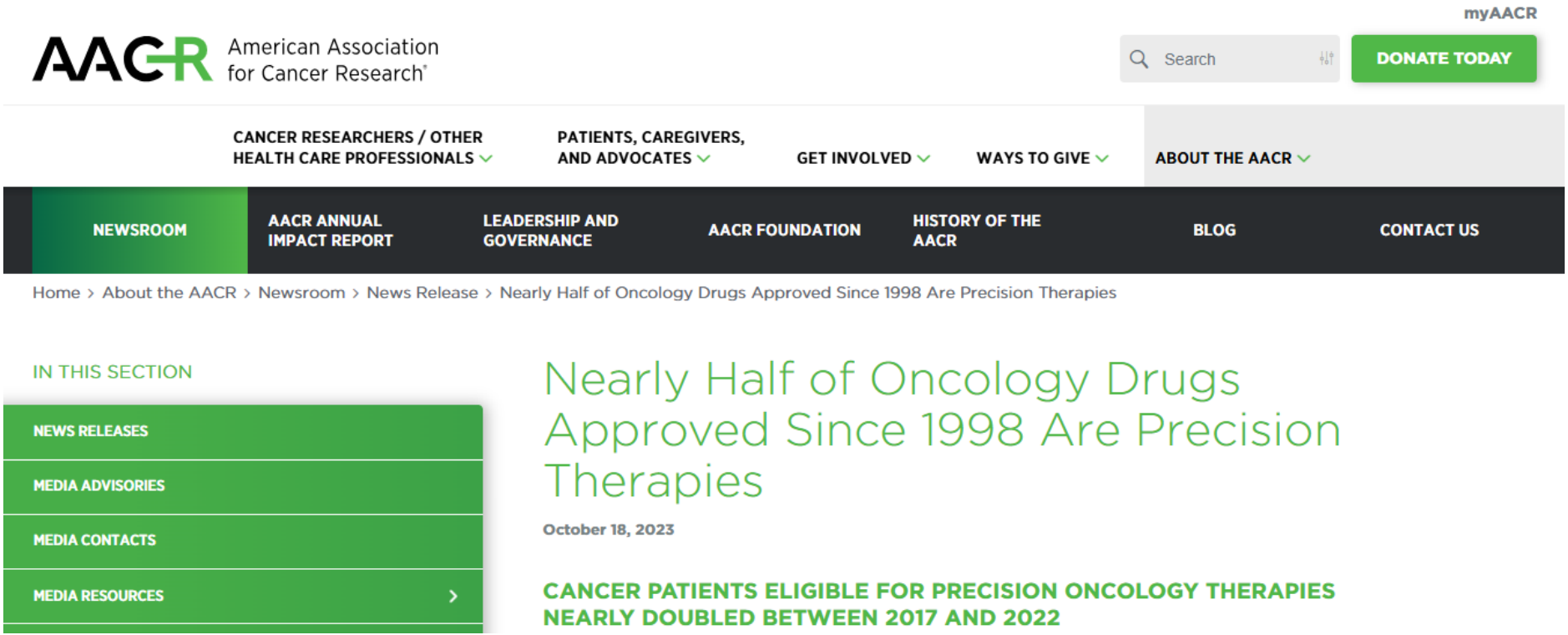


Precision Medicine

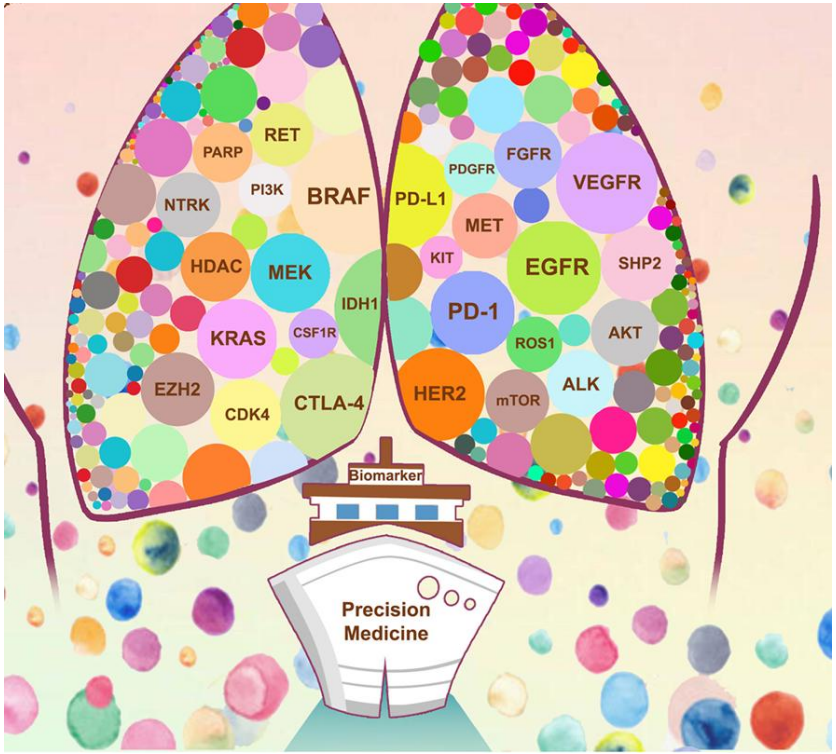
Personalized

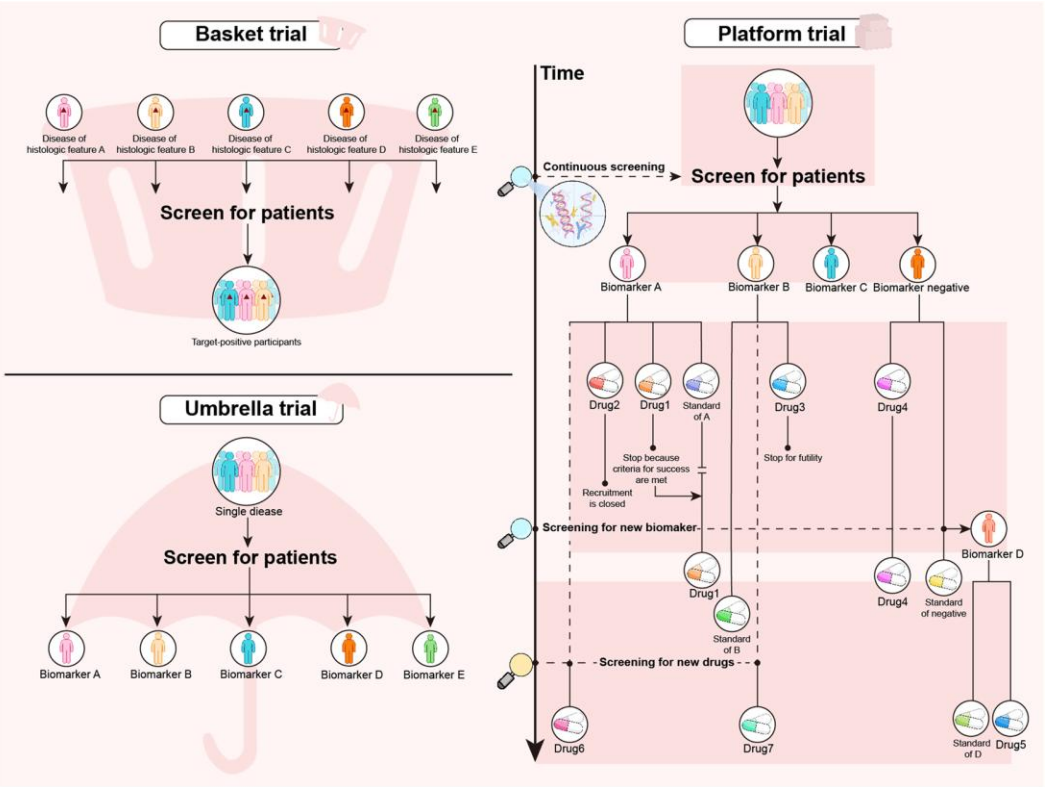


Precision Oncology



Clinical Trial Design in Precision Medicine





Source: Xiao-Peng Duan et al, Nature Signal transduction & targeted therapy, 2024

Challenges in Biomarker-guided Clinical Trials

Patient recruitment and selection

Data Challenges

Biomarker Assay validation

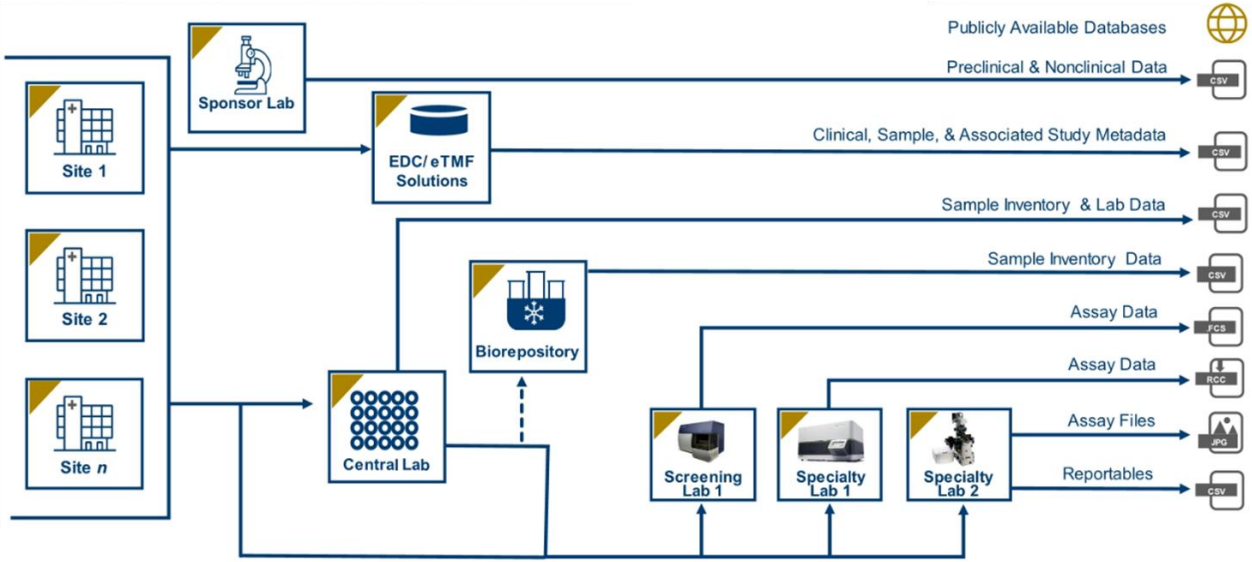
Ethical considerations

Regulatory aspects

Cost considerations

Disconnected Data, Samples, Technology

Data streams siloed across decentralized locations and within sponsor organizations



- Manual, time-consuming data processing
- Inability to map, transform, integrate, query data from various vendors/file formats
- Hard to analyze and visualize data in one place
- Difficult to generate shareable reports to key stakeholders

About me – Dr Sapna

- **Lead Subject Matter Expert**
  Clinical Solutions, PointCross Life Sciences
- **Scientist**
  Indian Council of Medical Research, ICMR-NCDIR
- **Regulatory Affairs**
- **PostGraduate**
  Oral Pathology , Microbiology & Forensic Medicine

Research Areas

- **Oncology**
- **Immunotherapy**
- **Infectious Diseases**
- **Virology**
- **Forensic Medicine**

Challenges of Biomarker Data

Data Transfer Spec

Variation on DTS by vendor

Vendors ranging from a university lab to large assay platform

Assay Methodology Variability

Inconsistent definition & Classification

Inconsistent naming conventions across labs and assay types

Time-consuming manual standardization

BIG DATA

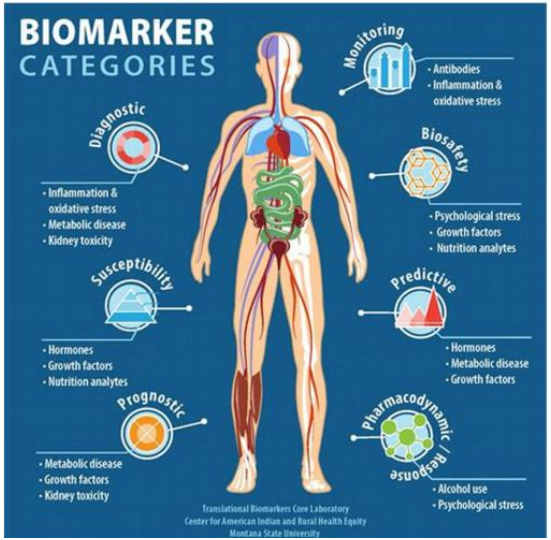
Control Terms

Limited Guidance /database from CDISC

Interdisciplinary knowledge across multiple roles such as scientists, data managers, programmers

Data standard evolution

Evolving CDISC standard in biomarker data standardization



Biomarker Validation & Standardization Process

Automated Validation & Data Transformation

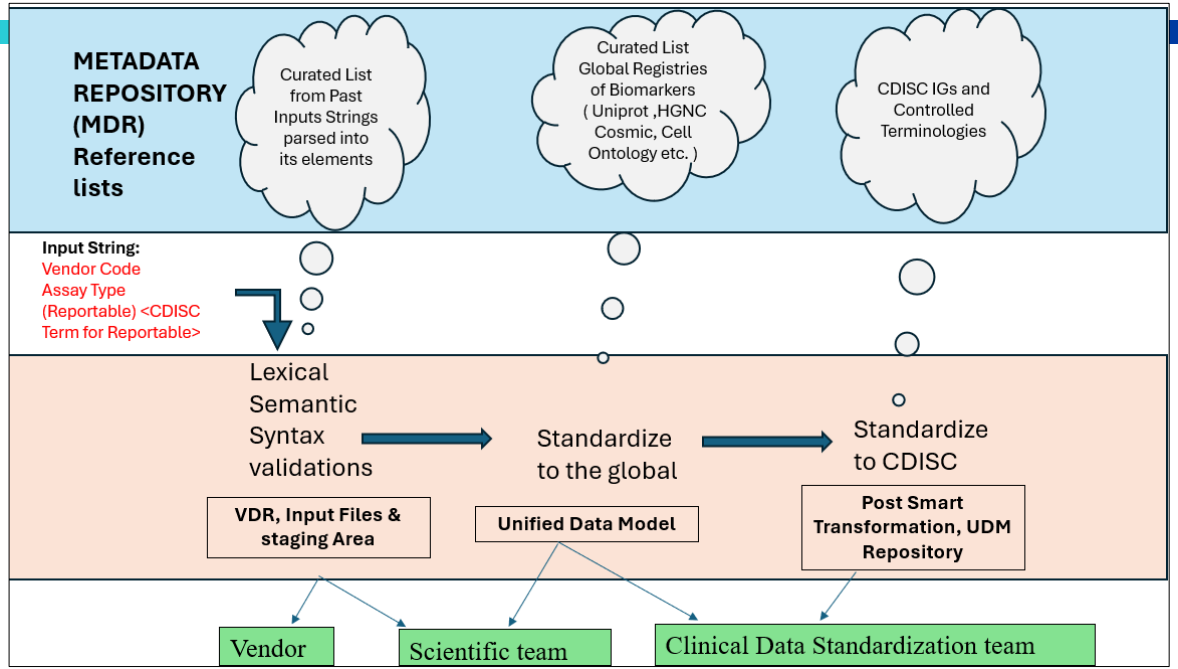
-To ensure reliability and reproducibility in clinical trials

-To confirm their predictive power and clinical relevance, thereby enhancing the credibility of trial outcomes.

MDR - "the ontology engine".

-Intelligent Standards Management & Integrations

Scientific-Regulatory Bridge Framework



DOMAIN	ISSUE	EXAMPLE	PROMPT QUESTION	DECISION
GF	When Gene Symbol cannot be identified from HGNC	ZBA1	Gene Symbol not found in the HUGO database	Request advice from Scientific team

Example :Genomic Findings

- **Description**
  To include assessments & results for genetic variation , transcription, gene expression & fusion
- **Dataset name**
  gf.xpt, Genomic findings
- **Structure**
  One record per finding per observation per specimen per subject
- **Key Variables**

Study ID, Subject ID , Method of Test or Examination , Specimen Material Type , Visit Number, Name of Genomic Measurement; Genome Reference

Subject Identifier	Sample ID	Sample Category	Processed Specimen Type	Visit	Assay Method	Assay Lab/ Assay Name	Assay Lab Analyte Name	Analyte Result	DNA sequence change	Protien description	Variant Allele Frequency	Reference sequence
S12345	R001	Blood	RNA	D1	qRT-PCR	Transcript Lab/RNA Analysis	BRCA1	Detected	c.68_69del	BRCA1 - Breast Cancer	0.002	GRCh38
S12346	D002	Blood	DNA	D2	PCR	Genomics Lab/DNA Sequencing	TP53	Not Detected	c.215C>T	TP53 - Tumor Suppressor	0.01	GRCh38

GFSPEC (Specimen Material Type)

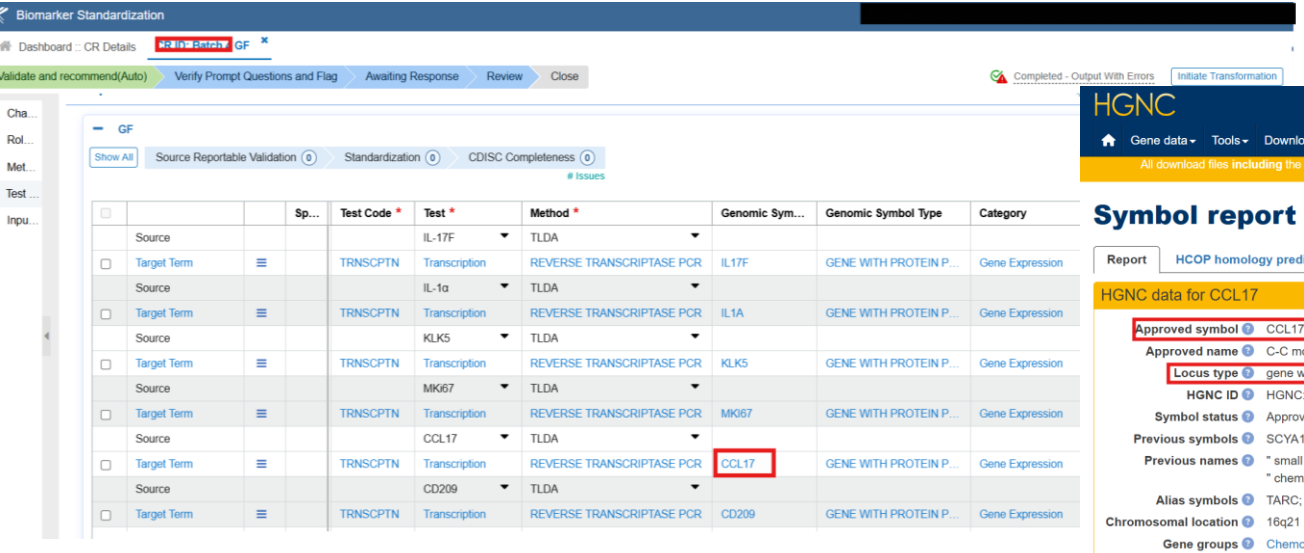
GFMETHOD (Method of Test)

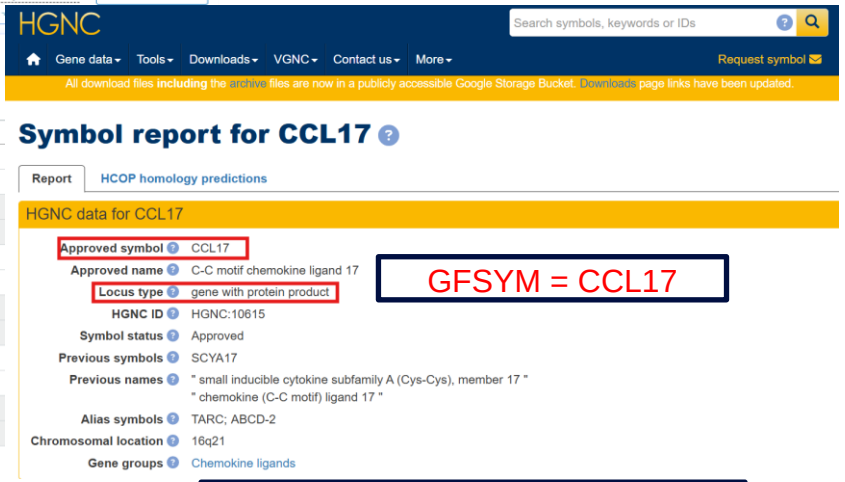
GFSYM (Genomic Symbol)

GFORRES(Result /Finding in Units)

GFSEQID(Sequence Identifier)

Standardizing to Global : HUGO Registry



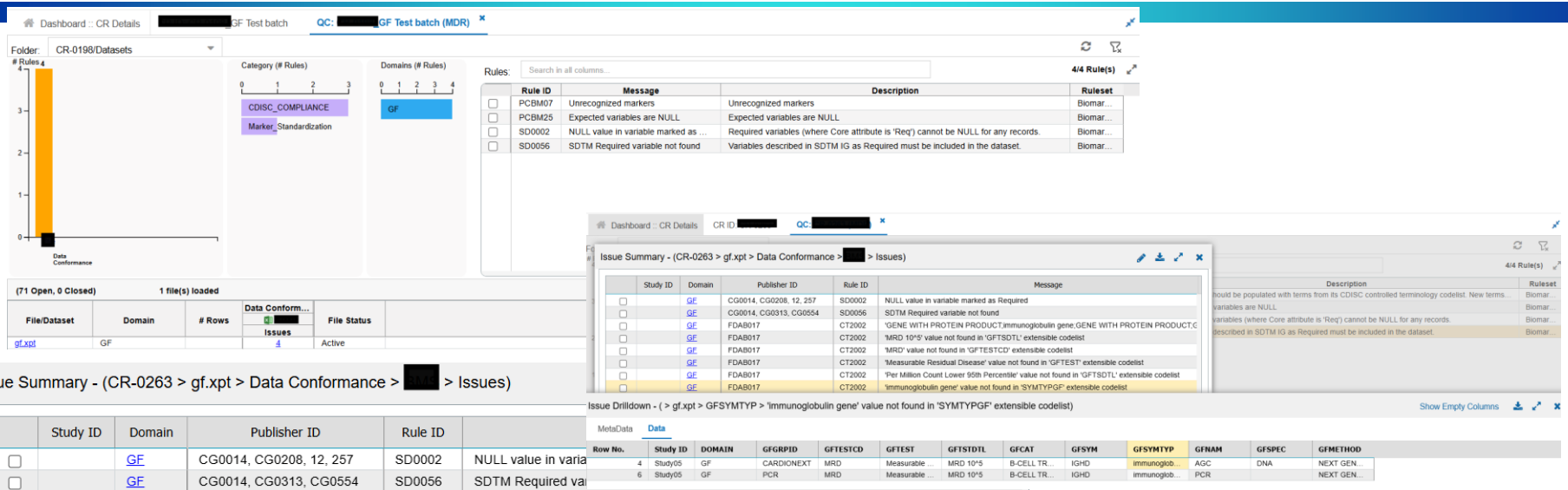


GFSYM = CCL17

GFSYMTYP = GENE WITH PRODUCT

Vendor provided data		Text Interpretation-based on CDISC Linkage			Text Interpretation- derived from HUGO database			
Vendor Reportable Name	Vendor Genomic Symb	Genomic Findings Test Name	Category	Method of Test or Examination	Approved Name	Genomic Symbol Type	Genetic Location	HGNC ID
PREDICTED CODING SEQUENCE CHANGE	BAG3	Single Nucleotide Variation	Genetic Variati	TARGETED GENOME SEQUENCING	BAG cochaperone 3	GENE WITH PROTEIN PRODUCT	121410891-121437331	939
PREDICTED AMINO ACID CHANGE	EMD	Single Nucleotide Variation	Genetic Variati	TARGETED GENOME SEQUENCING	emerin	GENE WITH PROTEIN PRODUCT	153607654-153609883	3331
Gene expression	STAT1	Transcription	Gene Expressic	REVERSE TRANSCRIPTASE PCR	Signal transducer and activator of transcription 1	GENE WITH PROTEIN PRODUCT	2q32.2	11362

Data Quality : Validation with eDV



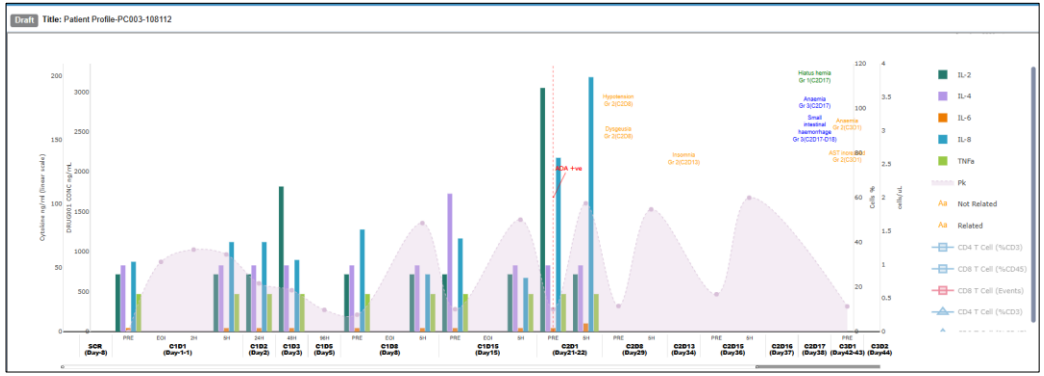
Issue Summary - (CR-0263 > gf.xpt > Data Conformance > [redacted] > Issues)

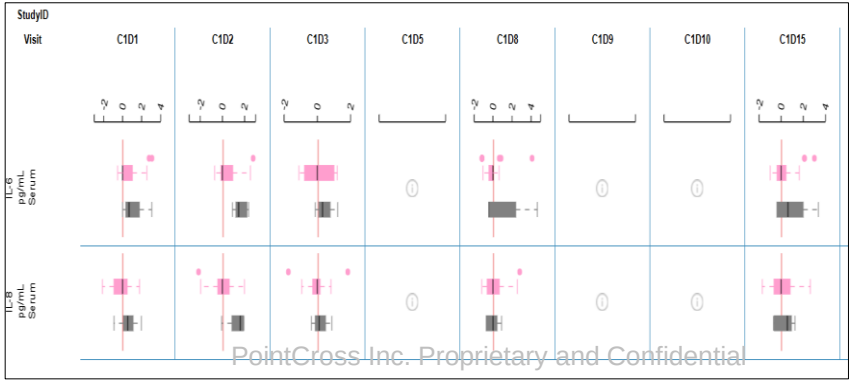
	Study ID	Domain	Publisher ID	Rule ID	
☐		GF	CG0014, CG0208, 12, 257	SD0002	NULL value in varia
☐		GF	CG0014, CG0313, CG0554	SD0056	SDTM Required va
☐		GF	FDAB017	CT2002	'GENE WITH PROTEIN PRODUCT;immunoglobulin gene;GENE WITH PROTEIN PRODUCT;G
☐		GF	FDAB017	CT2002	'MRD 10^5' value not found in 'GFTSDTL' extensible codelist
☐		GF	FDAB017	CT2002	'MRD' value not found in 'GFTESTCD' extensible codelist
☐		GF	FDAB017	CT2002	'Measurable Residual Disease' value not found in 'GFTEST' extensible codelist
☐		GF	FDAB017	CT2002	'Per Million Count Lower 95th Percentile' value not found in 'GFTSDTL' extensible codelist
☐		GF	FDAB017	CT2002	'immunoglobulin gene' value not found in 'SYMTYPGF' extensible codelist
☐		GF		PCBM25	Expected variables are NULL
☐		GF		PCBM25	Expected variables are NULL
☐		GF		PCBM25	Expected variables are NULL
☐		GF		PCBM25	Expected variables are NULL
☐		GF		PCBM25	Expected variables are NULL

Genomic Finding : Mapping to CDISC Standards

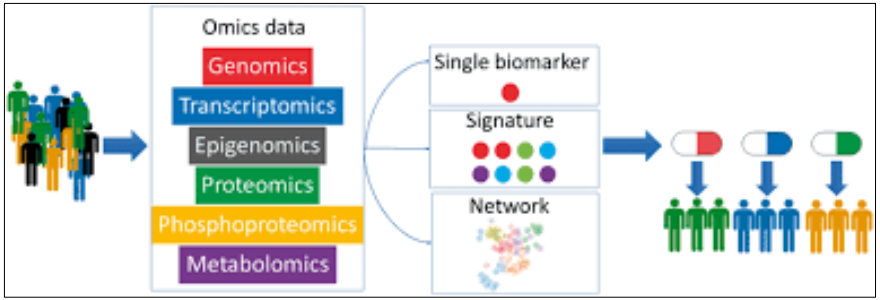
Subject Identifier	Sample ID	Sample Category	Genetic Material Sample	Visit	Assay Method	Assay Lab/ Assay Name	Assay Lab Analyte Name	Analyte Result	DNA sequence change	Protein description	Variant Allele Frequency	Reference sequence
S12345	R001	SKIN TISSUE	RNA	D1	TaqMan Low-Density Array (TLDA)	Transcript Lab/RNA Analysis	MMP12	CT	c.442C>T (p.Arg148C	Matrix Metalloproteinase-12 (MMP-12)	0.002	NM_002425.4 (for MMP12)
S12346	D002	BLOOD	DNA	D2	Targeted Genome Sequencing	Genomics Lab/DNA Sequencing	ALPK3	Detected	c.1300G>A (p.Val434	Alkaline Phosphatase 3 (ALPP)	0.01	NM_003770.3 (for ALKP3)

Domain Abbreviation	Ref.ID	Sequence Number	Group ID	Specimen Material	Method of Test or Examination	Category for Genomic Finding	Short Name of Genomic Measurement	Name of Genomic Measurement	Measurement Test or Examination Detail	Genomic Symbol	Genomic Symbol Type	Results or Findings in original Units	Sequence Identifier	Visit
Domain	GFREFID	GFSEQ	GFGRPID	GFSPEC	GFMETHOD	GFCAT	GFTESTCD	GFTEST	GFTSTDTL	GFSYM	GFSYMTYP	GFORRES	GFSEQID	VISIT
GF	R001	1	1	RNA	REVERSE TRANSCRIPTASE PCR	Gene Expression	TRNSCPTN	Transcription	GENETIC TRANSCRIPTION INDICATOR	MMP12	GENE WITH PROTEIN PRODUCT	Ct	NM_002425.4	D1
GF	D002	2	2	DNA	TARGETED GENOME SEQUENCING	Genetic Variation	SNV	Single Nucleotide Variation	PREDICTED CODING SEQUENCE CHANGE	ALPK3	GENE WITH PROTEIN PRODUCT		NM_003770.3	D2





Harmonizing the Complexity



- Centralized, Version Controlled Standards Repository (MDR)
- Intelligent Classification System/Agile CT Management
- AI/ML based data mapping/transformations
- Automated Validation/Quality Control
- Unified Repository for Patient data
- Visualization tools

Thank You!

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