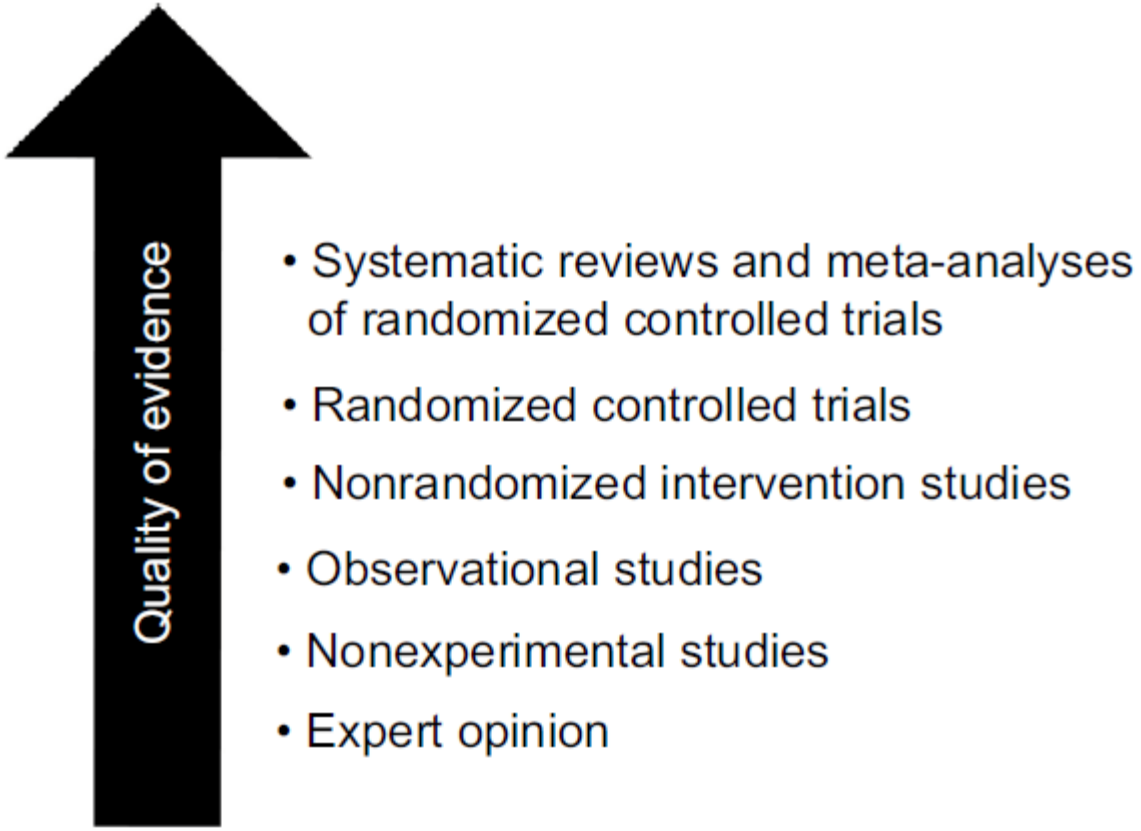
Session 5: Updates in Policy Improvement of PBM

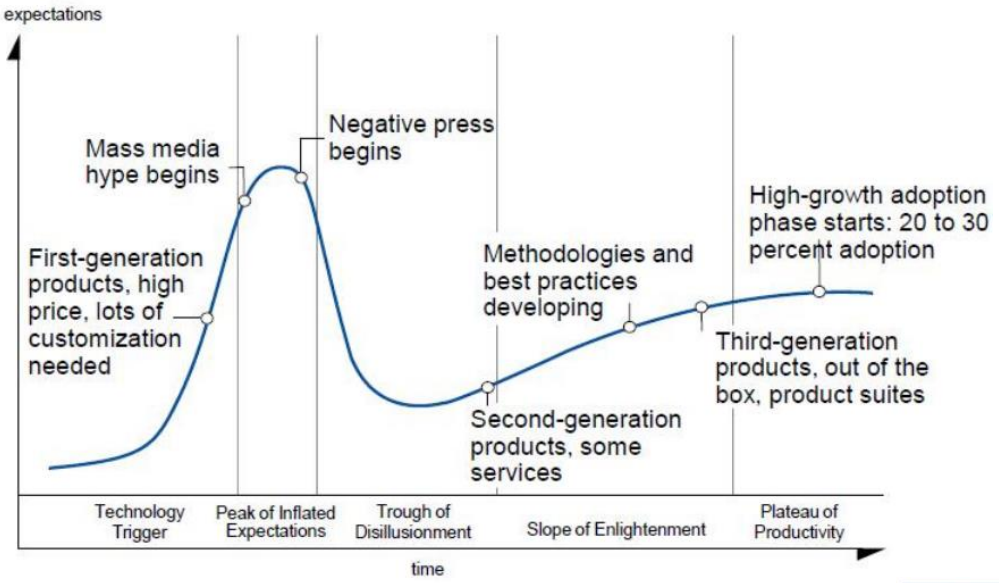
Role of Omics associated with Transfusion

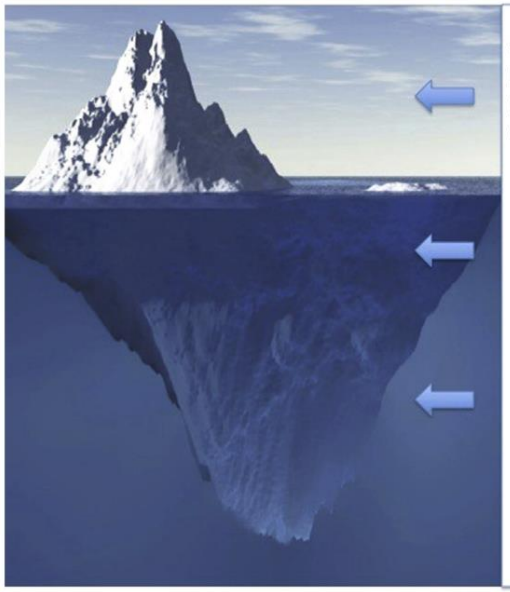
박경운
서울의대 검사의학교실
분당서울대병원 진단검사의학과

- Real-World Data (RWD)
- Real-World Evidence (RWE)



Innovation (Gartner) / Diagnostic pyramid (CMI 2018)





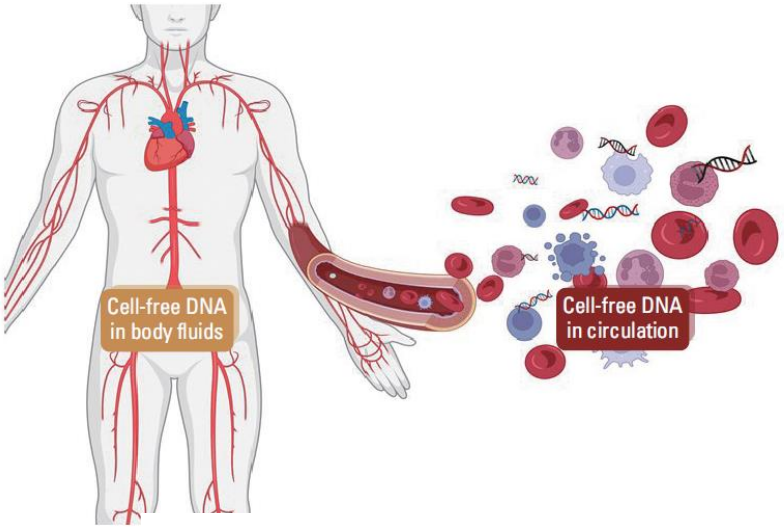
WHAT YOU KNOW: THERANOSTICS
Diagnosis of treatable etiologies
Routine
Commercial applications

WHAT YOU SHOULD KNOW:
Differential diagnosis of known etiologies
Diagnostics less common, may not inform treatment

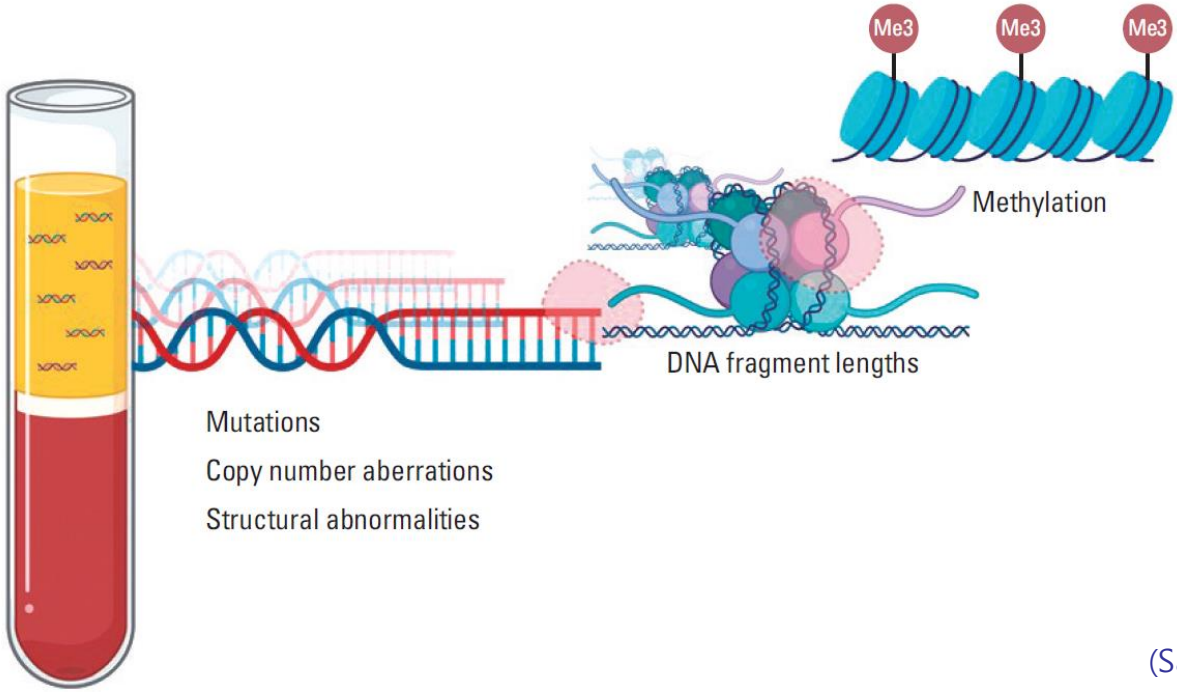
WHAT YOU MAY NEVER KNOW:
Unknown pathogens, emerging diseases, novel platforms for discovery

Clinical circulating tumor DNA testing for precision oncology

(SNUCM LM, Cancer Res Treat 2023)



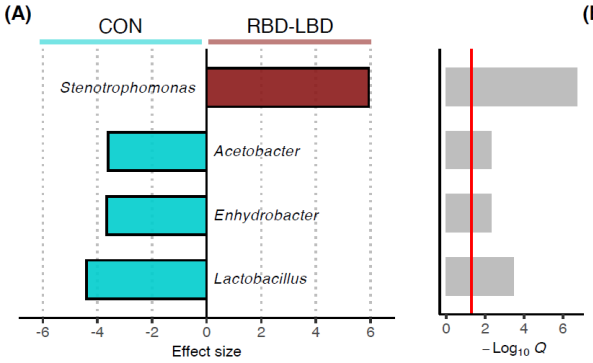
Oncology	Tumor cell-free DNA	Oncogenomics
Prenatal testing	Fetal cell-free DNA	IH Genomics
Post-transplant surgery surveillance	Transplanted cell-free DNA	Transplant genomics
Microbial cell-free DNA		Metagenomics

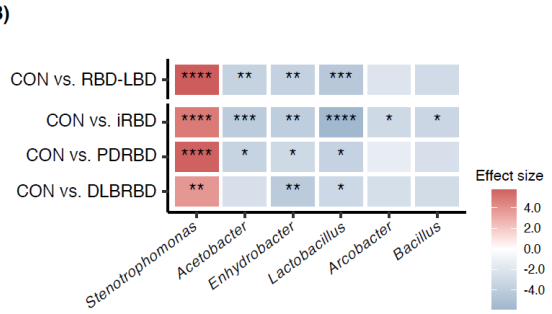


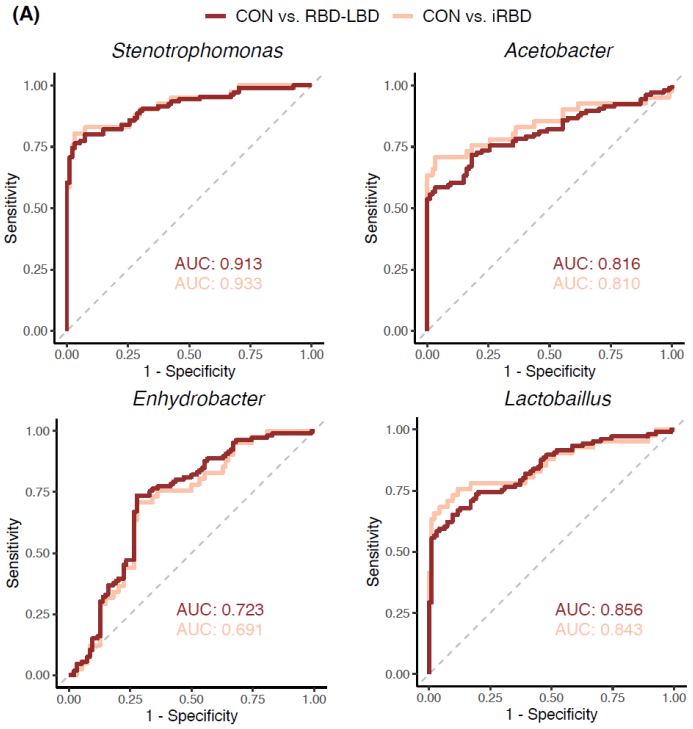
SNUH
Next Generation Diagnostics Research Group

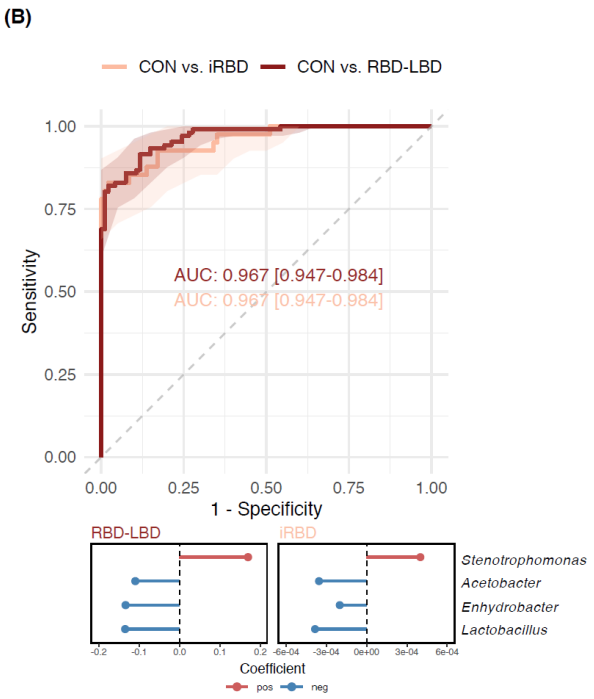
NGD Research Group
(Saliva, Liquid Biopsy, Microbiome)

Blood microbiome signatures in the REM sleep behavior disorder - Lewy body disease continuum [SNUCM LM, J Neural Transm (Vienna) 2025]





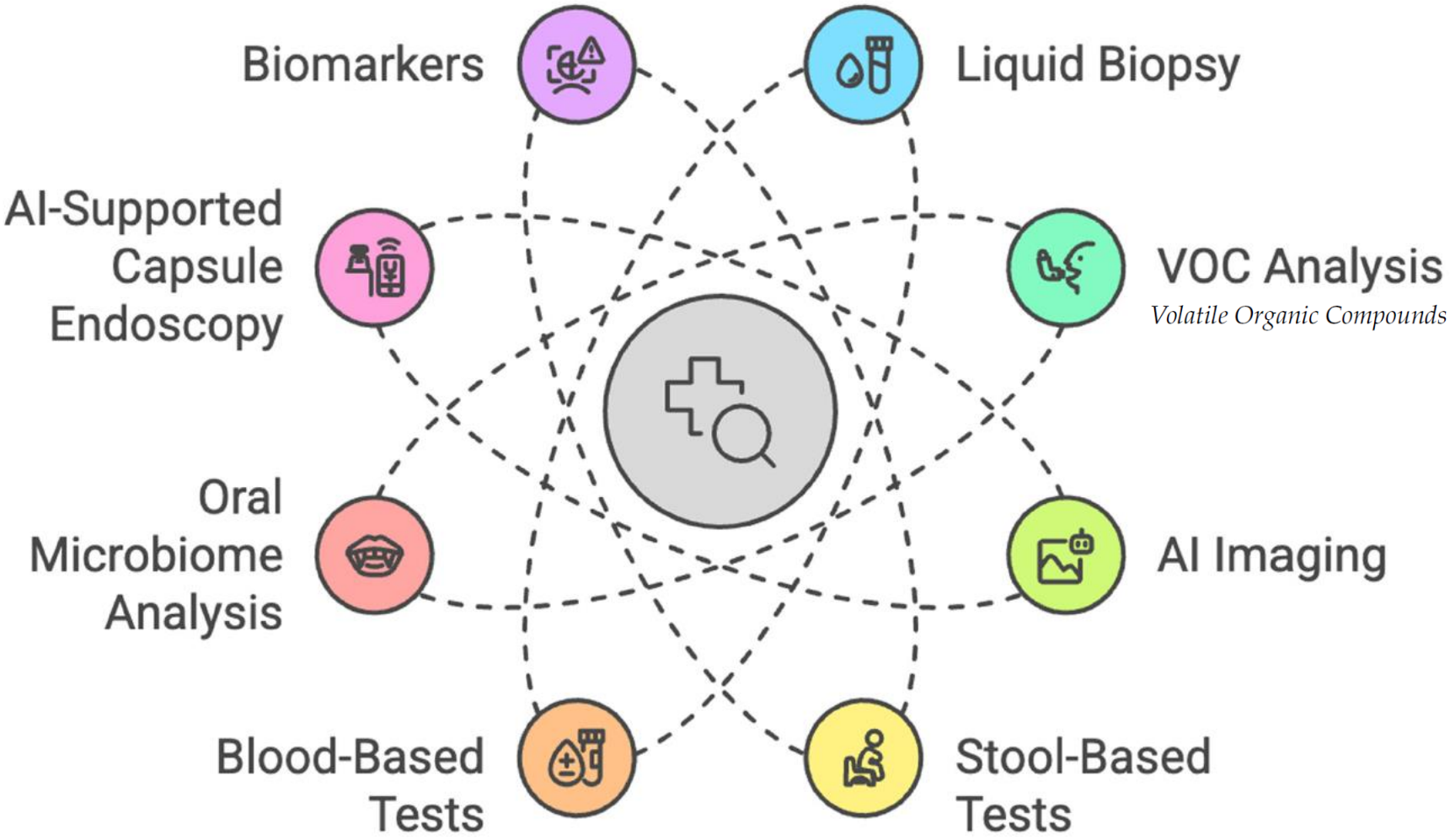




iRBD (isolated RBD), PDRBD (Parkinson's disease with probable RBD), DLBRBD (dementia with Lewy bodies with probable RBD)

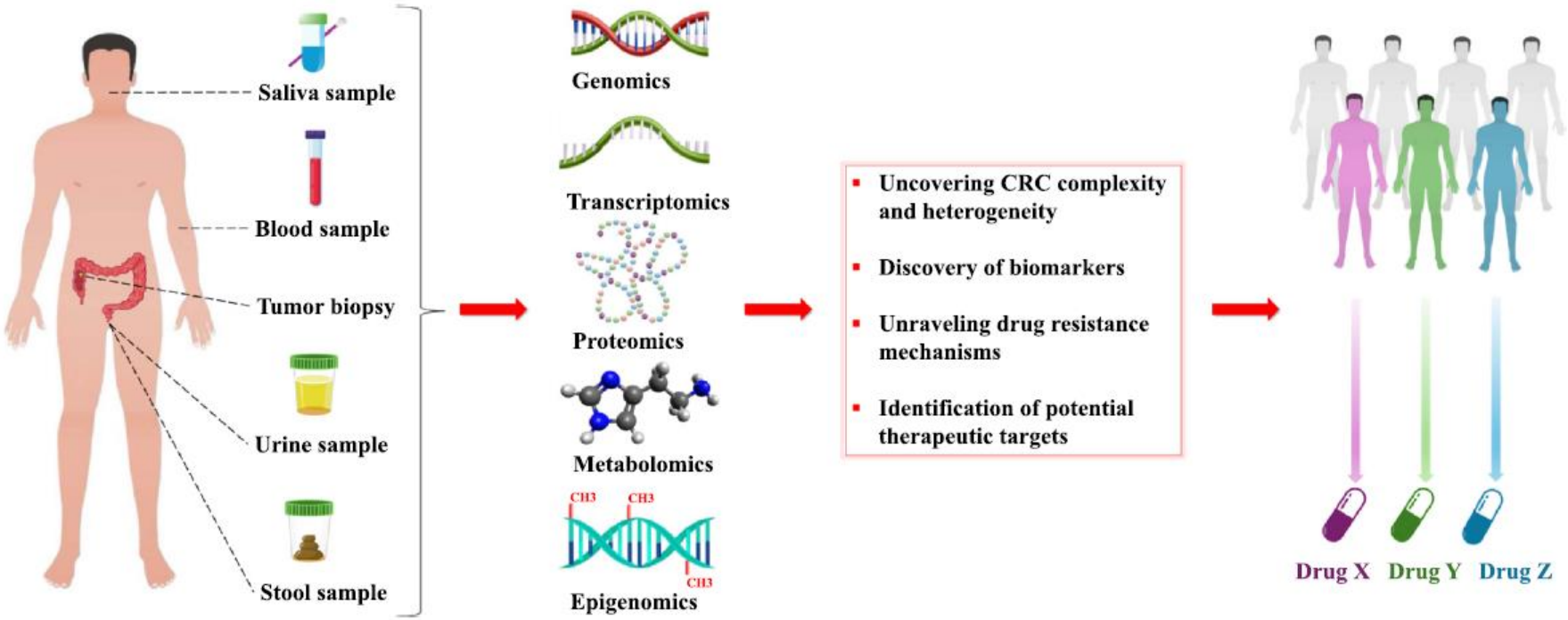
Non-invasive cancer screening for gastrointestinal cancers

[Cancers (Basel) 2025]



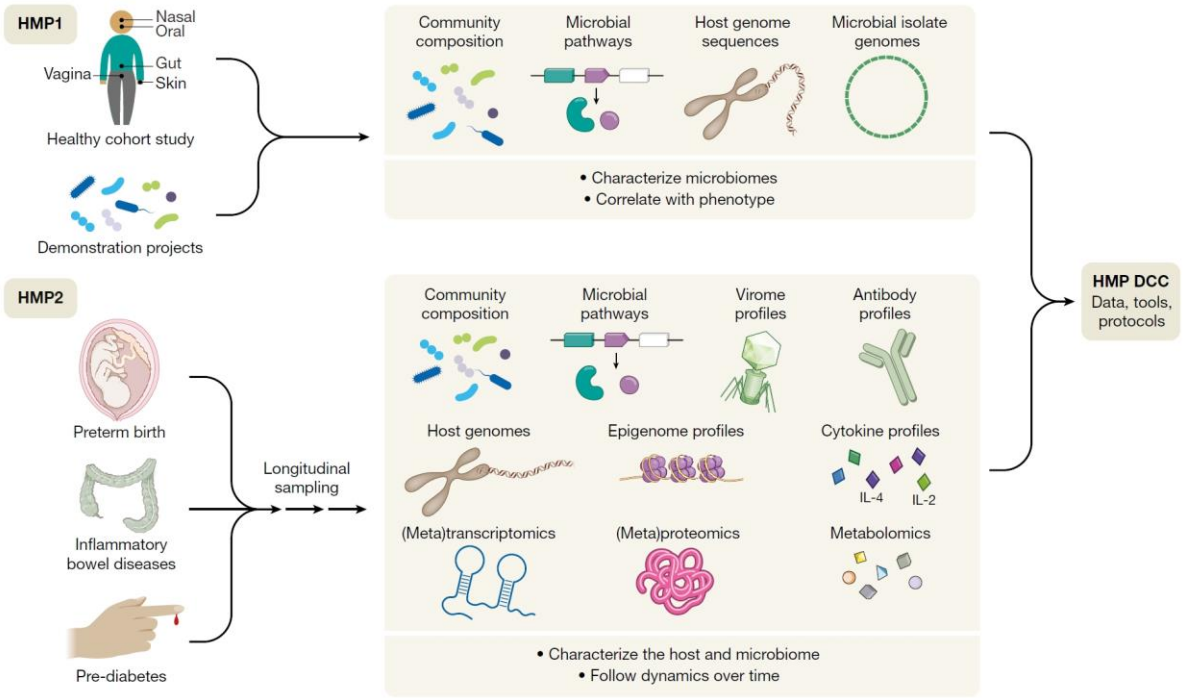
Omics technologies as powerful approaches to unravel CRC complexity

(Mol Cells 2025)



The Integrative Human Microbiome Project (iHMP or HMP2)

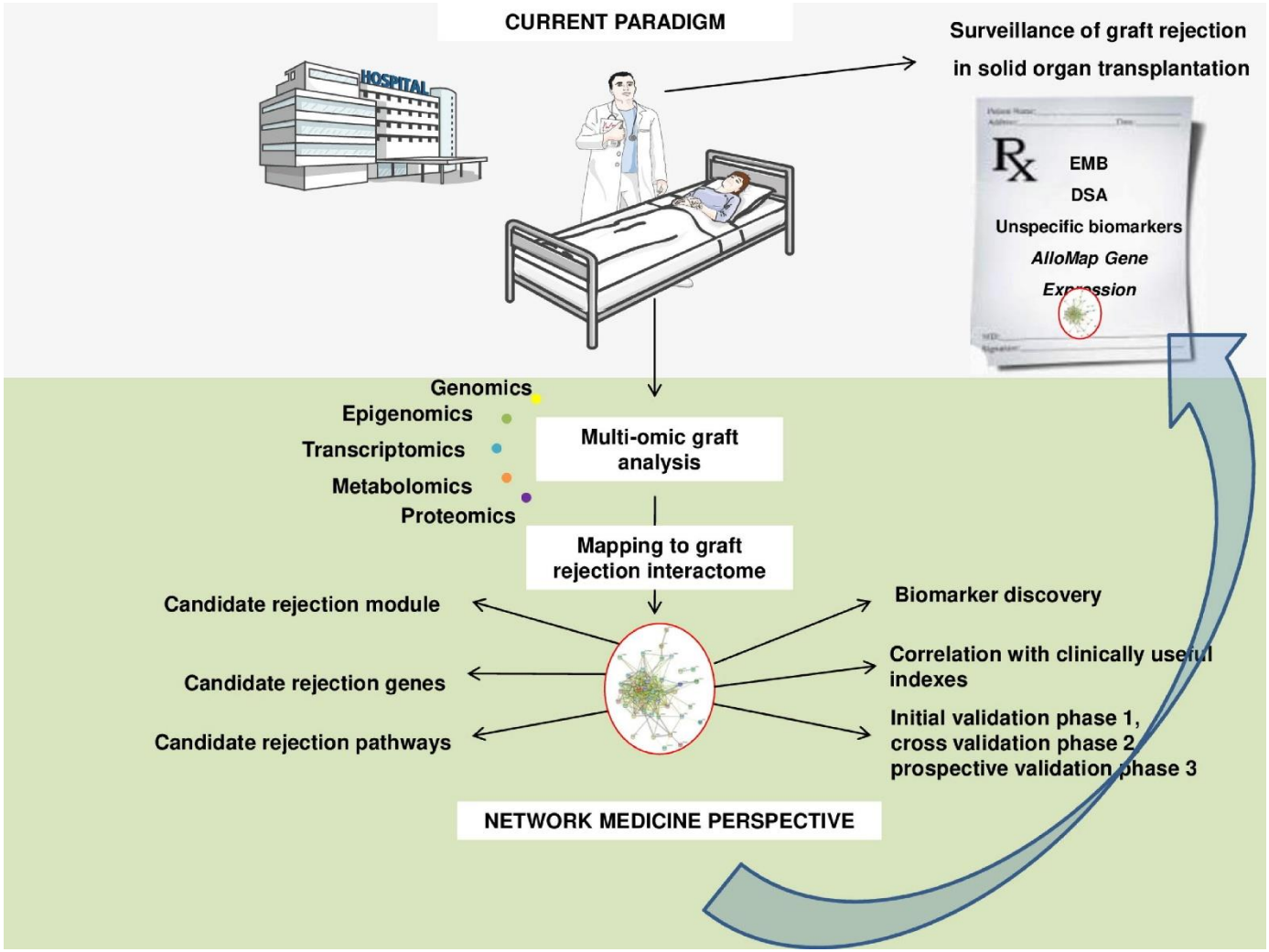
(Nature 2019)



HMP DCC (Data Coordination Center, http://ihmpdcc.org)
MOMS-PI (Multi-Omic Microbiome Study: Pregnancy Initiative) - pregnancy and preterm birth
IBDMDB (Inflammatory Bowel Disease Multi'omics Database - inflammatory bowel disease
IPOP (Integrated Personal 'Omics Project) - prediabetes

Network medicine at the bedside of patients undergoing SOT

(Hum Immunol 2023)



Clinical transplantomics-derived applications to detect solid organ rejection

(Hum Immunol 2023)

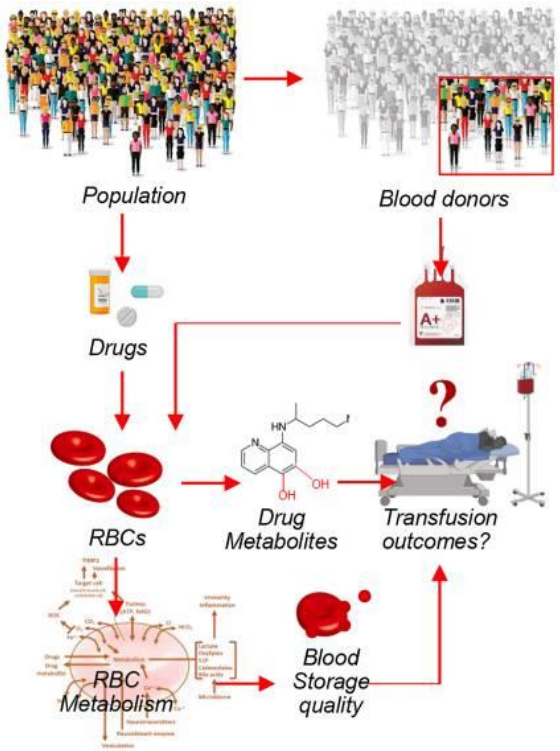
Omics	Test	Organ	Sample source	Principle	Status
Transcriptomics	*AlloMap*™	Heart	Pheripheral blood	Detection of gene expression levels of a 11 informative gene-panel in PBMCs in transplant recipients	-Used -Non-invasive surveillance of ACR
	The TruGraf®	Kidney and liver	Peripheral blood	Microarray-based quantification of differentially expressed genes in transplant recipients	-Used -Non-invasive surveillance of patients adequately/ inadequately immunosuppressed
	B-HOT panel	Kidney, liver, heart, and lung	FFPE biopsy	Microarray-based quantification of 770 differentially expressed genes in transplant recipients	-Research only -Advanced molecular characterization of the in-situ response in the allograft
Genomics	*Signatera*™	Liver	Pheripheral blood	Detection of cfDNA levels in graft recipient	-Used -Clinical research -To detect pre-and post-transplant MRD
	Prospera™	Liver	Pheripheral blood	Massively multiplex PCR to detect cfDNA levels in donor-recipient pairs	-Used -Clinical research -Diagnosis of active rejection
	AlloSure	Heart, kidney	Plasma	NGS-based detection of a targeted SNP panel across all somatic chromosomes to quantify the fraction of dd-cfDNA in donor-recipient pairs	-Used -Non-invasive surveillance of acute rejection in heart transplantation -Non-invasive surveillance of clinical and subclinical AMR risk in kidney transplantation
	Viracor TRAC®	Liver, heart, and lung			-Clinical validation -Non-invasive surveillance of acute rejection in liver, heart, and lung transplantation
Metabolomics	*ImmuKnow (Cylex)*	Kidney	Peripheral blood	Measurement of $CD4^+$ T cell-related ATP production	-Clinical validation -Non-invasive surveillance of patients adequately/ inadequately immunosuppressed
Combination of transcriptomics and genomics	*OmniGraf*™	Kidney	Peripheral blood and plasma	Combination of *TruGraf*® and *Viracor TRAC*®	-Clinical validation -Simultaneous noninvasive surveillance of "silent" subclinical and clinical acute rejection
Combination of genomics, epigenomics, and traditional biochemical parameters	*QSant*™	Kidney	Urine	Measurement of 6 kidney-specific biomarkers (cfDNA, methylated-cfDNA, clusterin, CXCL10, creatinine, and total proteins) to determine the transplant Q-Score	-Clinical validation -Non-invasive surveillance of acute rejection risk in both adult and pediatric kidney transplant recipients

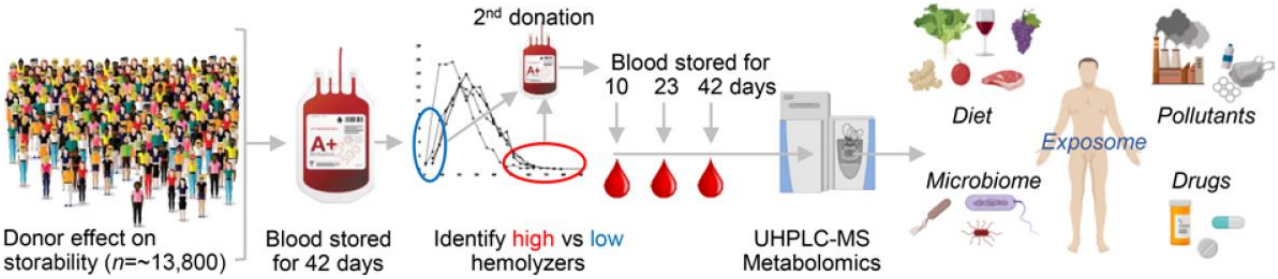
Abbreviations: **ACR**: acute cellular rejection; **AMR**: Antibody Mediated Rejection; **ctDNA**: circulating tumor DNA; **dd-cfDNA**: donor derived-circulating free DNA; **FFPE**: formalin-fixed paraffin-embedded; **MRD**: molecular residual disease; **NGS**: next generation sequencing; **PBMCs**: peripheral blood mononuclear cells; **SNP**: single nucleotide polymorphism.

Donor exposome & impact of common drugs on RBC metabolism

- Recipient Epidemiology and Donor Evaluation Study III Red Blood Cell-Omics (REDS-III RBC-Omics) Study -

(JCI Insight 2021) (Nat Med 2025)



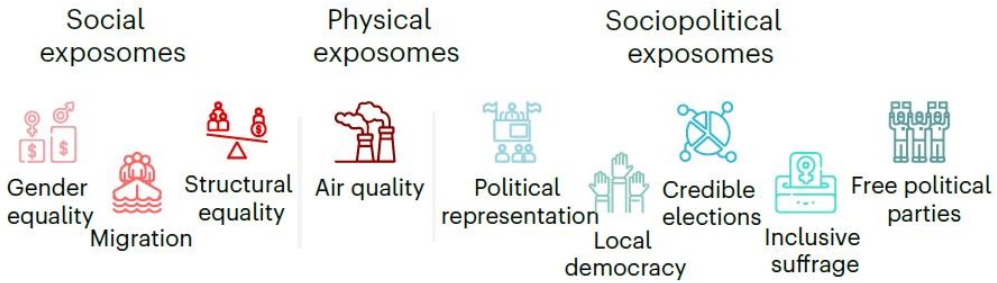


- Exposome
  - The combined physical & social exposures experienced throughout life
  - Different exposomal factors

    Social (gender equality, migration, structural equality) variable

    Physical (air quality) variable

    Sociopolitical (democracy indicators) variable



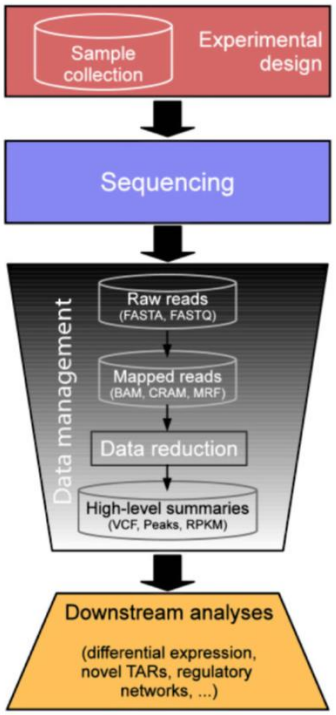
NGS & complementary methods (Semin Thromb Hemost 2019)

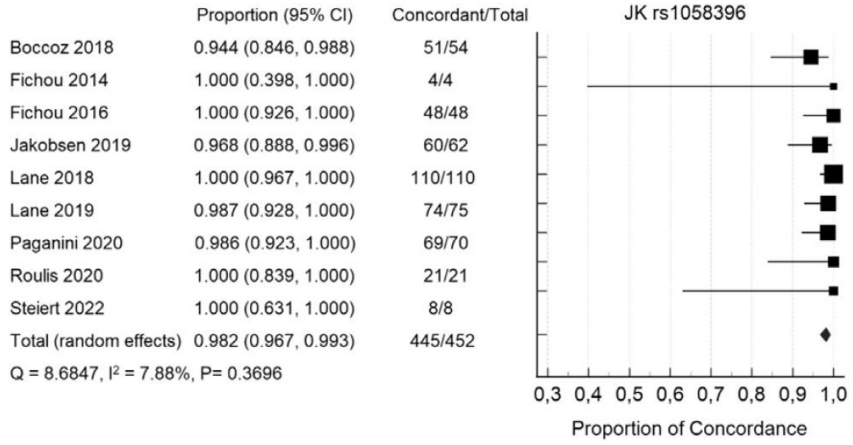
- NGS Nucleic Acid Sequencing
  - Second-Generation (Short-Read) Sequencing
    - Short-Read Sequencing by Synthesis (Illumina)
    - Ion Semiconductor Sequencing (ThermoFisher Scientific)
    - Nanoball Sequencing (Beijing Genomics Institute)
  - Third-Generation (Long-Read and Real-Time) Sequencing
    - Single-Molecule Real-Time Sequencing (Pacific Biosciences)
    - Nanopore Sequencing (Oxford Nanopore Technologies)
    - Synthetic Long Reads (Illumina and 10X Genomics)
- NGS Data Output and Prebioinformatics Processing

- Optical Mapping (Bionano Genomics Irys and Saphyr)
- Hybrid Sequencing (Combining 2nd- & 3rd-Generation Sequencing)
  - NanoString
  - RNA-Seq
  - Chromatin Immunoprecipitation with Seq
  - Single-Cell RNA/DNA Sequencing

- Prediction of various blood group systems using Korean whole-genome sequencing data (SNUCM LM, PLoS One 10.1371/journal.pone.0269481)

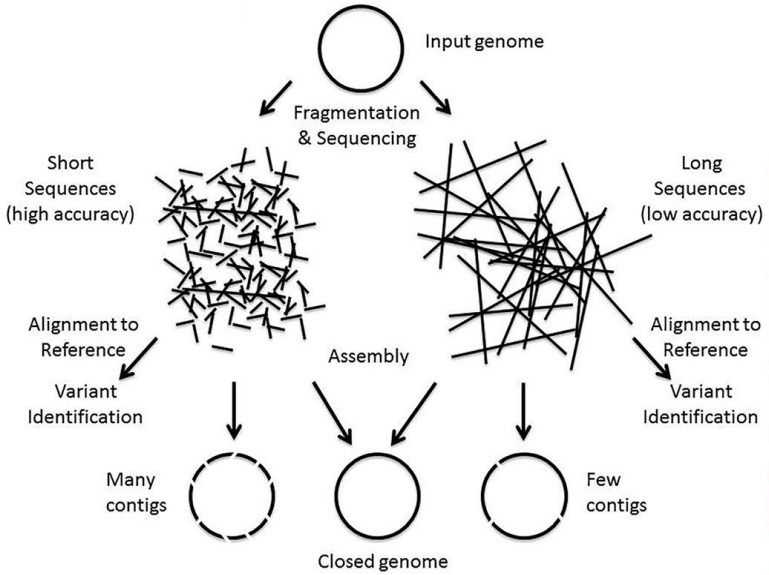
- NGS compared to other standard molecular methods (JK*01/JK*02) (TMR 10.1016/j.tmrv.2023.150776)

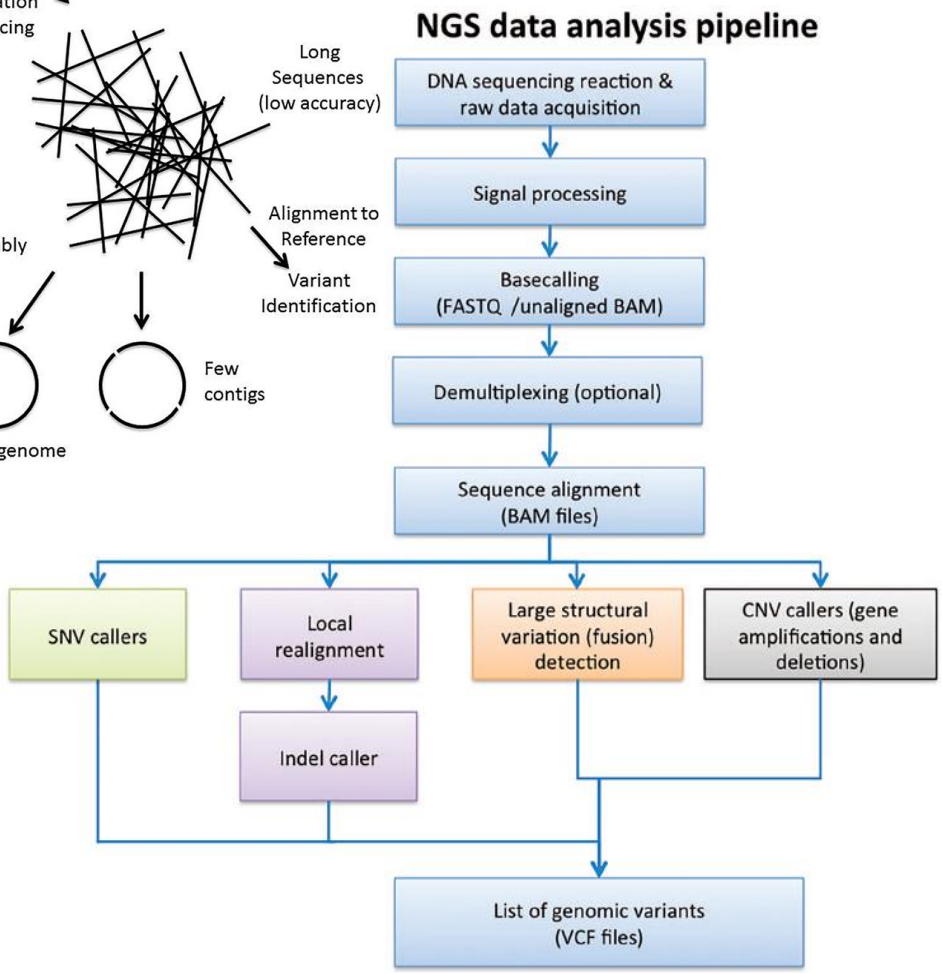


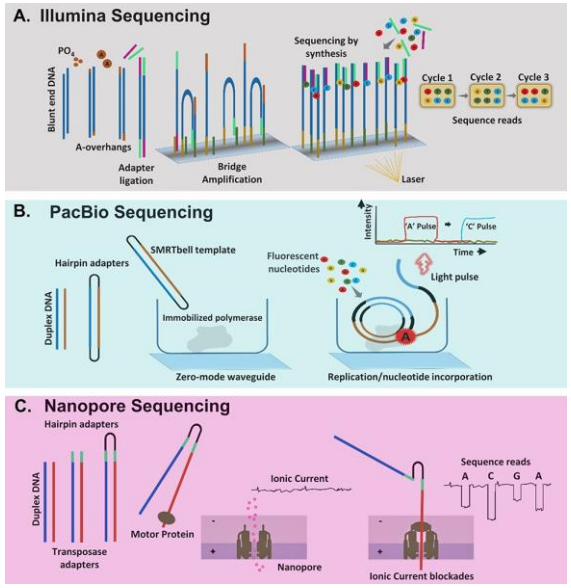


General schema for bioinformatics workflow for NGS

(Arch Pathol Lab Med 2016) (Brief Bioinform 2021)







File size range

Terabytes

Gigabytes

Megabytes / Kilobytes

Comparative analysis of short- and long-read SQ of VRE for application to molecular epidemiology

Factors influencing oral microbiome analysis: from saliva sampling methods to NGS platforms

Recommendations regarding practical DEL typing strategies for serologically D-negative Asian donors

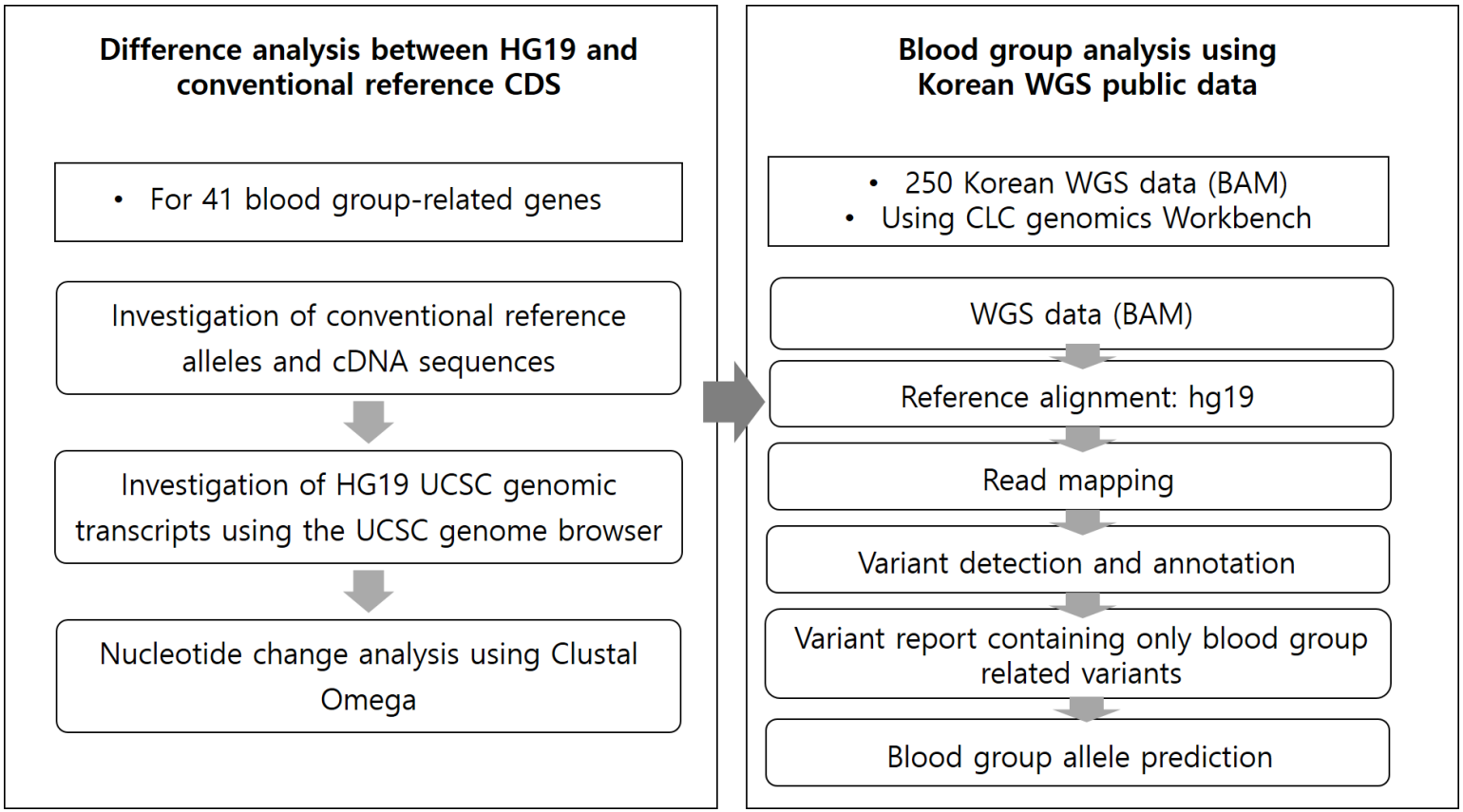
(SNUCM LM, Transfus Med Hemother 2020)

	RhCE phenotyping	Adsorption-elution test	*RHD* genotyping
Cost[1] TAT[1] Hands-on time[1]	USD 34.5 (USD 5.8/sample) 30 min 30 min (5 min/sample)	USD 120.0 (USD 20.0/sample) 4.5 h 3.5 h (35 min/sample)	USD 106.5 (USD 17.8/sample) 2.5 h 1.5 h (15 min/sample)
Advantages	Rapid, inexpensive, and no special instruments required	No special instruments required, phenotypic characterization of novel alleles	Relatively rapid and an accurate (reference method)
Disadvantages	Only used to exclude D-negative samples with *RHD* null alleles	Technically demanding, laborious, and time-consuming	Usually unable to detect all DEL alleles High initial costs for instruments

[1] Cost, TAT, and hands-on time were estimated, assuming that 6 samples were tested simultaneously.

Prediction of various blood group systems using Korean WGS data

(SNUCM LM, PLoS One 2022)



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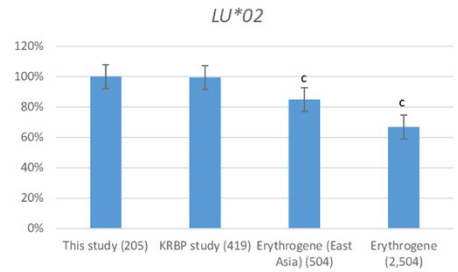
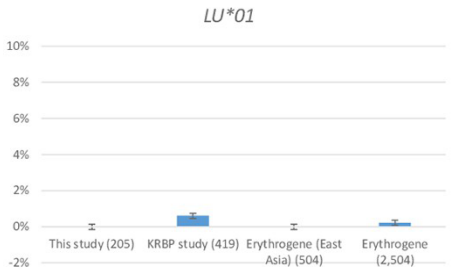
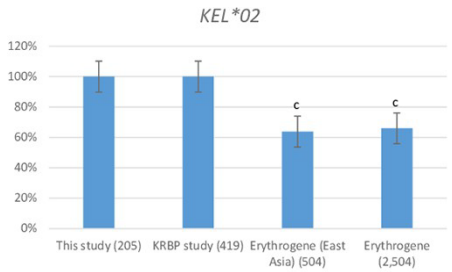
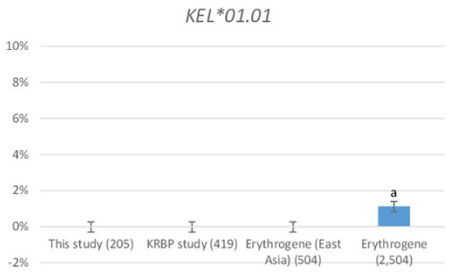
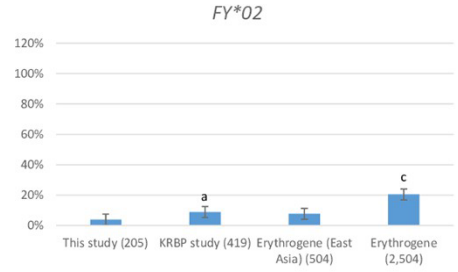
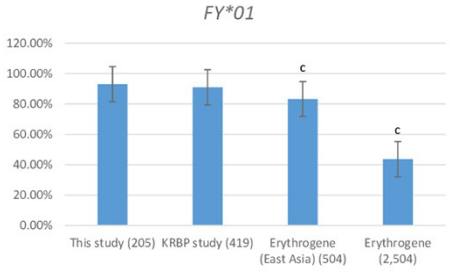


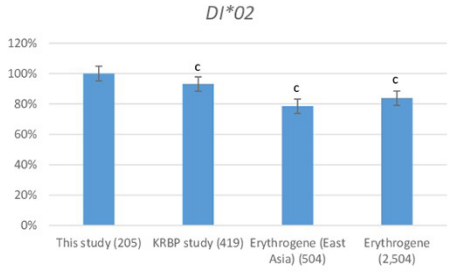


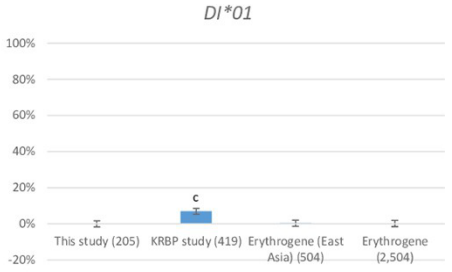


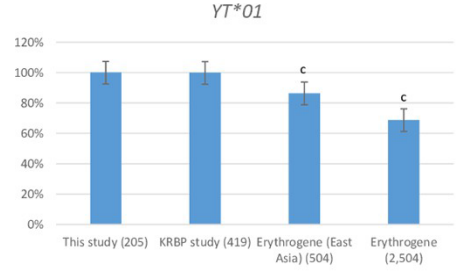


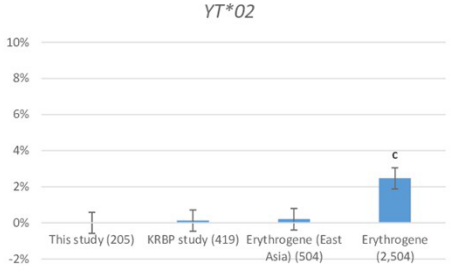


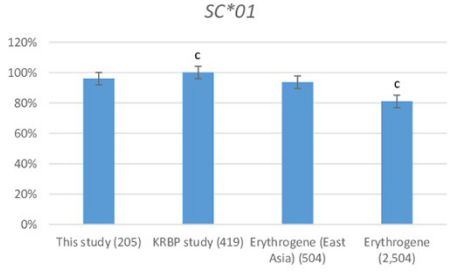


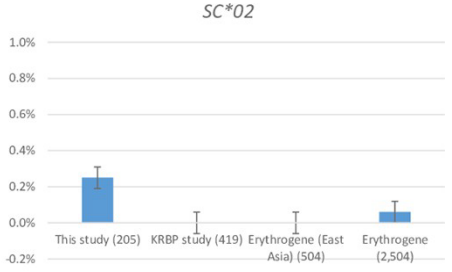


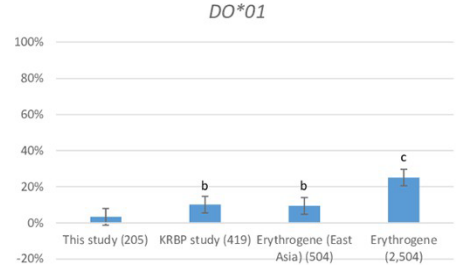


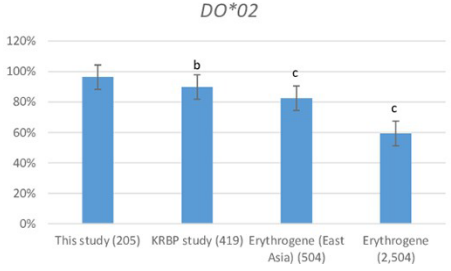


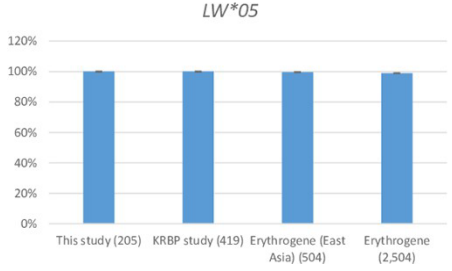


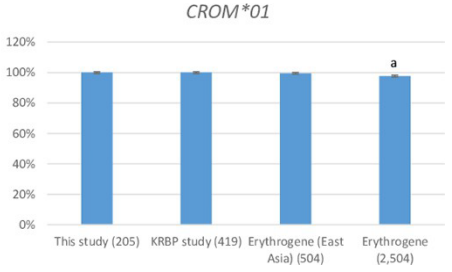






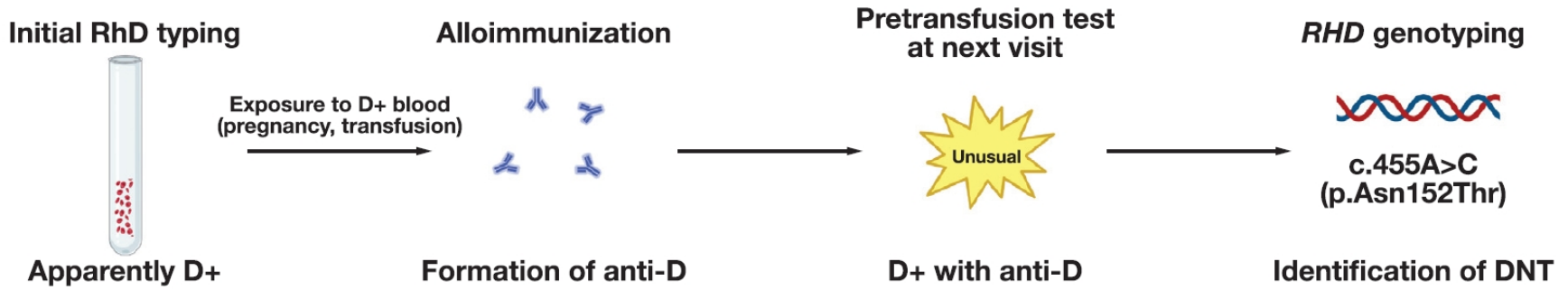


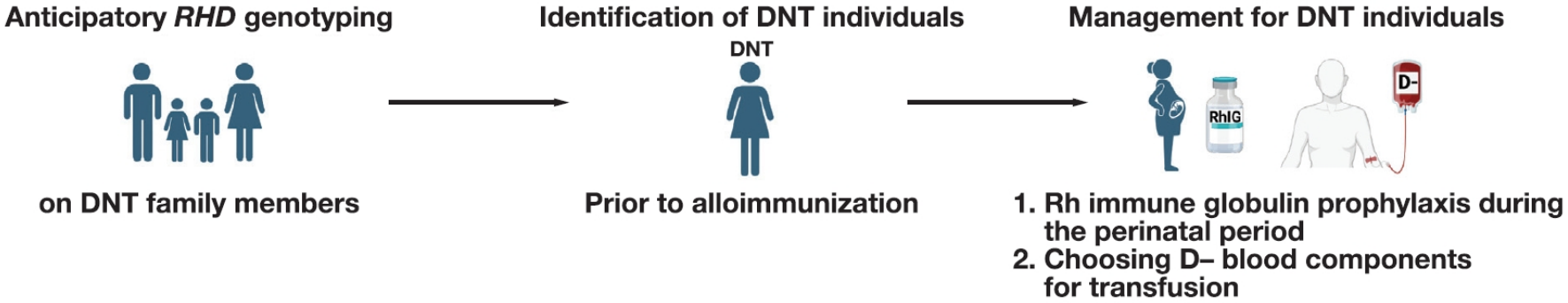




A Korean family with *RHD*DNT* only detectable after anti-D alloimmunization

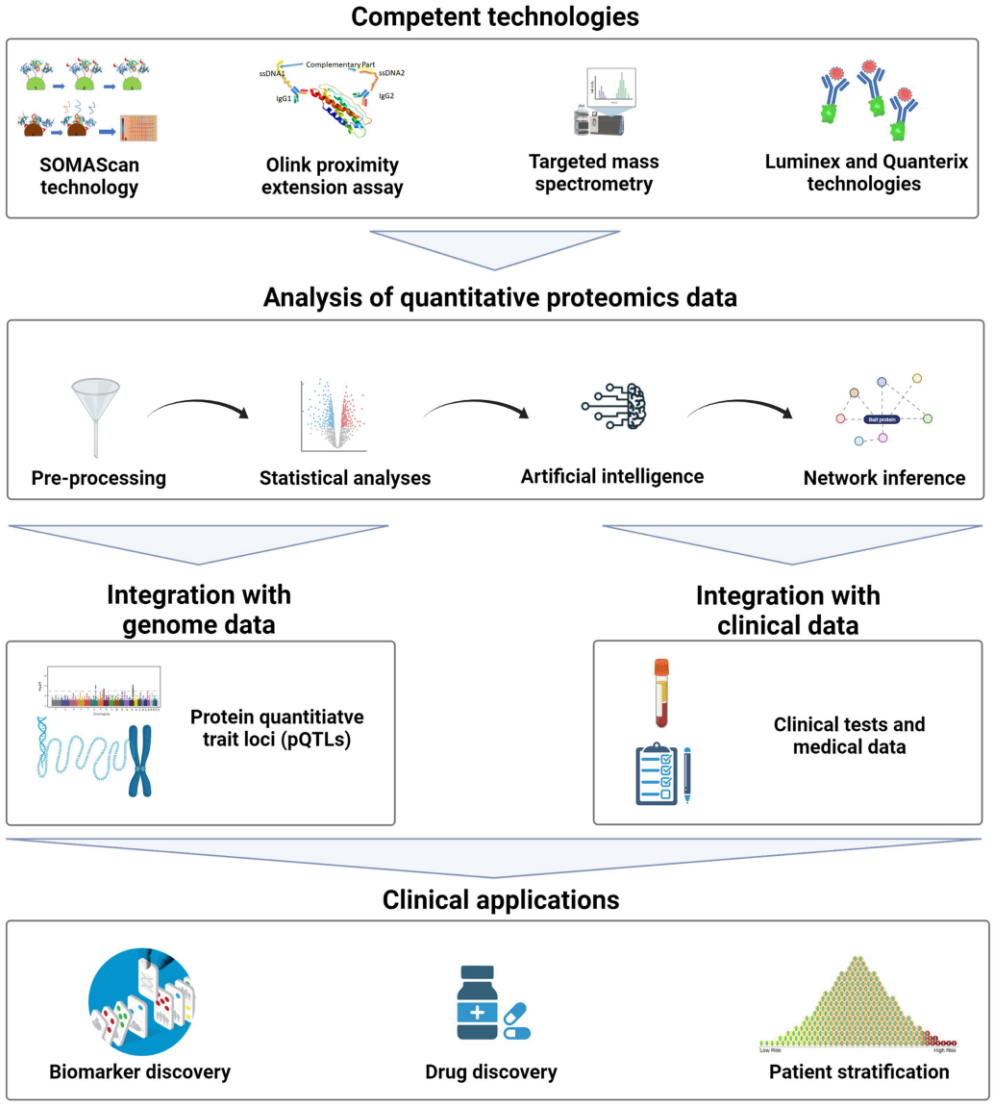
(SNUCM LM, Am J Clin Pathol 2024)

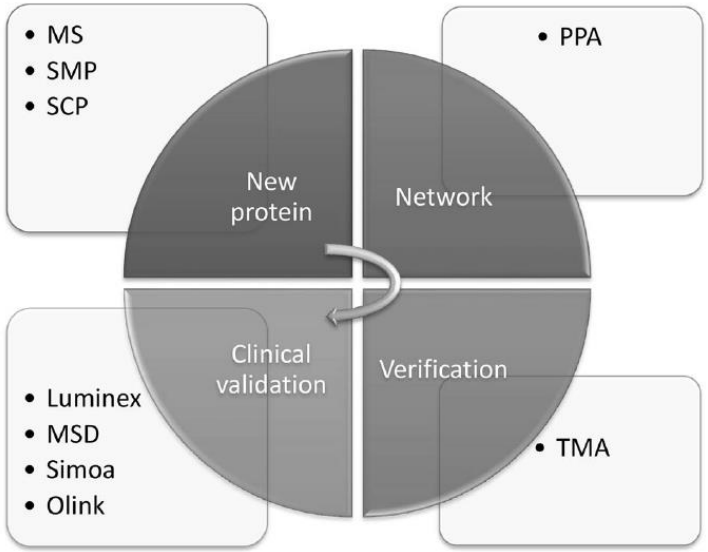




Building a quantitative proteomics toolbox / High-throughput proteomics

(Front Physiol 2021) / (Lab Invest 2022)





MS: mass spectrometry

SMP: single-molecule proteomics

SCP: single-cell proteomics

PPA: protein pathway array

MSD: meso-scale discovery

TMA: tissue microarray

21-45 (Anti-I Auto Pan) / 21-49 (Anti-Jr^a Allo Pan) / 25-40 (Nonspecific Allo Pan)

(SNUCM LM, in prep)

Assay	Gene	N_21-45	N_21-49	Threshold
IL8	CXCL8	12.023590	7.195790	Significant
VEGFA	VEGFA	13.398980	11.568980	Significant
MCP-3	CCL7	4.465240	2.060990	Significant
CDCP1	CDCP1	6.681280	3.246990	Significant
OPG	TNFRSF11B	11.580990	10.215410	Significant
IL6	IL6	7.443930	1.918520	Significant
IL-17A	IL17A	3.724100	0.792710	Significant
CXCL11	CXCL11	12.873800	10.046440	Significant
CXCL9	CXCL9	10.816710	7.085210	Significant
OSM	OSM	9.175960	5.800680	Significant
CCL4	CCL4	9.763530	7.062910	Significant
SCF	KITLG	8.381090	10.083000	Significant
IL18	IL18	14.393260	9.356180	Significant
SLAMF1	SLAMF1	5.176260	3.123620	Significant
TGF-alpha	TGFA	6.518760	3.383010	Significant
TNFSF14	TNFSF14	8.499300	6.331090	Significant
FGF-23	FGF23	4.819110	2.611720	Significant
MMP-1	MMP1	13.896340	12.665060	Significant
FGF-21	FGF21	7.142490	3.689370	Significant
CCL19	CCL19	14.022980	10.700000	Significant
IL-15RA	IL15RA	2.068200	0.743950	Significant
IL-22 RA1	IL22RA1	1.066910	2.636770	Significant
PD-L1	CD274	8.038190	6.651240	Significant
CXCL5	CXCL5	12.038260	14.014920	Significant
HGF	HGF	11.451480	9.327360	Significant
IL-12B	IL12B	7.631720	5.994970	Significant
MMP-10	MMP10	12.328060	9.647370	Significant
IL10	IL10	4.545480	3.334260	Significant
CCL3	CCL3	10.584180	5.781720	Significant
Flt3L	FLT3LG	10.881170	9.431450	Significant
CXCL6	CXCL6	9.133030	10.452190	Significant
CXCL10	CXCL10	11.263650	7.595610	Significant
4E-BP1	EIF4EBP1	7.318930	8.817020	Significant
CD40	CD40	12.770980	11.598960	Significant
IL4	IL4	0.056290	2.152930	Significant
CASP-8	CASP8	12.575030	9.552500	Significant
CX3CL1	CX3CL1	4.470480	3.165340	Significant
TNFRSF9	TNFRSF9	7.341360	4.987090	Significant
NT-3	NTF3	0.358640	2.272350	Significant
TWEAK	TNFSF12	6.740000	9.452830	Significant
CCL20	CCL20	9.473740	6.141430	Significant
TNFB	LTA	4.496650	3.474970	Significant
DNER	DNER	7.910810	9.058800	Significant
IFN-gamma	IFNG	8.017120	6.220470	Significant
TNF	TNF	4.970300	3.164570	Significant

Assay	Gene	N_21-45	N_25-40	Threshold
VEGFA	VEGFA	13.398980	12.126140	Significant
MCP-3	CCL7	4.465240	2.784600	Significant
CDCP1	CDCP1	6.681280	5.141360	Significant
IL6	IL6	7.443930	3.023740	Significant
IL-17C	IL17C	2.672540	1.496020	Significant
IL-17A	IL17A	3.724100	0.487220	Significant
CXCL11	CXCL11	12.873800	9.561280	Significant
CXCL9	CXCL9	10.816710	8.592350	Significant
CXCL1	CXCL1	12.123290	11.030180	Significant
CCL4	CCL4	9.763530	8.141450	Significant
SCF	KITLG	8.381090	10.263810	Significant
SLAMF1	SLAMF1	5.176260	3.326750	Significant
TGF-alpha	TGFA	6.518760	4.773840	Significant
CCL11	CCL11	8.504900	7.479810	Significant
FGF-23	FGF23	4.819110	2.586600	Significant
CCL19	CCL19	14.022980	10.523320	Significant
IL-15RA	IL15RA	2.068200	0.807940	Significant
IL-22 RA1	IL22RA1	1.066910	4.183440	Significant
PD-L1	CD274	8.038190	7.026490	Significant
TRANCE	TNFSF11	5.057910	3.659510	Significant
IL-12B	IL12B	7.631720	6.440490	Significant
IL-24	IL24	1.639460	-0.516800	Significant
MMP-10	MMP10	12.328060	9.464270	Significant
CCL23	CCL23	13.169030	11.734310	Significant
CD5	CD5	7.500550	6.470610	Significant
CCL3	CCL3	10.584180	8.628490	Significant
Flt3L	FLT3LG	10.881170	9.101180	Significant
CXCL10	CXCL10	11.263650	7.879460	Significant
4E-BP1	EIF4EBP1	7.318930	9.430590	Significant
EN-RAGE	S100A12	7.588260	6.485280	Significant
CD40	CD40	12.770980	11.684810	Significant
FGF-19	FGF19	10.061460	6.561580	Significant
IL4	IL4	0.056290	-1.478890	Significant
NRTN	NRTN	0.568100	2.868320	Significant
CASP-8	CASP8	12.575030	9.271130	Significant
TNFRSF9	TNFRSF9	7.341360	5.733210	Significant
NT-3	NTF3	0.358640	1.626330	Significant
TWEAK	TNFSF12	6.740000	9.093150	Significant
CCL20	CCL20	9.473740	7.073150	Significant
ST1A1	SULT1A1	9.481720	8.093750	Significant
TNFB	LTA	4.496650	3.383670	Significant
DNER	DNER	7.910810	9.007550	Significant
CD8A	CD8A	7.759110	6.200750	Significant
IFN-gamma	IFNG	8.017120	5.086660	Significant
TNF	TNF	4.970300	3.494970	Significant

희귀혈액등록체계 (Korean Rare Blood Program)

- Transfusion registry (KRBP database) & Case registry (KRBP case archive) -

(bloodgroupimmunogenetics.org / safeblood.or.kr) [SNUCM LM, KFDA Fund]

ISBT 번호	혈액형군 이름(기호)	항원	양성(수)	음성(수)	총합(수)	특정항원음성(%)
002	MNS (MNS)	M	254	84	338	24.9
		N	270	68	338	20.1
		S	27	310	337	92.0
		s	335	2	337	0.6
004	Rh (RH)	c	249	89	338	26.3
		C	218	117	335	34.9
		e	312	26	338	7.7
		E	128	210	338	62.1
005	Lutheran (LU)	Lu^a	1	335	336	99.7
		Lu^b	336	0	336	0.0
006	Kell (KEL)	K	0	338	338	100.0
		k	338	0	338	0.0
		Kp^a	0	338	338	100.0
		Kp^b	338	0	338	0.0
		Kp^c	0	338	338	100.0
		Js^a	0	338	338	100.0
		Js^b	338	0	338	0.0
008	Duffy (FY)	Fy^a	337	0	337	0.0
		Fy^b	62	275	337	81.6
009	Kidd (JK)	Jk^a	250	88	338	26.0
		Jk^b	266	72	338	21.3
010	Diego (DI)	Di^a	45	291	336	86.6
		Di^b	332	4	336	1.2
		Wr^a	1	335	336	99.7
		Wr^b	336	0	336	0.0
011	Yt* (YT)	Yt^a	335	1	336	0.3
		Yt^b	1	335	336	99.7
013	Scianna (SC)	Sc1	335	1	336	0.3
		Sc2	0	336	336	100.0
014	Dombrock (DO)	Do^a	65	273	338	80.8
		Do^b	334	4	338	1.2
		Hy	336	0	336	0.0
		Jo^a	336	0	336	0.0
015	Colton (CO)	Co^a	335	1	336	0.3
		Co^b	1	335	336	99.7
016	Landsteiner-Wiener (LW)	LW^a	335	1	336	0.3
		LW^b	1	335	336	99.7
021	Cromer (CROM)	Cr^a	336	0	336	0.0
022	Knops (KN)	Kn^a	335	1	336	0.3
		Kn^b	1	335	336	99.7
		McC^a	335	1	336	0.3
		McC^b	1	335	336	99.7
		Sl1	335	1	336	0.3
		Sl2	0	335	335	100.0

* ISBT 명명법에서 Cartwright 혈액형군의 이름이 Yt로 변경됨

A voluntary transfusion recipient registry in Korea as a database for blood group antibodies

(SNUCM LM, Blood Transfus 2024)

Specificity	Cases
Single antibodies	**(n=4,913)**
Anti-E	2,202
Anti-Le^a	618
Anti-M	383
Anti-Jk^a	323
Anti-Fy^b	283
Anti-Le^b	278
Anti-P1	202
Anti-Di^a	116
Anti-c	113
Anti-Jk^b	94
Anti-S	87
Anti-C	67
Anti-e	59
Anti-D	31
Anti-Xg^a	15
Anti-N	13
Anti-Lu^a	11
Anti-Fy^a	7
Anti-K	4
Anti-Lu^b	4
Anti-Di^b	2
Anti-k	1
Two antibodies	**(n=2,862)**
Anti-E, c	1,792
Anti-C, e	757
Anti-Le^a, Le^b	62
Anti-E, Fy^b	42
Anti-E, Jk^a	32
Anti-e, Fy^b	19
Anti-E, Jk^b	16
Anti-Le^a, P1	16
Anti-E, M	15
Anti-Fy^b, Le^a	14
Anti-E, K	12

Specificity	Cases
Anti-E, Le^a	7
Anti-D, E	6
Anti-C, c	6
Anti-C, Jk^a	5
Anti-Jk^a, S	5
Anti-D, C	4
Anti-E, P1	4
Anti-E, S	4
Anti-C, E	3
Anti-C, Fy^b	3
Anti-E, Xg^a	3
Anti-e, Le^a	3
Anti-P1, M	3
Anti-C, Le^a	2
Anti-E, Le^b	2
Anti-c, e	2
Anti-Fy^a, Le^a	2
Anti-Jk^a, Le^a	2
Anti-Le^a, S	2
Anti-E, Di^a	2
Anti-C, Jk^b	1
Anti-C, Le^b	1
Anti-E, Kp^a	1
Anti-c, Le^a	1
Anti-e, Jk^a	1
Anti-e, Jk^b	1
Anti-f, Le^a	1
Anti-K, M	1
Anti-Fy^b, Jk^a	1
Anti-Le^a, N	1
Anti-Le^a, Lu^a	1
Anti-Lu^a, Lu^b	1
Anti-Di^a, S	1
Anti-E, Di^b	1
Anti-E, Wr^a	1

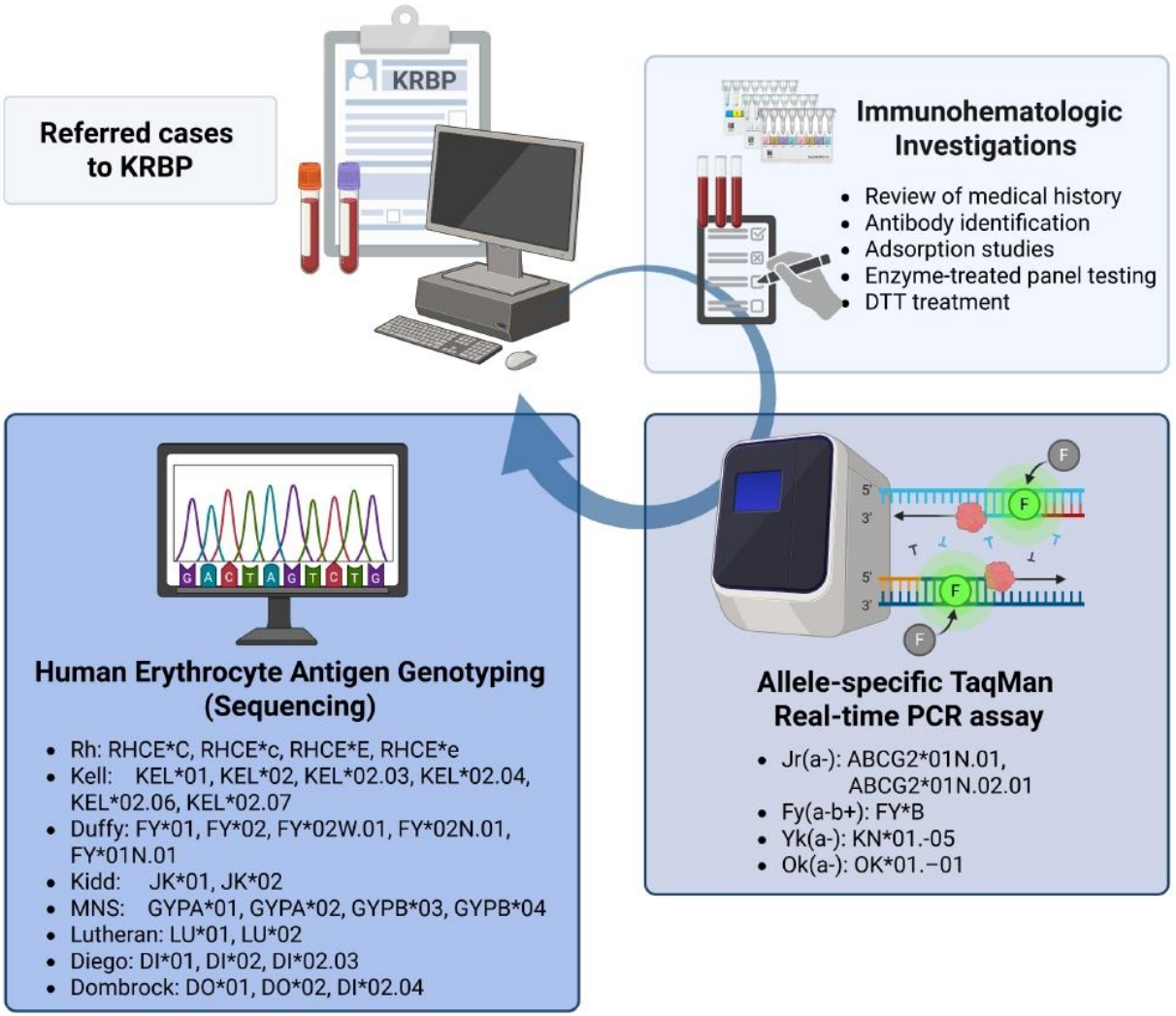
Specificity	Cases
Three antibodies	**(n=197)**
Anti-C, e, Jk^a	37
Anti-E, c, Jk^a	33
Anti-E, c, Jk^b	30
Anti-E, c, Le^a	24
Anti-E, c, N	9
Anti-E, c, M	8
Anti-E, c, S	8
Anti-C, e, Jk^b	7
Anti-E, c, Le^b	7
Anti-E, c, Fy^b	6
Anti-C, e, Di^a	5
Anti-C, e, S	4
Anti-C, e, M	3
Anti-E, Jk^b, M	3
Anti-C, e, Le^a	2
Anti-E, c, P1	2
Anti-E, c, Di^a	2
Anti-C, e, Fy^b	1
Anti-C, K, Js^a	1
Anti-E, Jk^a, S	1
Anti-c, e, S	1
Anti-Fy^a, M, S	1
Anti-Fy^b, Jk^a, S	1
Anti-Fy^b, Di^a, Lu^a	1
Four antibodies	**(n=9)**
Anti-E, Jk^b, Le^a, M	3
Anti-E, c, Le^a, Le^b	2
Anti-C, E, c, e	1
Anti-C, e, K, Jk^b	1
Anti-C, e, Fy^b, S	1
Anti-E, c, Fy^b, Jk^a	1

Antibody (anti-)	Cases	Proportion	Antigen-typed cases	Antigen-typed units	Obtained units	Antigen(s)-egative frequency	Units required for typing*
E	2,202	27.6%	1,305	4,194	3,027	72.2%**	2
E, c	1,792	22.5%	1,343	4,251	2,957	69.6%**	2
C, e	757	9.5%	555	1,880	1,091	58.0%**	2
Le^a	618	7.7%	110	451	313	69.4%	2
M	383	4.8%	197	1,902	415	21.8%	5
Jk^a	323	4.0%	215	1,741	491	28.2%	4
Fy^b	283	3.5%	228	1,001	743	74.2%	2
Le^b	278	3.5%	62	319	163	51.1%	2
P1	202	2.5%	137	731	421	57.6%	2
Di^a	116	1.5%	37	135	98	72.6%	2
c	113	1.4%	99	425	283	66.6%**	2
Jk^b	94	1.2%	67	811	185	22.8%	5
S	87	1.1%	61	272	180	66.2%	2
C	67	0.8%	29	94	46	48.9%**	3
Le^a, Le^b	62	0.8%	17	132	46	34.9%	3
e	59	0.7%	36	82	64	78.1%**	2
E, Fy^b	42	0.5%	25	108	83	76.9%**	2
C, e, Jk^a	37	0.5%	11	450	28	6.2%**	17
E, c, Jk^a	33	0.4%	22	162	68	42.0%**	3
E, Jk^a	32	0.4%	26	191	54	28.3%**	4

*Mean number of units needed to be typed in order to find one compatible unit. **Antigen(s)-negative frequencies including C, E, c, and/or e were overestimated because many blood banks preselected C-, E-, c-, and/or e-negative units through the Blood Information Sharing System (BISS) and performed retyping (see **Table III**).

Genotype-driven resolution of panagglutination

over a decade of Korean Rare Blood Program Case Archives (SNUCM LM, in submission)



thank you!

From Concept to Commercialization

Initiation → Negotiation → Scope of Work → Development → Set Up → Pilot → Validation