Directii de cercetare in GENOMICA UMANA UMFCraiova

Anca Lelia (Riza) Costache
Universitatea de Medicina si Farmacie din Craiova
Centrul Regional de Genetica Medicala Dolj
Radboud University Medical Centre

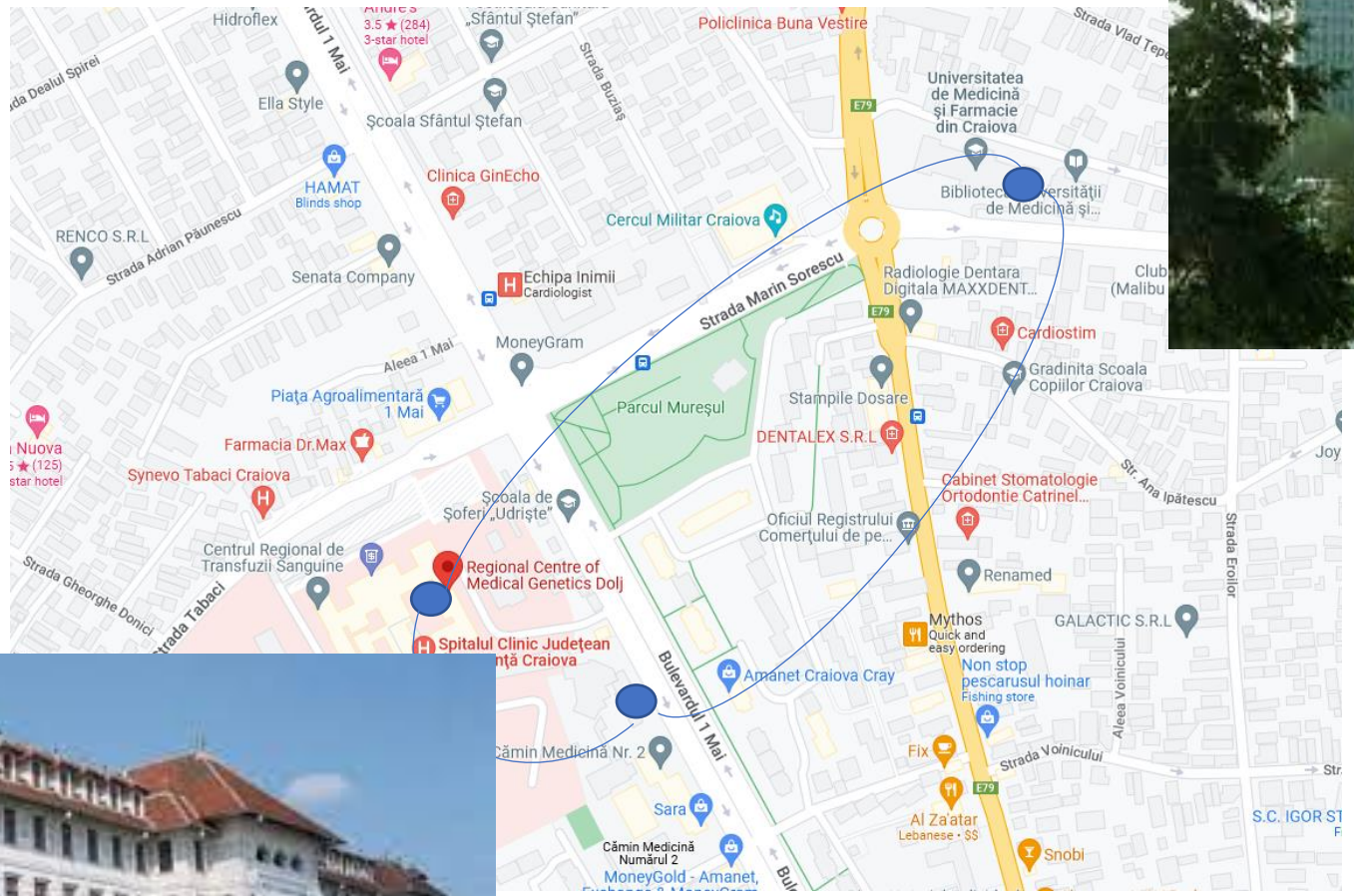
prof. dr. Mihai Netea

prof. dr. Reinout van Crevel

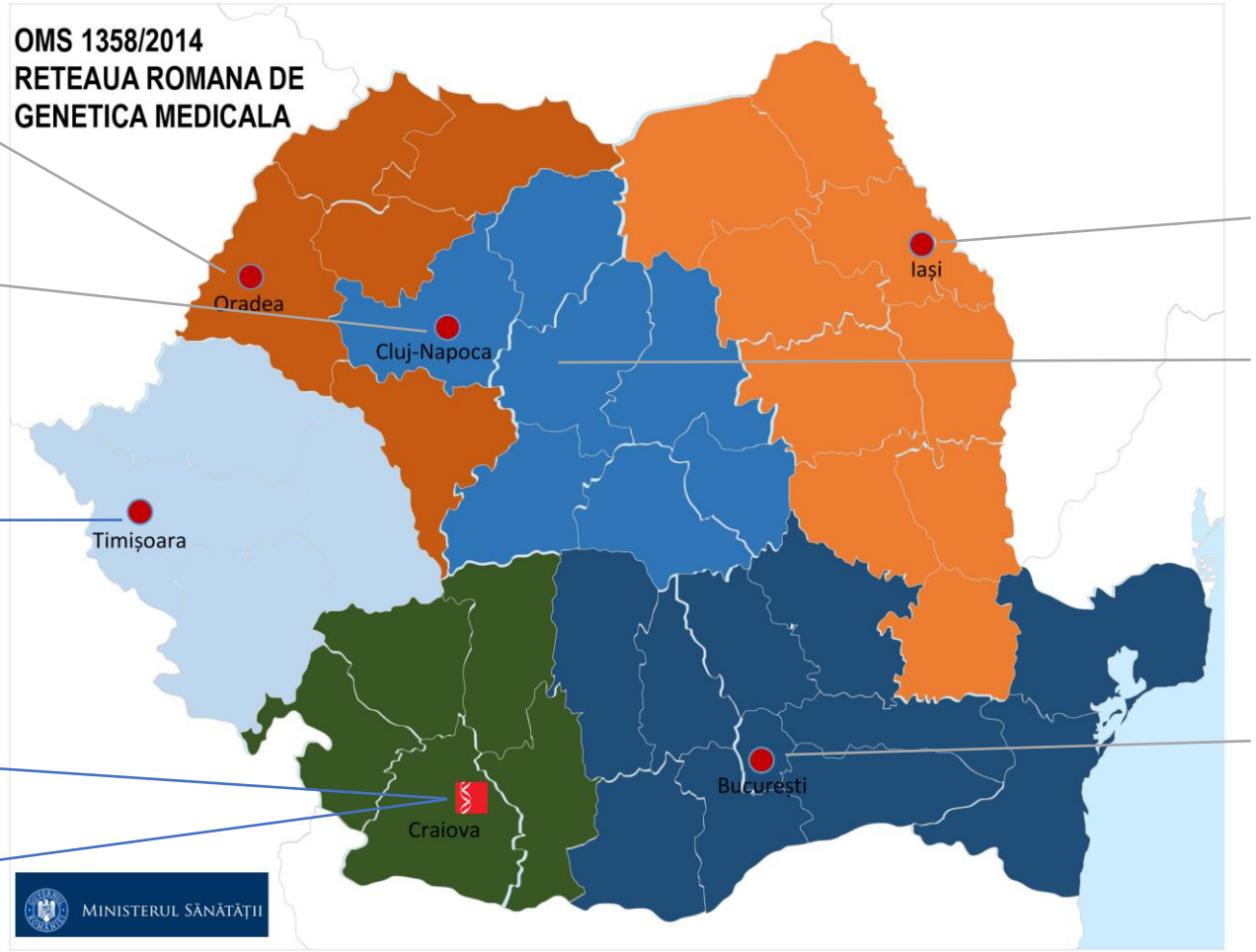
dr. Vinod Kumar Magadi

prof. dr. Cisca Wijmenga

prof. dr. Mihai Ioana


Hidroflex
Ella Style
Școala Sfântul Ștefan
Clinica GinEcho
HAMAT
Blinds shop
RENCO S.R.L
Strada Adrian Păunescu
Senata Company
Echipa Inimii
Cardiologist
Cercul Militar Craiova
Policlinica Buna Vestire
Universitatea de Medicină și Farmacie din Craiova
Strada Marin Sorescu
Radiologie Dentara Digitala MAXXDENT...
Cardiostim
Gradinita Scoala Copiilor Craiova
MoneyGram
Aleea 1 Mai
Piața Agroalimentară 1 Mai
Parcul Mureșul
Stampile Dosare
DENTALEX S.R.L
Farmacia Dr.Max
Synevo Tabaci Craiova
Școala de Șoferi „Udriște"
Cabinet Stomatologie Ortodontie Catrinel...
Oficiul Registrului Comerțului de pe...
Centrul Regional de Transfuzii Sanguine
Regional Centre of Medical Genetics Dolj
Renamed
Mythos
Quick and easy ordering
GALACTIC S.R.L
Amanet Craiova Cray
Non stop pescarusul hoinar
Fishing store
Fix
Al Za'atar
Lebanese · $$
Snobi
Sara
Cămin Medicină Nr. 2
Cămin Medicină Numărul 2
MoneyGold - Amanet,
Strada Gheorghe Donici
Strada Tabaci
Bulevardul 1 Mai
Strada Eroilor
Str. Ana Ipătescu
Aleea Voinicului
Strada Voinicului
E79

MINISTERUL SĂNĂTĂȚII



Oradea

Cluj

Timisoara

LGM – CRGM – SCJUC

LGU- UMFCV

Iasi

TgMures

Lab IOMC

prof. Mixich, prof. Ioana

ML, CCR, HCV, HPV

RT-PCR …
LGU

2008-2013
TARGET - LGU
echipamente, spatiu

2013-2017
TANDEM
etichetare, criostocare, 2017 NGS non-self RUMC

2015
donatie GUDB MC

2015-2017
RID-TB
echipamente, resursa umana

2016
donatie server AC

2016-2021
FUSE
echipamente functional, resursa umana

2015-prezent

dupa ordin 2014 infiintare
PN.VI.3.3. Malformatii

2015

QF-PCR aneuploidii
comodat ABI

2016

aCGH
MLPA

2020
HINT
resursa umana

proiecte gastro
resursa umana

2018-prezent
DRD-ME – non-self

2019
Bal caritabil

2018-2022
PROGENERARE

2017
Asoc DRAVET
MutationSurveyor

2020

primele 2 runuri NextSeq
PN.I.2. Infectioase
Contracost
echipamente MS
personal angajat

2019

licitatie NextSeq
spatiul initial in cadrul Laboratorului de Analize Medicale al SCJUC

2018

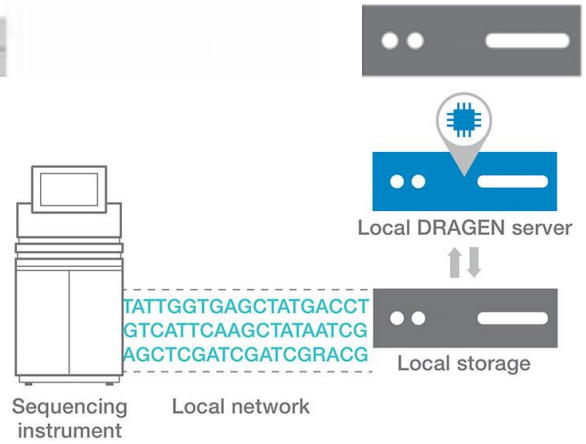
QF-PCR CNAS
Contracost
donatie ABI
dec 2017 SEQ
workskop MiSeq

2021-2022
POIM - echipamente

2022

…

Core-facility



Core-facility

PROGRAMUL OPERAȚIONAL INFRASTRUCTURĂ MARE

FORMULARUL CERERE DE FINANȚARE

★★★★★★★★★★★★★★

Axa Prioritară 9
Protejarea sănătății populației în contextul pandemiei cauzate de COVID-19

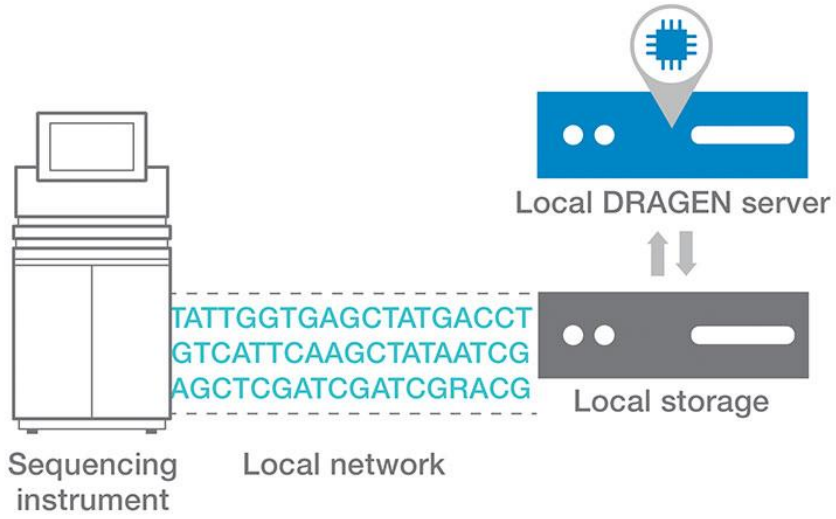
Obiectivul Specific 9.1
Creșterea capacității de gestionare a crizei sanitare COVID-19

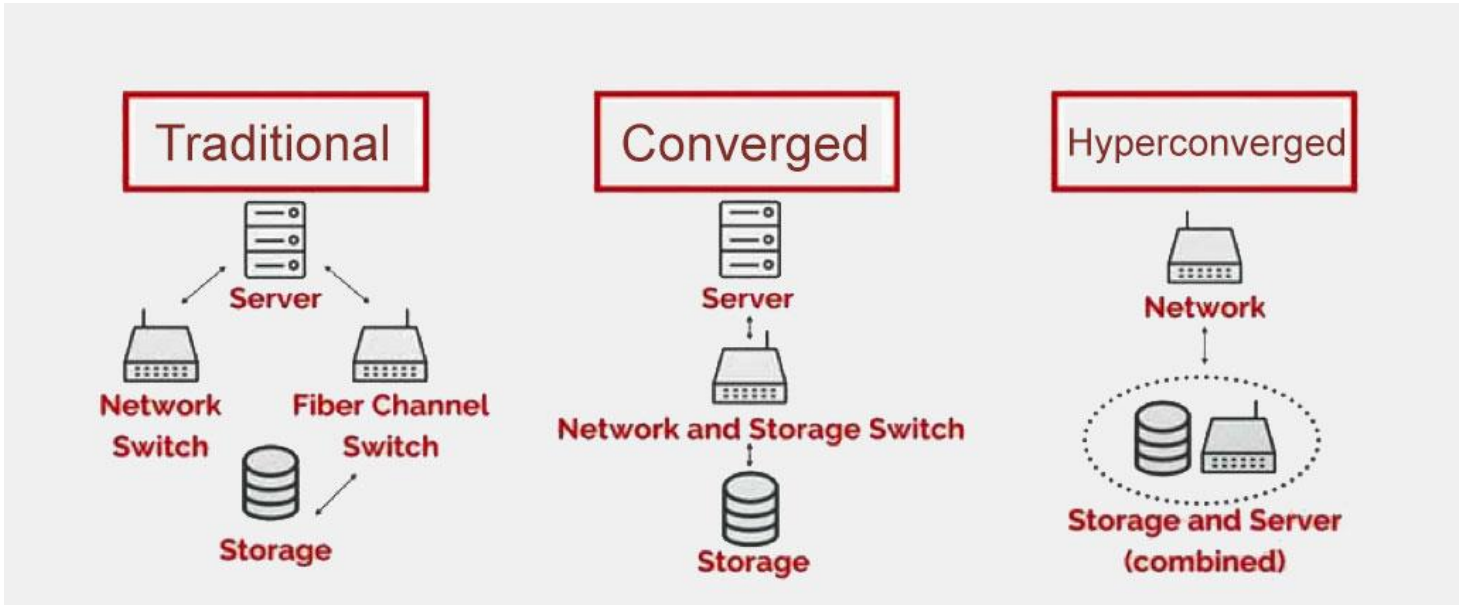
Titlul Proiectului

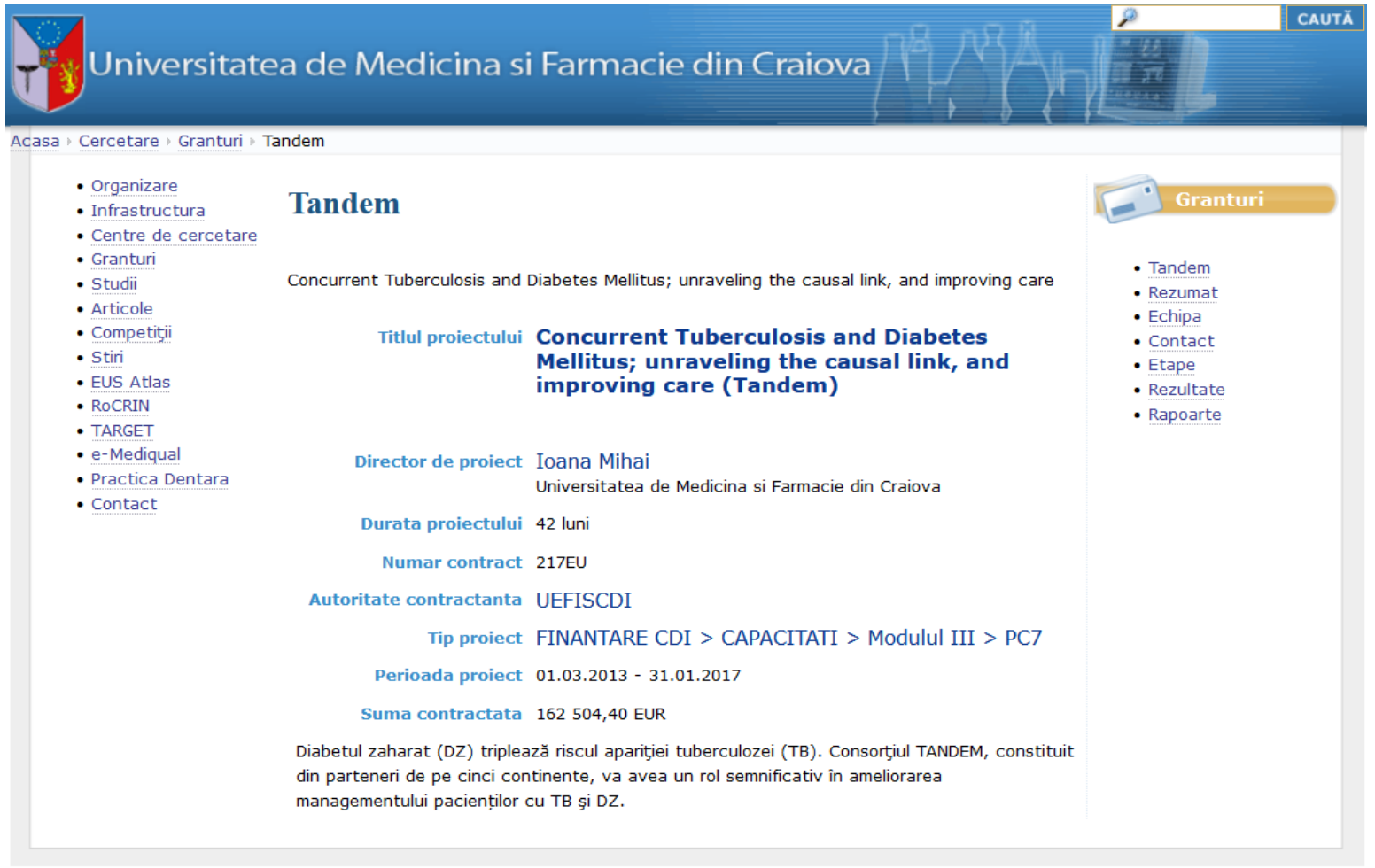
Cresterea capacitatii de diagnostic prin RT PCR la nivelul SCJUC in vederea asigurarii unui management eficient al pacientilor suspecti COVID19 din regiunea Sud – Vest Oltenia

Solicitant

Digitalizarea activității educaționale și de cercetare în cadrul UMF din Craiova
C15: Educație
Investiția 16: Digitalizarea universităților și pregătirea acestora pentru profesiile digitale ale viitorului





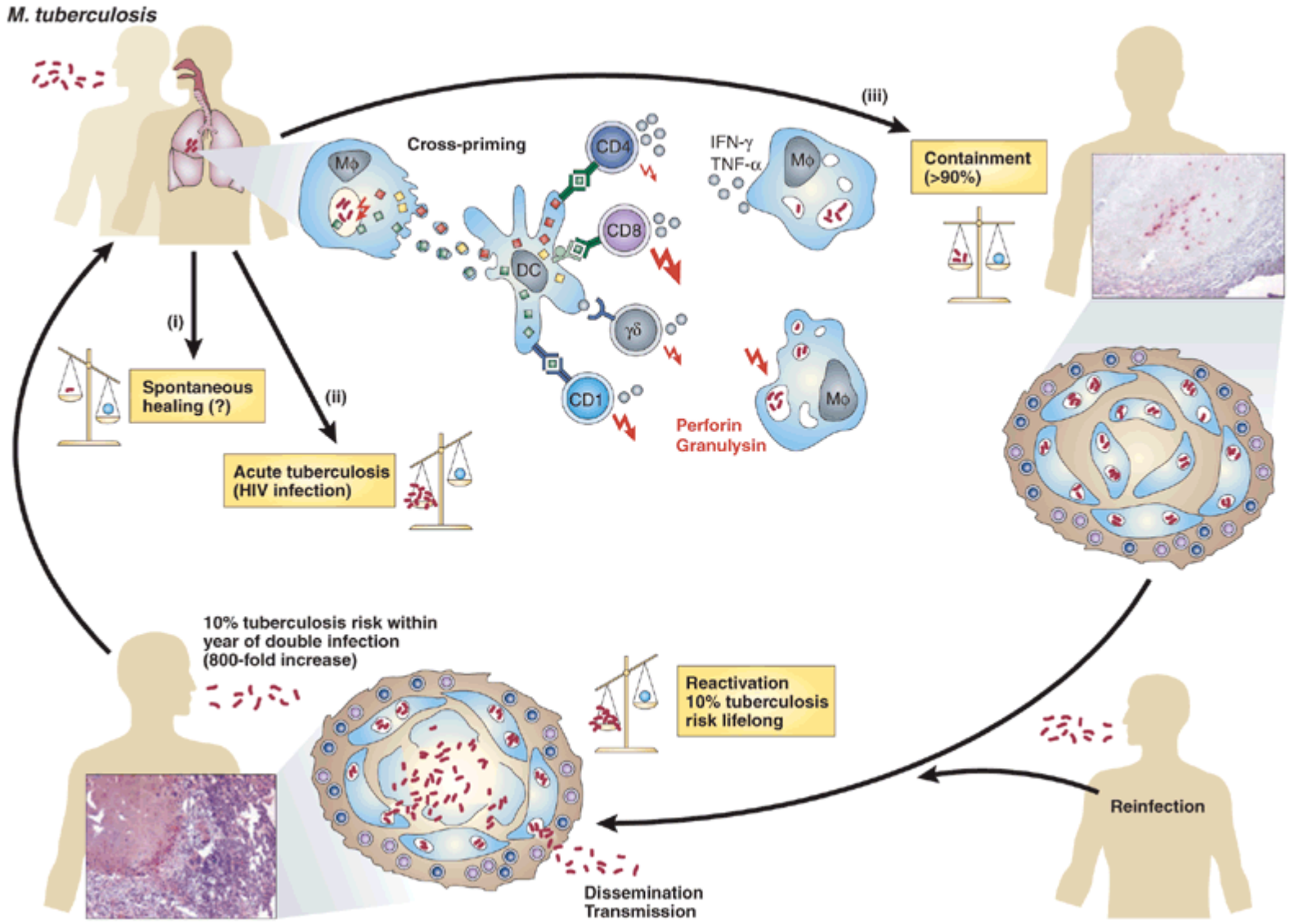

Universitatea de Medicina si Farmacie din Craiova
CAUTĂ
Acasa › Cercetare › Granturi › Tandem
Organizare
Infrastructura
Centre de cercetare
Granturi
Studii
Articole
Competiţii
Stiri
EUS Atlas
RoCRIN
TARGET
e-Mediqual
Practica Dentara
Contact
Tandem
Concurrent Tuberculosis and Diabetes Mellitus; unraveling the causal link, and improving care
Titlul proiectului
Concurrent Tuberculosis and Diabetes Mellitus; unraveling the causal link, and improving care (Tandem)
Director de proiect
Ioana Mihai
Universitatea de Medicina si Farmacie din Craiova
Durata proiectului
42 luni
Numar contract
217EU
Autoritate contractanta
UEFISCDI
Tip proiect
FINANTARE CDI > CAPACITATI > Modulul III > PC7
Perioada proiect
01.03.2013 - 31.01.2017
Suma contractata
162 504,40 EUR
Diabetul zaharat (DZ) triplează riscul apariţiei tuberculozei (TB). Consorţiul TANDEM, constituit din parteneri de pe cinci continente, va avea un rol semnificativ în ameliorarea managementului pacienţilor cu TB şi DZ.
Granturi
Tandem
Rezumat
Echipa
Contact
Etape
Rezultate
Rapoarte


Universitatea de Medicina si Farmacie din Craiova
CAUTĂ
Acasa › Cercetare › Granturi › RID-TB
Organizare
Infrastructura
Centre de cercetare
Granturi
Studii
Articole
Competiţii
Stiri
EUS Atlas
RoCRIN
TARGET
e-Mediqual
Practica Dentara
Contact
RID-TB
Titlul proiectului
Rolul factorilor imunogenetici si al deficitului de vitamina D in tuberculoza (RID-TB)
Director de proiect
Conf. univ. dr. Mihai IOANA
UMF Craiova
Durata proiectului
2 ani
Numar contract
163/01.10.2015
Autoritate contractanta
UEFISCDI
Tip proiect
PN-II-RU-TE-2014
Perioada proiect
01.10.2015 - 30.09.2017
Suma contractata
550000 RON
Ipoteza de lucru propusa: deficitul de vitamina D este asociat cu risc crescut de infecţie TB si progresie spre TB activa, prin autofagie si raspuns citokinic inadecvat la M.tb.
Granturi
RID-TB
Rezumat
Contact
Echipa
Etape
Rezultate
Rapoarte
Universitate | Facultati | Cercetare | Servicii Medicale | Harta site

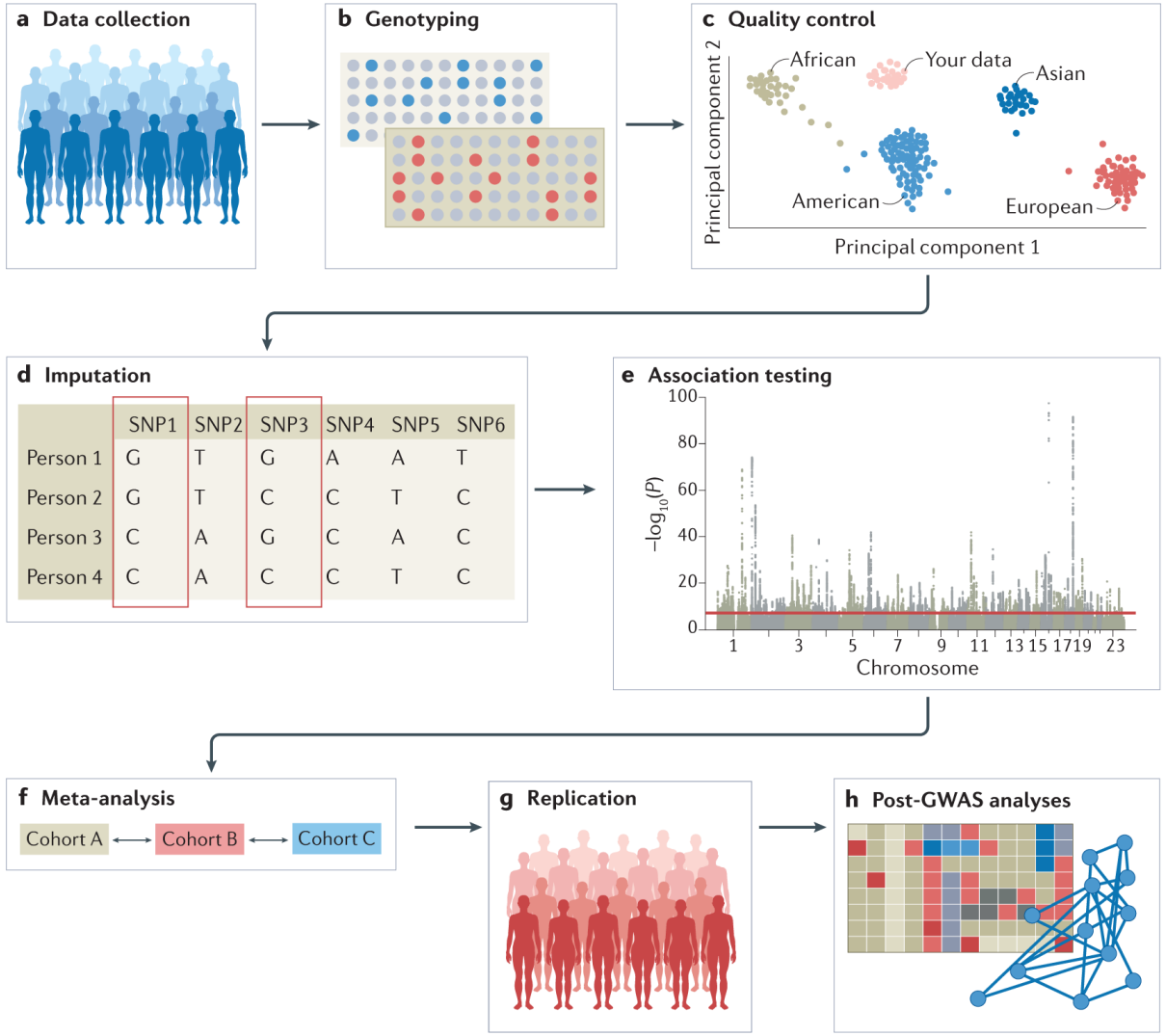
Illumina iScan platform was used for genotyping on HumanCore Exome chips, on previously established Indonesian and Romanian cohorts:

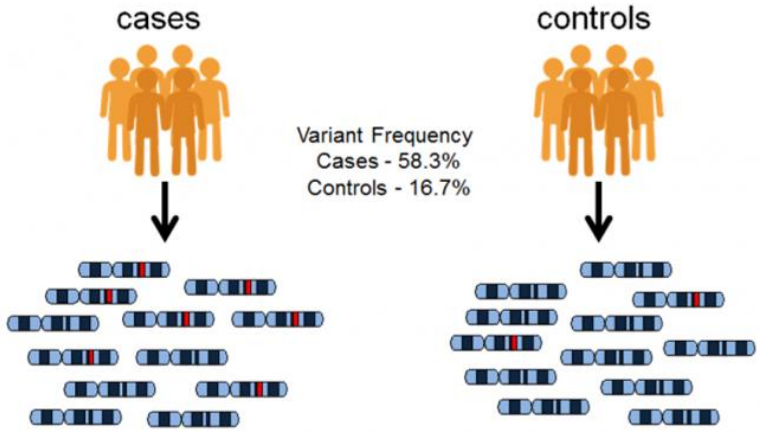
(1) TANDEM - Concurrent Tuberculosis and Diabetes Mellitus; unraveling the causal link, and improving care, conducted in 4 recruiting sites, out of which Romania and Indonesia have genotyping data (Collaborative project FP7-HEALTH-2012-INNOVATION-1 305279),
(2) INFECT - Innate Factors and Early Clearance of *Mycobacterium tuberculosis,* conducted in Bandung, Indonesia (funded by the University of Otago and Mercy Hospital, Dunedin, New Zealand),
(3) TBM - TB Meningitis research, conducted in Bandung, Indonesia, detailed in table 1 per phenotype (VIDI grant Reinout can Crevel and Indonesian support)

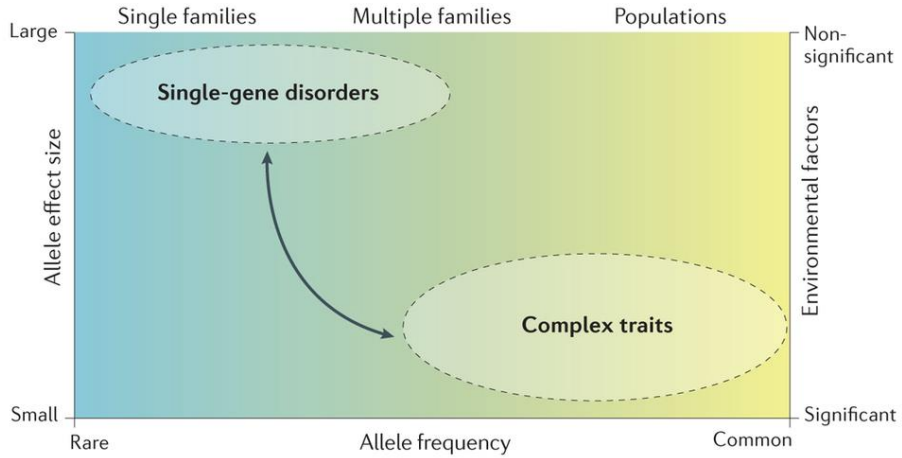
"The TANDEM Consortium brings together partners with complementary skills in clinical studies, epidemiology, health economics, human genetics and immunology."



Kaufmann, Stefan HE, and Andrew J. McMichael. "Annulling a dangerous liaison: vaccination strategies against AIDS and tuberculosis." *Nature medicine* 11.4s (2005): S33.

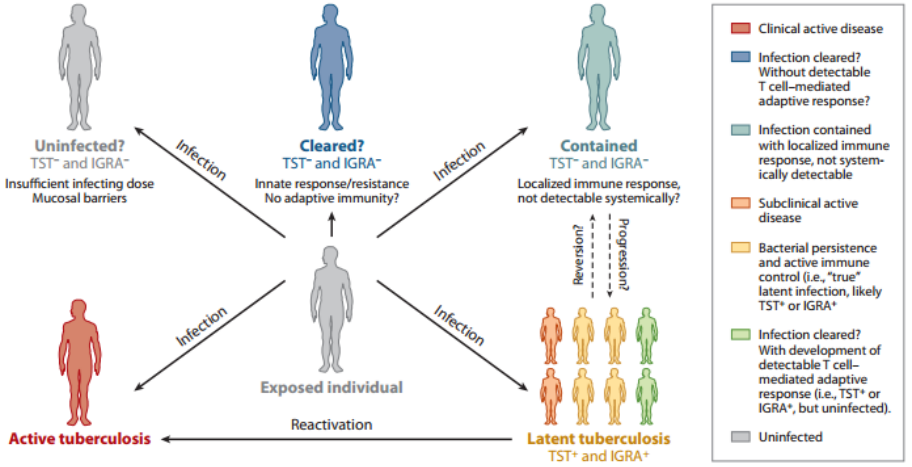




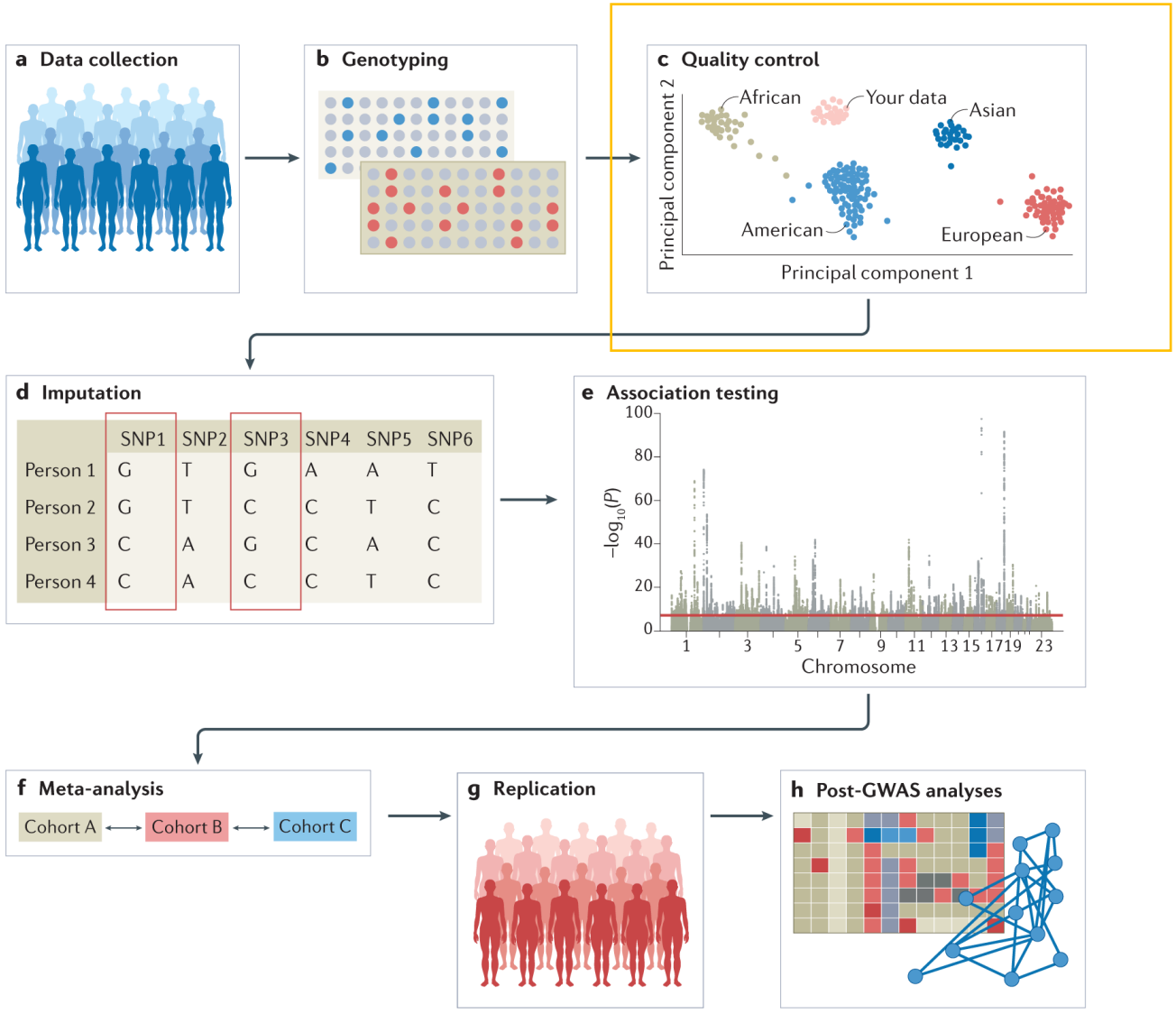


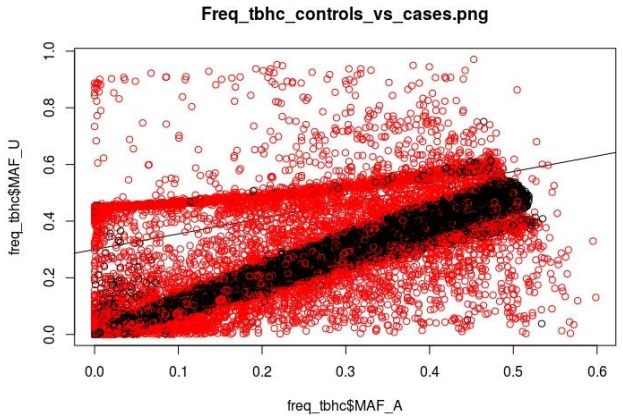
Uffelmann, E., Huang, Q.Q., Munung, N.S. et al. Genome-wide association studies. Nat Rev Methods Primers 1, 59 (2021). https://doi.org/10.1038/s43586-021-00056-9

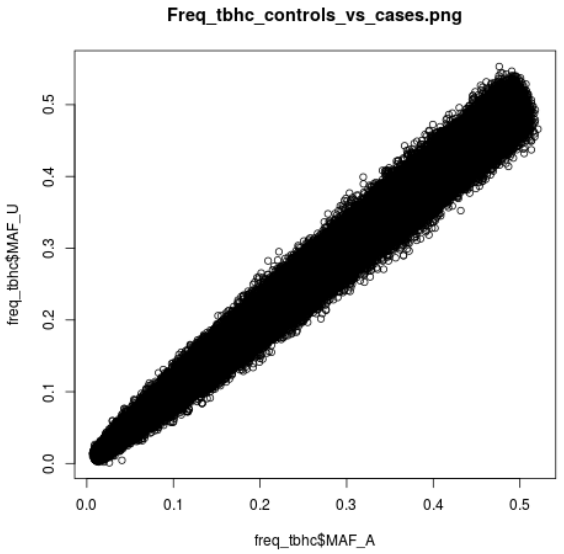
Tam, V., Patel, N., Turcotte, M. *et al.* Benefits and limitations of genome-wide association studies. *Nat Rev Genet* **20,** 467–484 (2019). https://doi.org/10.1038/s41576-019-0127-1

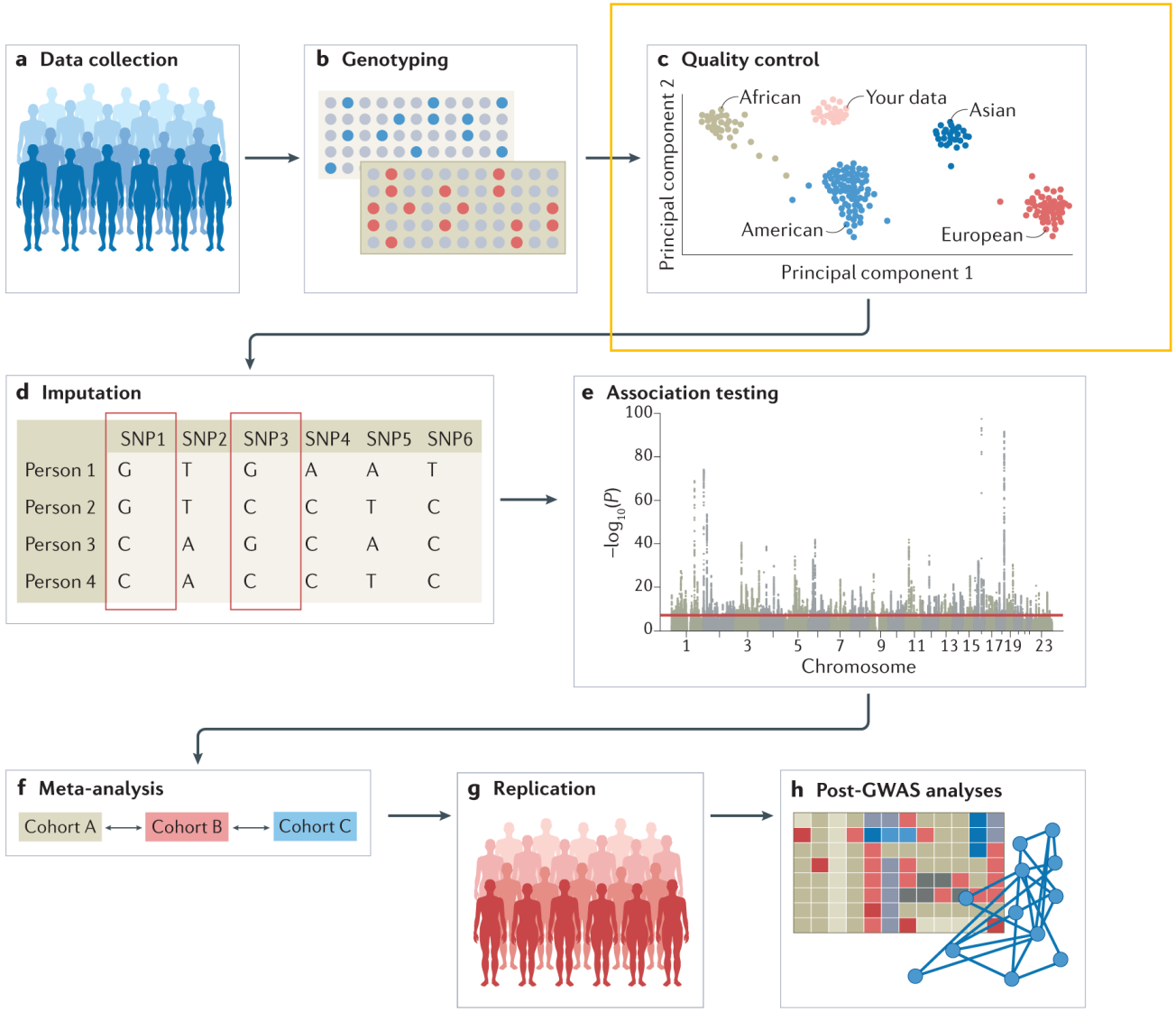


O'Garra et al, Ann Rev Imm 2013


a Data collection
b Genotyping
c Quality control
African
Your data
Asian
American
European
Principal component 2
Principal component 1
d Imputation
SNP1 SNP2 SNP3 SNP4 SNP5 SNP6
Person 1 G T G A A T
Person 2 G T C C T C
Person 3 C A G C A C
Person 4 C A C C T C
e Association testing
−log10(P)
Chromosome
f Meta-analysis
Cohort A
Cohort B
Cohort C
g Replication
h Post-GWAS analyses


Freq_tbhc_controls_vs_cases.png
freq_tbhc$MAF_U
freq_tbhc$MAF_A


Freq_tbhc_controls_vs_cases.png
freq_tbhc$MAF_U
freq_tbhc$MAF_A


a Data collection
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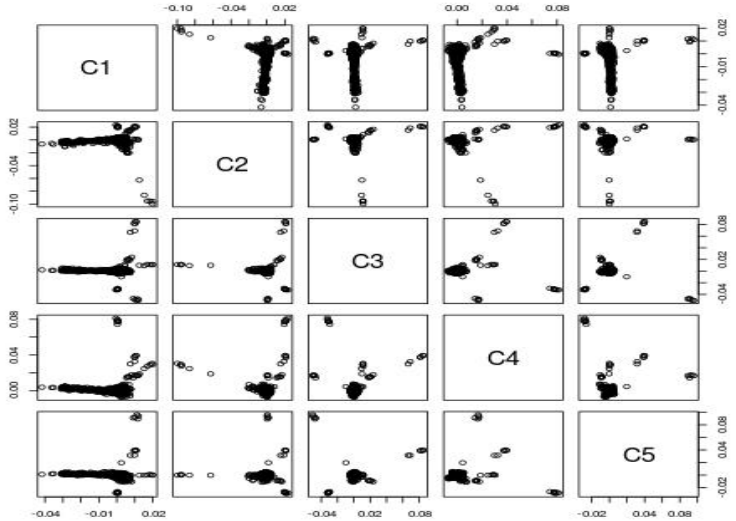
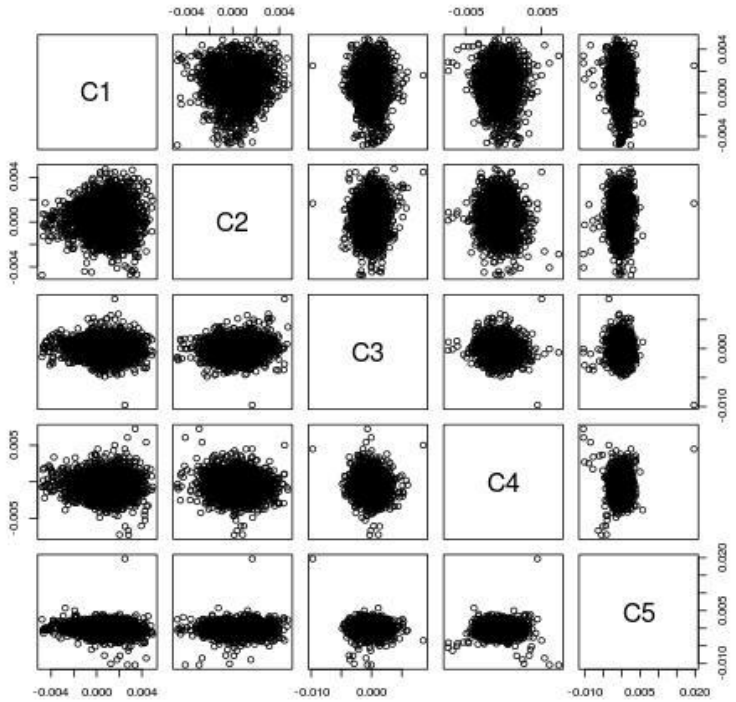
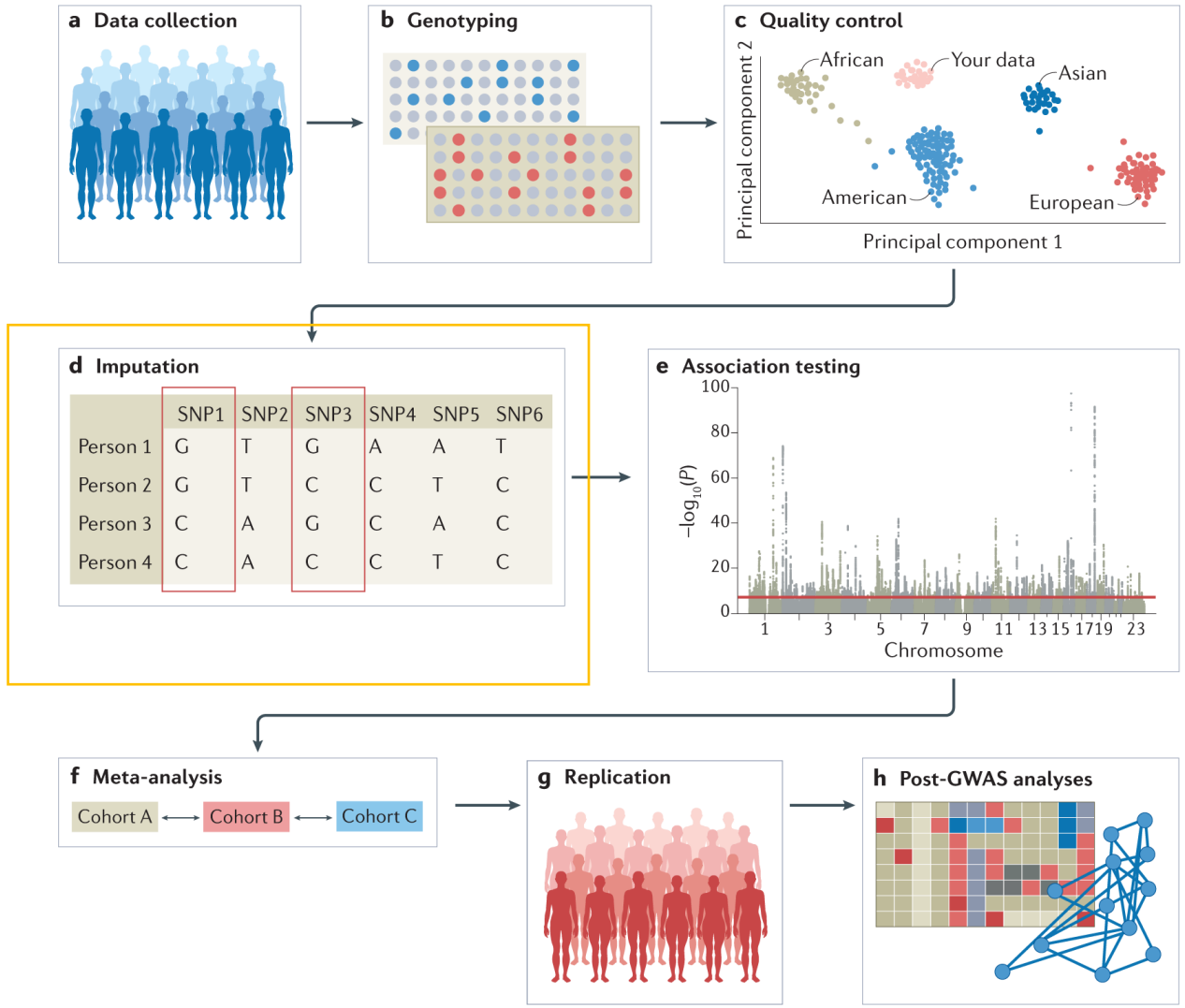
c Quality control
African
Your data
Asian
American
European
Principal component 2
Principal component 1
d Imputation
SNP1 SNP2 SNP3 SNP4 SNP5 SNP6
Person 1 G T G A A T
Person 2 G T C C T C
Person 3 C A G C A C
Person 4 C A C C T C
e Association testing
−log10(P)
Chromosome
f Meta-analysis
Cohort A
Cohort B
Cohort C
g Replication
h Post-GWAS analyses


C1
C2
C3
C4
C5

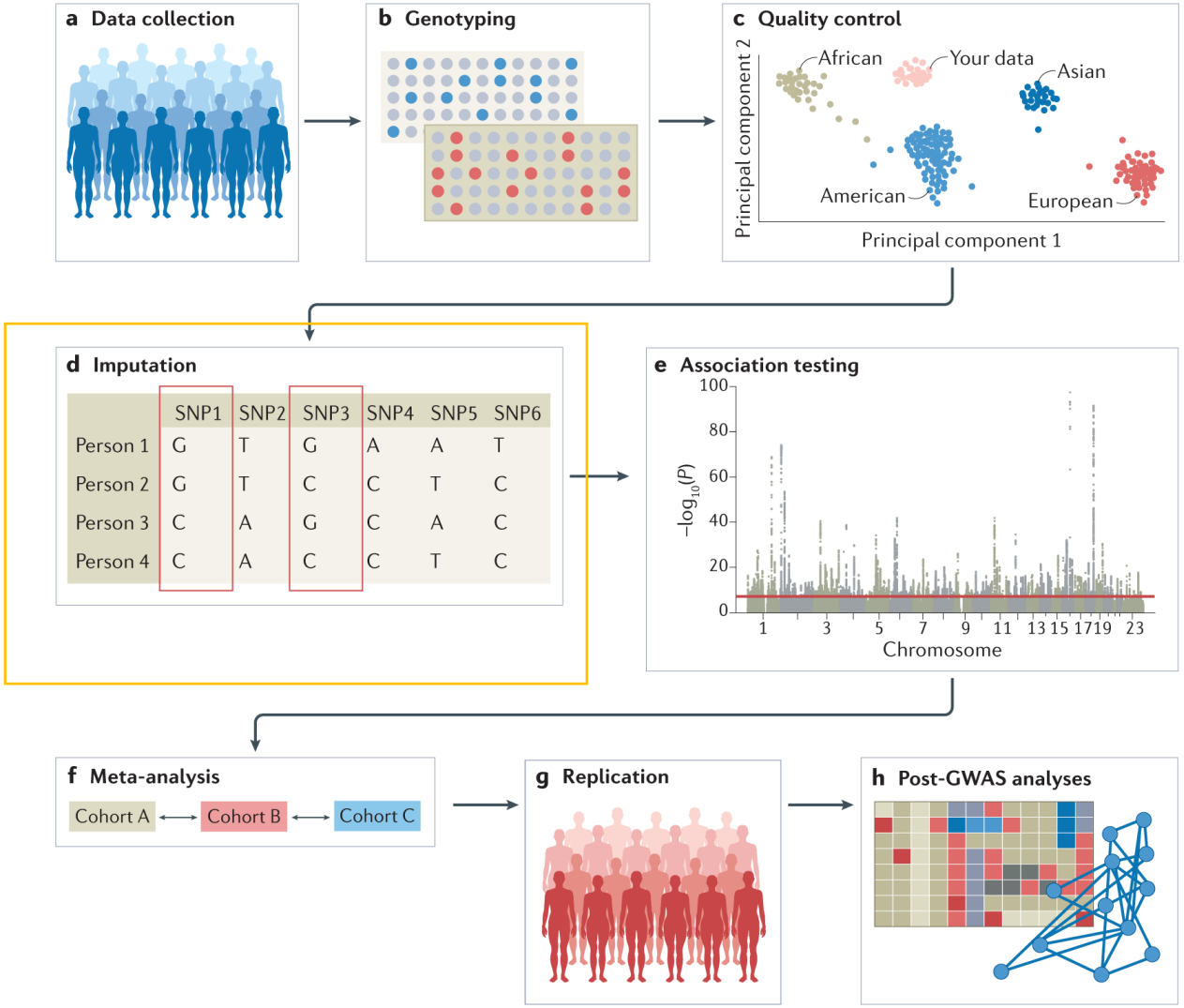

C1
C2
C3
C4
C5



The RIGHT reference panel for imputation?

Using population-specific add-on polymorphisms to improve genotype imputation in underrepresented populations

Zhi Ming Xu, Sina Rüeger, Michaela Zwyer, Daniela Brites, Hellen Hiza, Miriam Reinhard, Liliana Rutaihwa, Sonia Borrell, Faima Isihaka, Hosiana Temba, Thomas Maroa, Rastard Naftari, Jerry Hella, […],Jacques Fellay [view all]



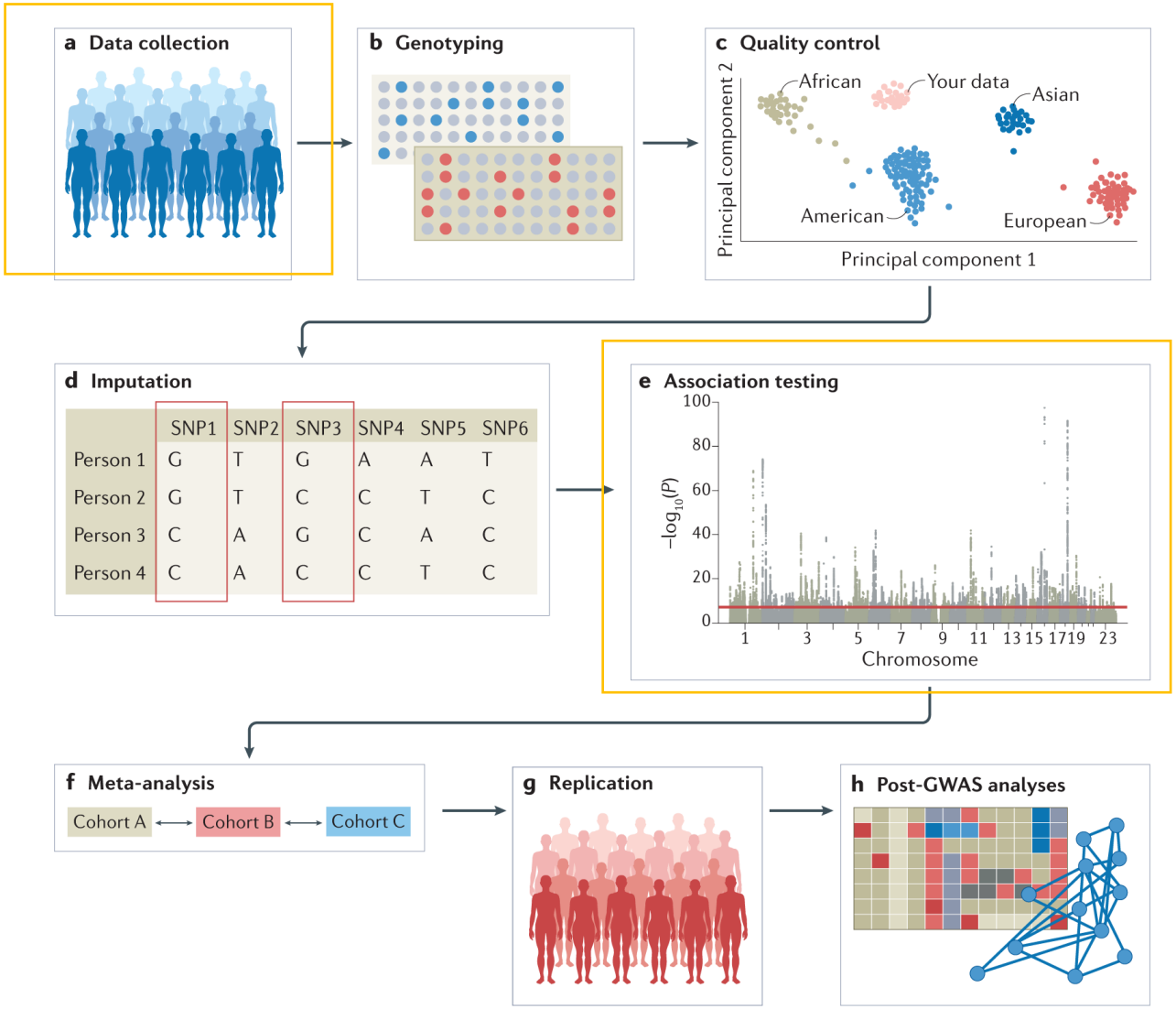
The RIGHT reference panel for imputation is:

?

Naïve overlap

Impute references

Joint calling


a Data collection
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Principal component 2
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SNP1 SNP2 SNP3 SNP4 SNP5 SNP6
Person 1 G T G A A T
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Person 3 C A G C A C
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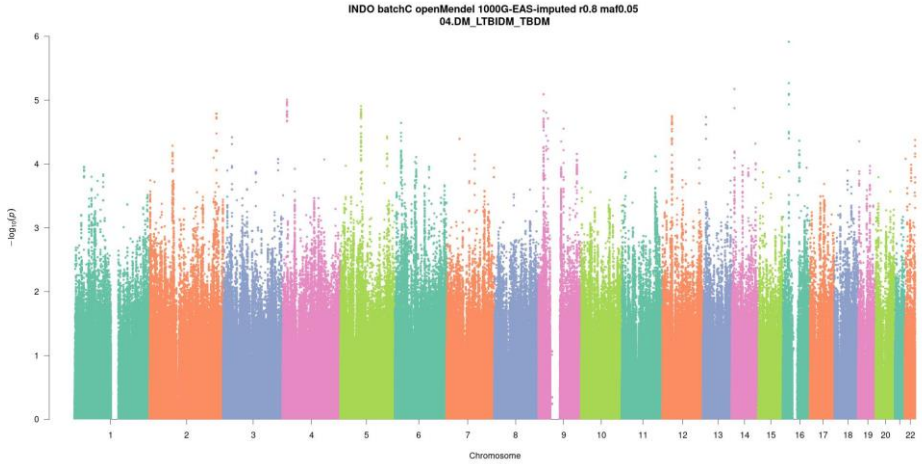
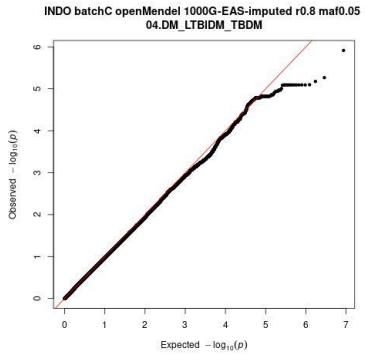
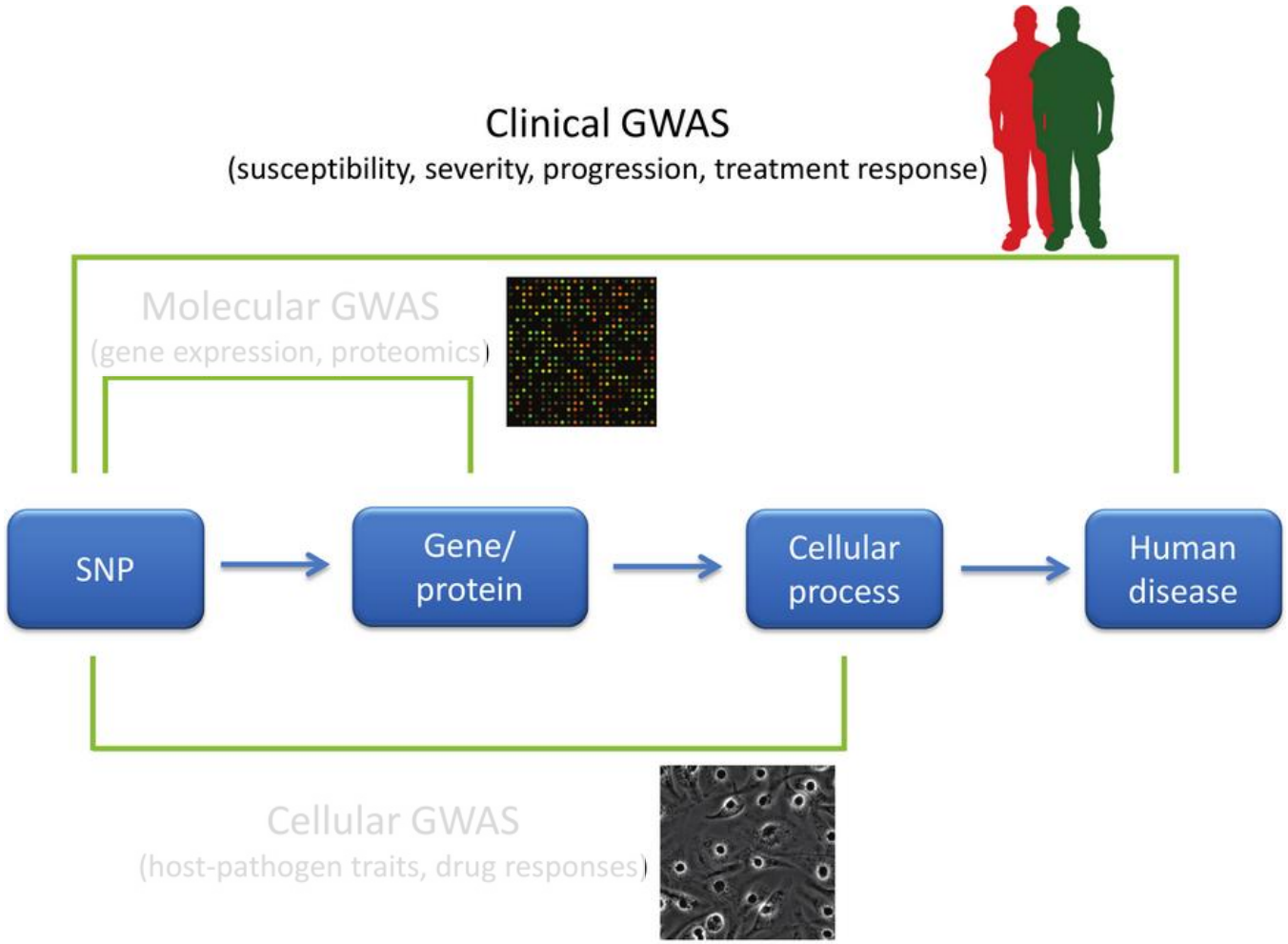
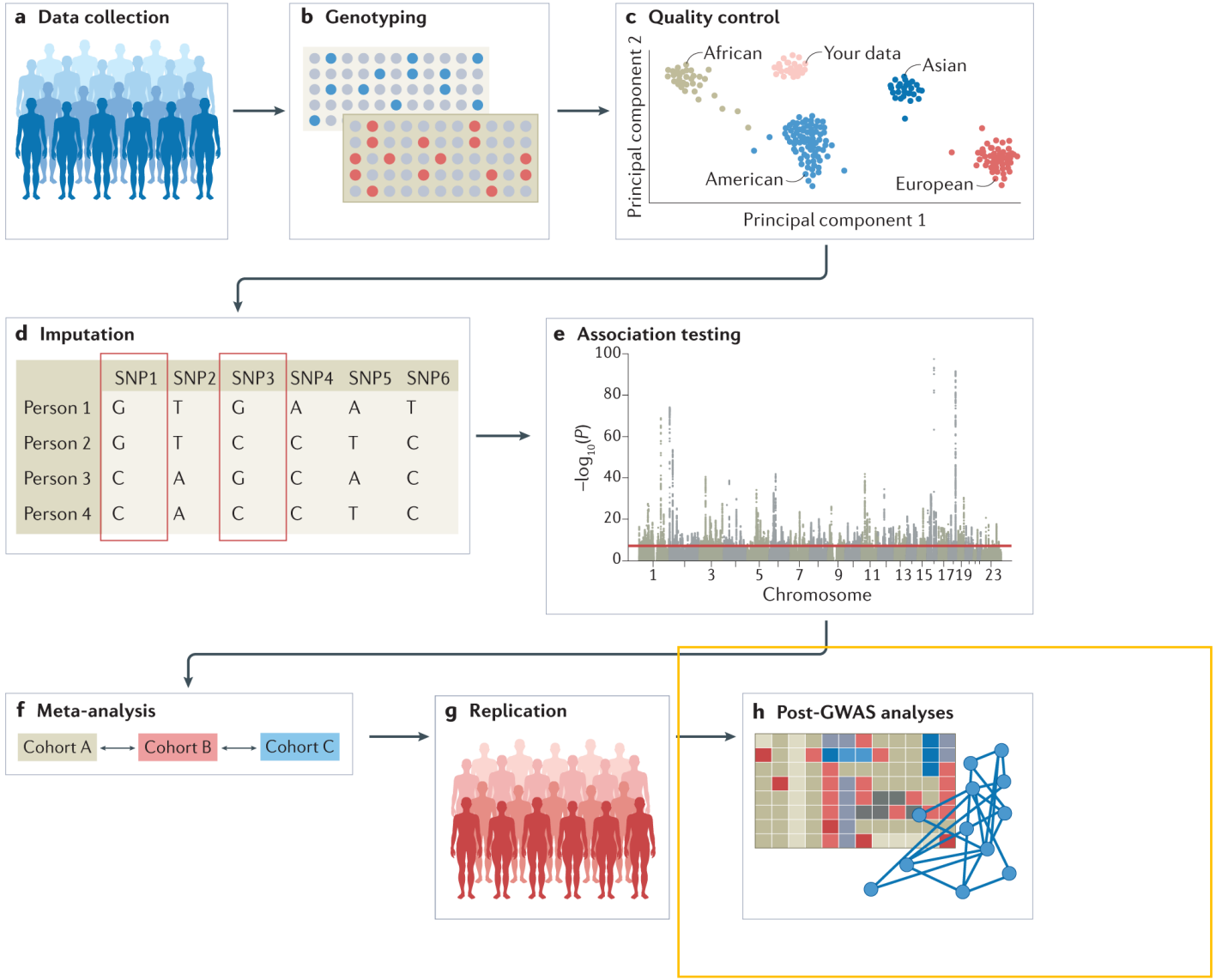
e Association testing
−log10(P)
Chromosome
f Meta-analysis
Cohort A
Cohort B
Cohort C
g Replication
h Post-GWAS analyses

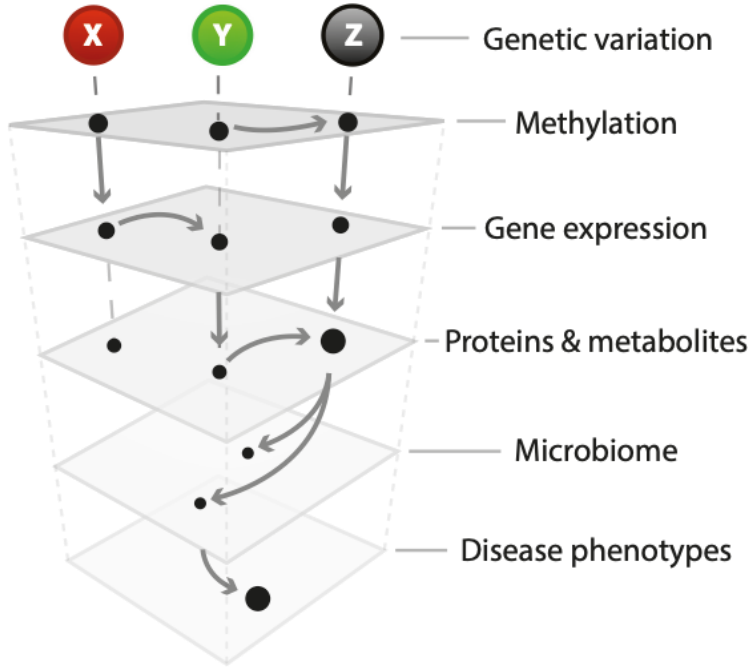

INDO batchC openMendel 1000G-EAS-imputed r0.8 maf0.05
04.DM_LTBIDM_TBDM
Chromosome


INDO batchC openMendel 1000G-EAS-imputed r0.8 maf0.05
04.DM_LTBIDM_TBDM
Expected −log10(p)

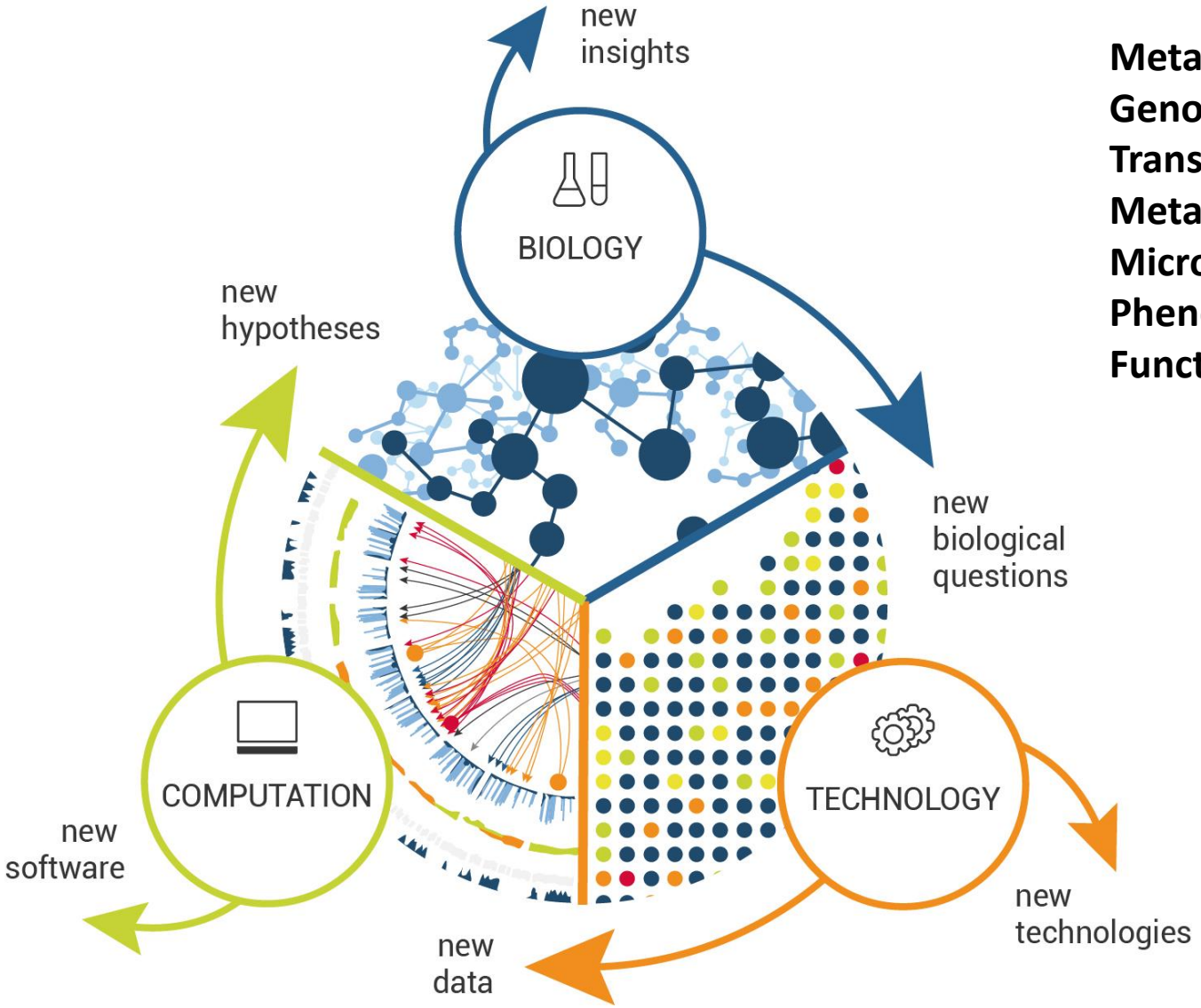
SNP -> gene -> pathway -> phenotype




a Data collection
b Genotyping
c Quality control
African
Your data
Asian
American
European
Principal component 2
Principal component 1
d Imputation
SNP1 SNP2 SNP3 SNP4 SNP5 SNP6
Person 1 G T G A A T
Person 2 G T C C T C
Person 3 C A G C A C
Person 4 C A C C T C
e Association testing
100
80
60
40
20
0
−log10(P)
1 3 5 7 9 11 13 15 17 19 23
Chromosome
f Meta-analysis
Cohort A
Cohort B
Cohort C
g Replication
h Post-GWAS analyses


X
Y
Z
Genetic variation
Methylation
Gene expression
Proteins & metabolites
Microbiome
Disease phenotypes

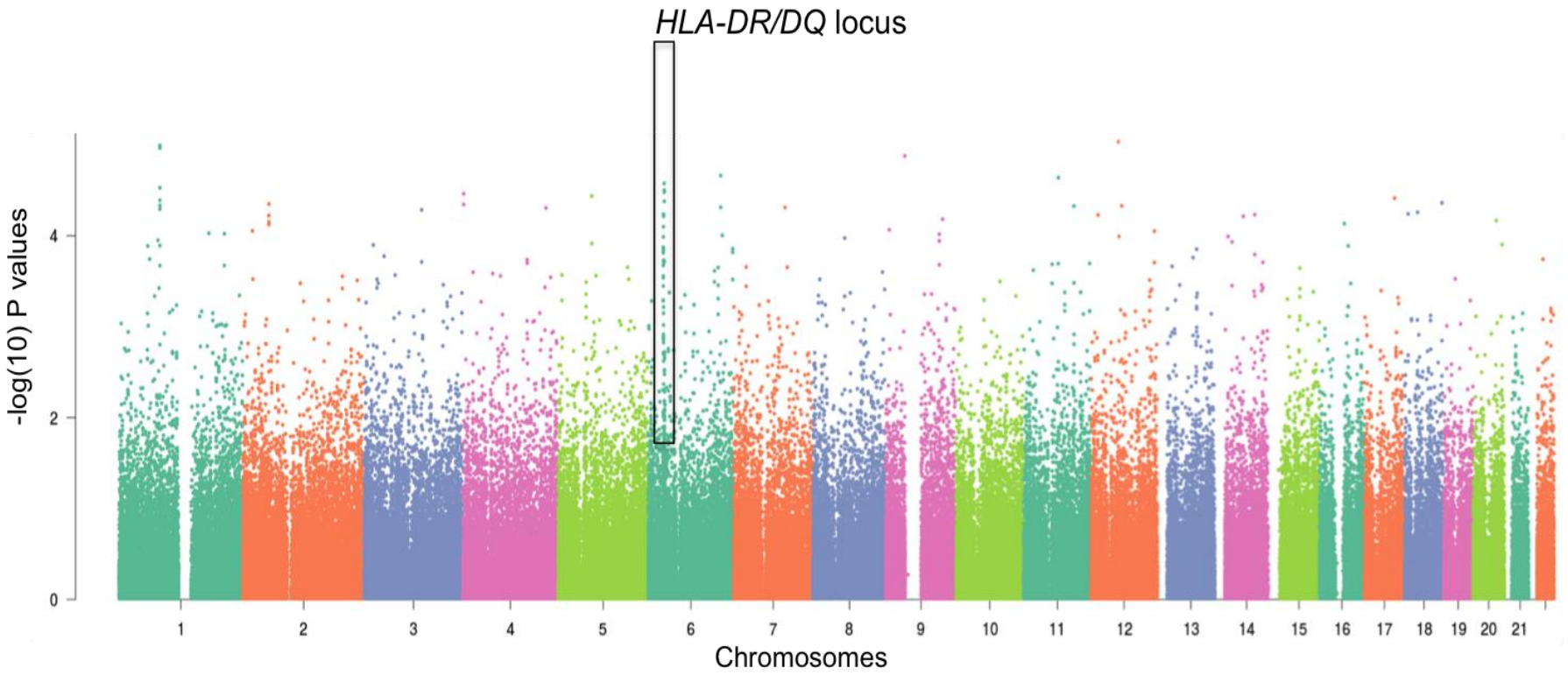
Indonesian data DM vs TBDM functional validation



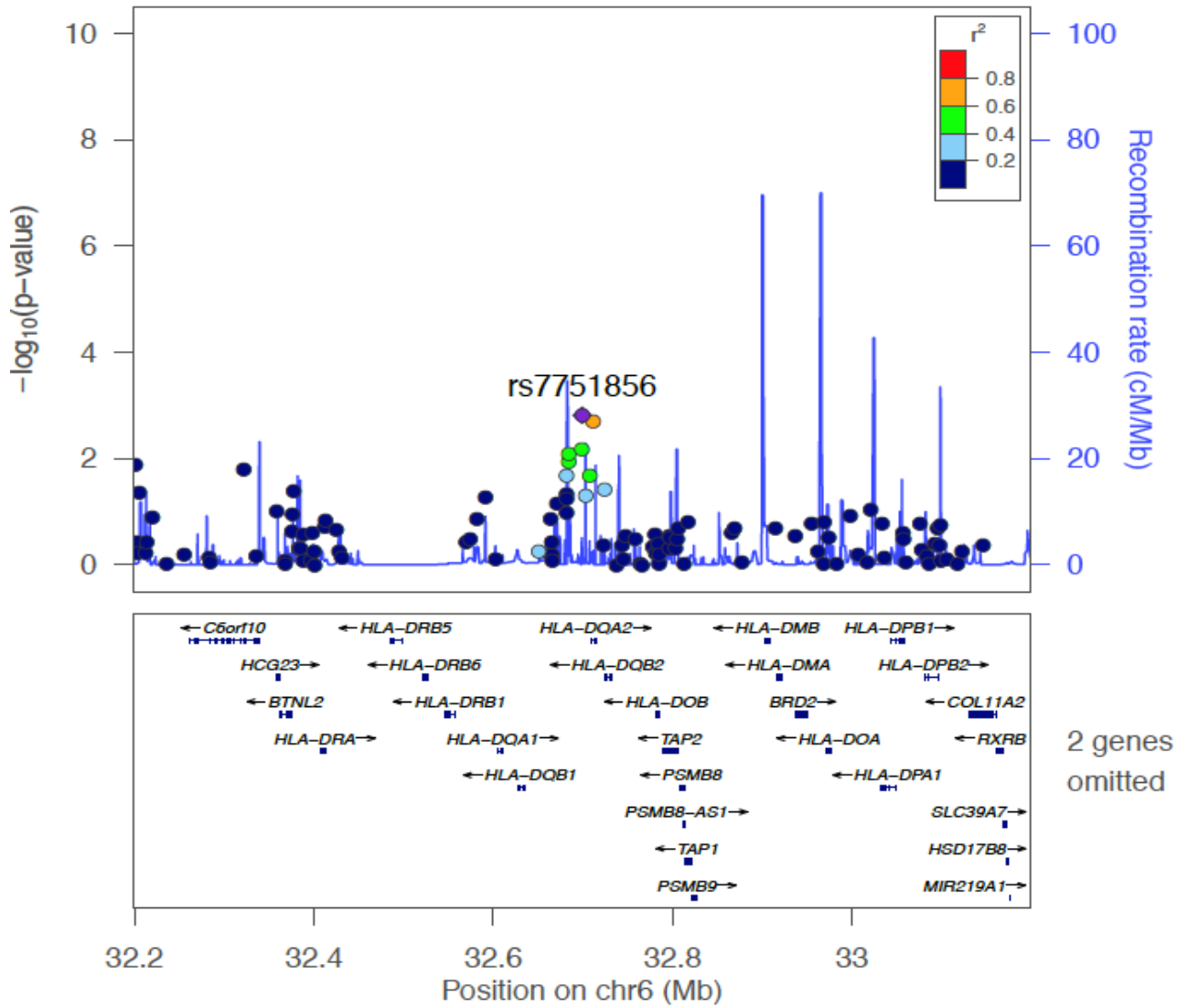
Metadata
Genome
Transcriptome
Metabolome
Microbiome
Phenotypical
Functional

immunological data

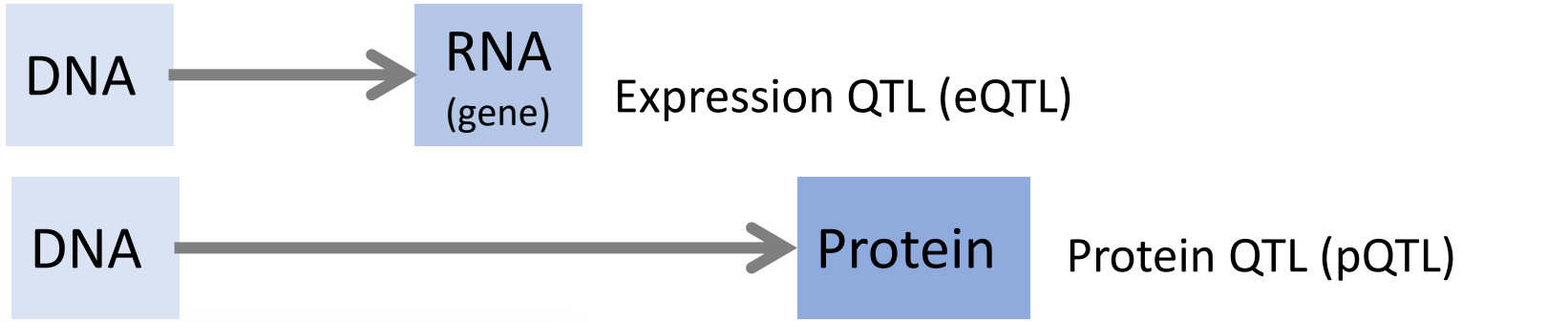
Indonesian data DM vs TBDM

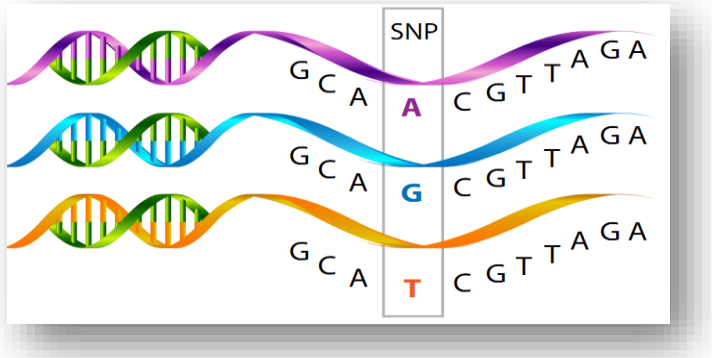


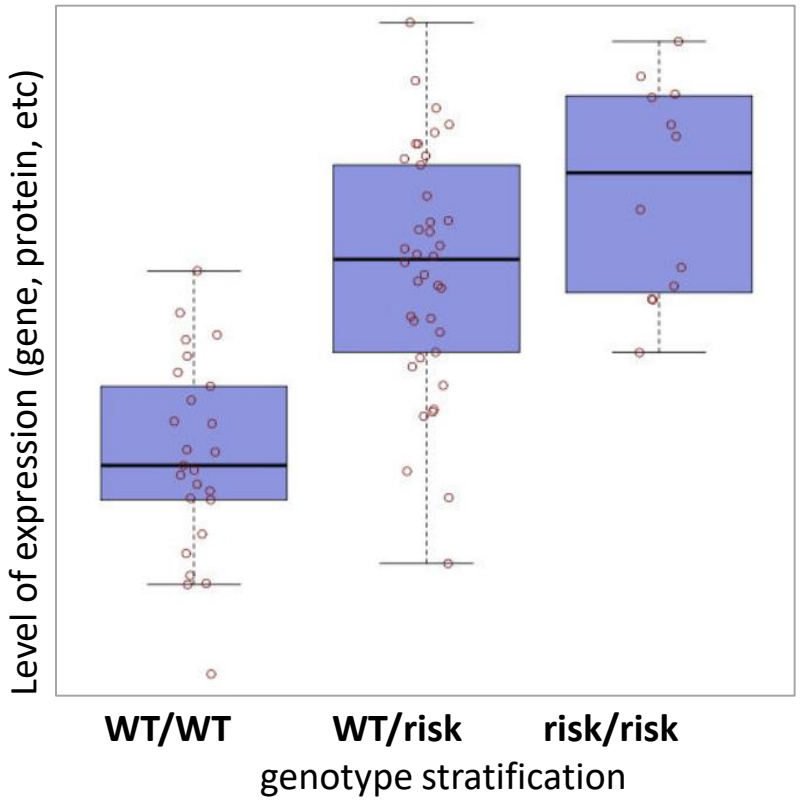
Indonesian data DM vs TBDM identifying genes, gene function prediction and pathways



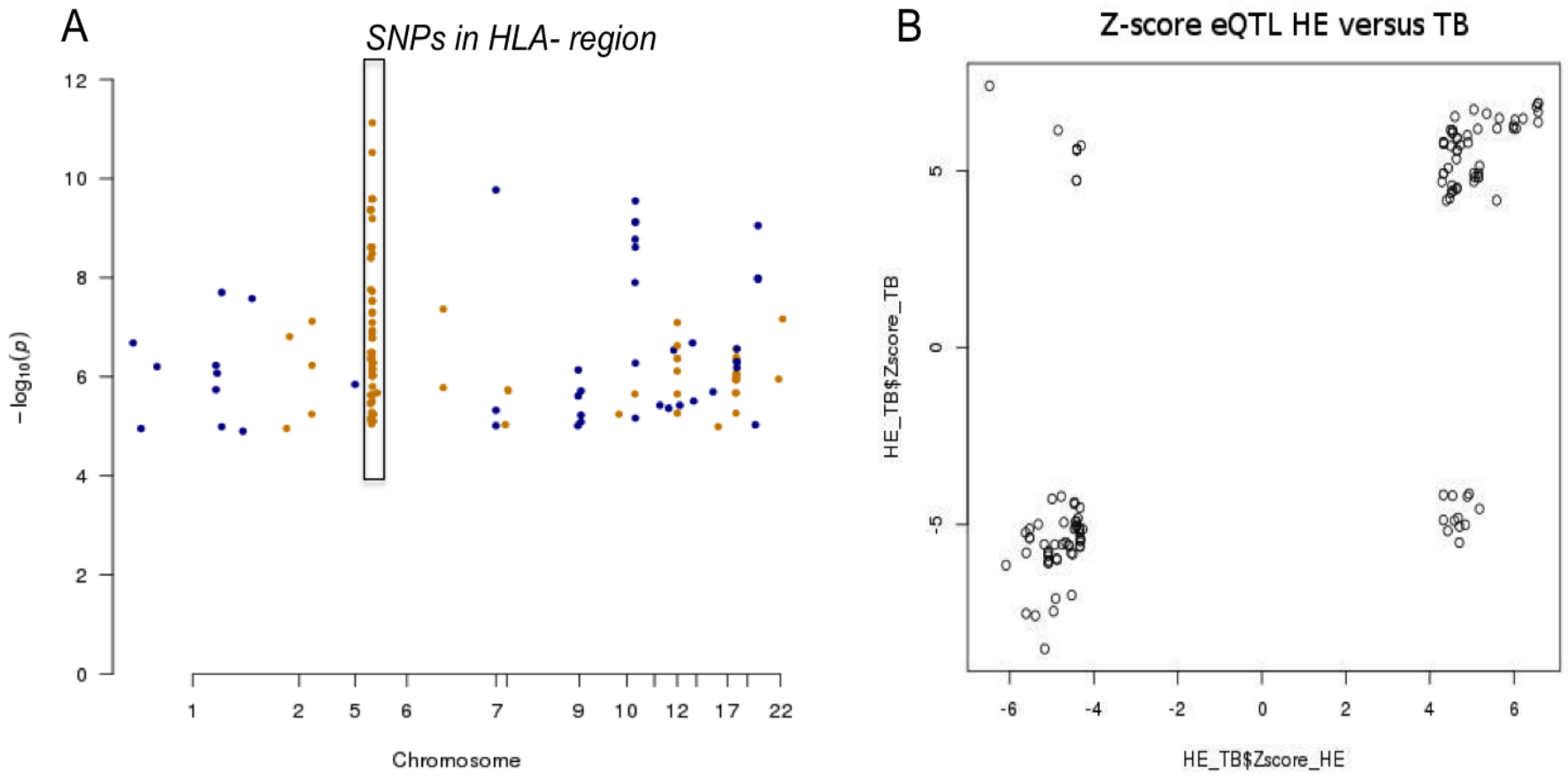
Quantitative trait loci (qtl):
correlation between genotypes and quantitative phenotypes







Indonesian data DM vs TBDM cis-eQTL



What we hope to do better

- good phenotyping
- choice of controls – the community and household model, extreme phenotype
- ethnicity-specific imputation panels
- analysis of different steps in the infectious process
- use of pathogen (mycobacteria) information

early clearer -> latent TB -> active pulmonary TB -> TB meningitis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Titlul proiectului Genomica FUnctionala in infectii SEvere (FUSE)
Director de proiect Netea Mihai Gheorghe
Durata proiectului 4 ani
Numar contract 31/01.09.2016
Autoritate contractanta ANCS
Tip proiect Componenta1 - Apel
Perioada proiect 01.09.2016 - 31.08.2020
Suma contractata 8 813 621.12 RON
Raspunsul imun este determinat de interactiunea dintre genomul uman, agentii patogeni si microbiom. Aceasta interactiune este alterata la pacientii cu sepsis. Identificarea acestor dezechilibre va duce la descoperirea de noi tinte terapeutice.
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- Sepsis is the primary cause of **death** from infection, especially if not recognized and treated promptly. Its recognition mandates urgent attention.
- Sepsis is a syndrome shaped by **pathogen** factors and **host** factors (eg, sex, race and other genetic determinants, age, comorbidities, environment) with characteristics that evolve over time. What differentiates sepsis from infection is an **aberrant or dysregulated host response** and the presence of organ dysfunction.
- Sepsis-induced organ dysfunction **may be occult**; therefore, its presence should be considered in any patient presenting with infection. Conversely, unrecognized infection may be the cause of new-onset organ dysfunction. Any unexplained organ dysfunction should thus raise the possibility of underlying infection.
- The **clinical and biological phenotype** of sepsis can be modified by preexisting acute illness, long-standing comorbidities, medication, and interventions.
- Specific infections may result in local organ dysfunction without generating a dysregulated **systemic** host response.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4968574/

Sequential [Sepsis-Related] Organ Failure Assessment Score[a]

	Score				
System	**0**	**1**	**2**	**3**	**4**
Respiration					
PaO_2/FIO_2, mm Hg (kPa)	≥400 (53.3)	<400 (53.3)	<300 (40)	<200 (26.7) with respiratory support	<100 (13.3) with respiratory support
Coagulation					
Platelets, $\times 10^3/\mu L$	≥150	<150	<100	<50	<20
Liver					
Bilirubin, mg/dL (μmol/L)	<1.2 (20)	1.2–1.9 (20–32)	2.0–5.9 (33–101)	6.0–11.9 (102–204)	>12.0 (204)
Cardiovascular	MAP ≥70 mm Hg	MAP <70 mm Hg	Dopamine <5 or dobutamine (any dose)[b]	Dopamine 5.1–15 or epinephrine ≤0.1 or norepinephrine ≤0.1[b]	Dopamine >15 or epinephrine >0.1 or norepinephrine >0.1[b]
Central nervous system					
Glasgow Coma Scale score[c]	15	13–14	10–12	6–9	<6
Renal					
Creatinine, mg/dL (μmol/L)	<1.2 (110)	1.2–1.9 (110–170)	2.0–3.4 (171–299)	3.5–4.9 (300–440)	>5.0 (440)
Urine output, mL/d				<500	<200

Open in a separate window

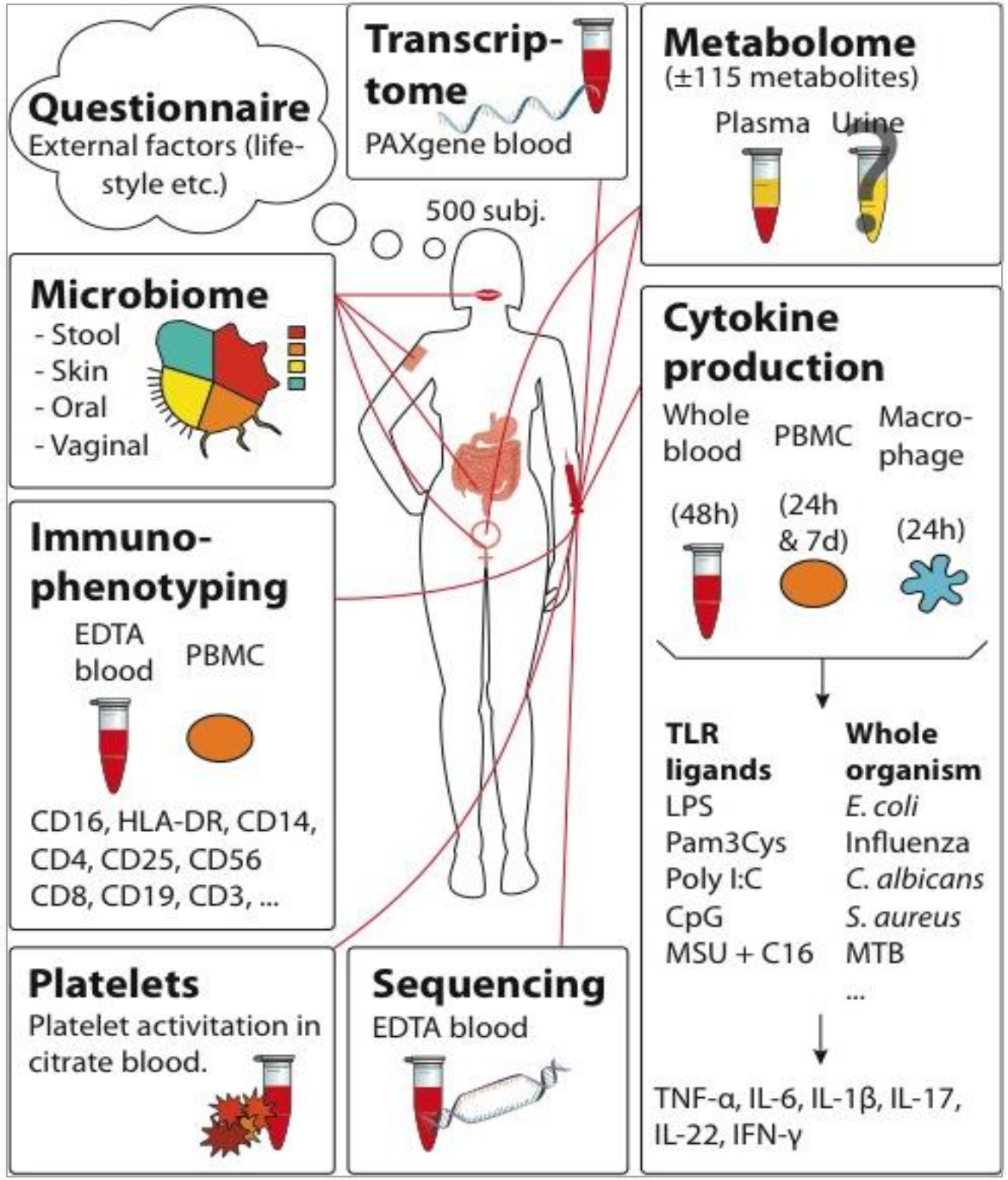
Abbreviations: FIO_2, fraction of inspired oxygen; MAP, mean arterial pressure; PaO_2, partial pressure of oxygen.

[a]Adapted from Vincent et al.[27]

[b]Catecholamine doses are given as μg/kg/min for at least 1 hour.

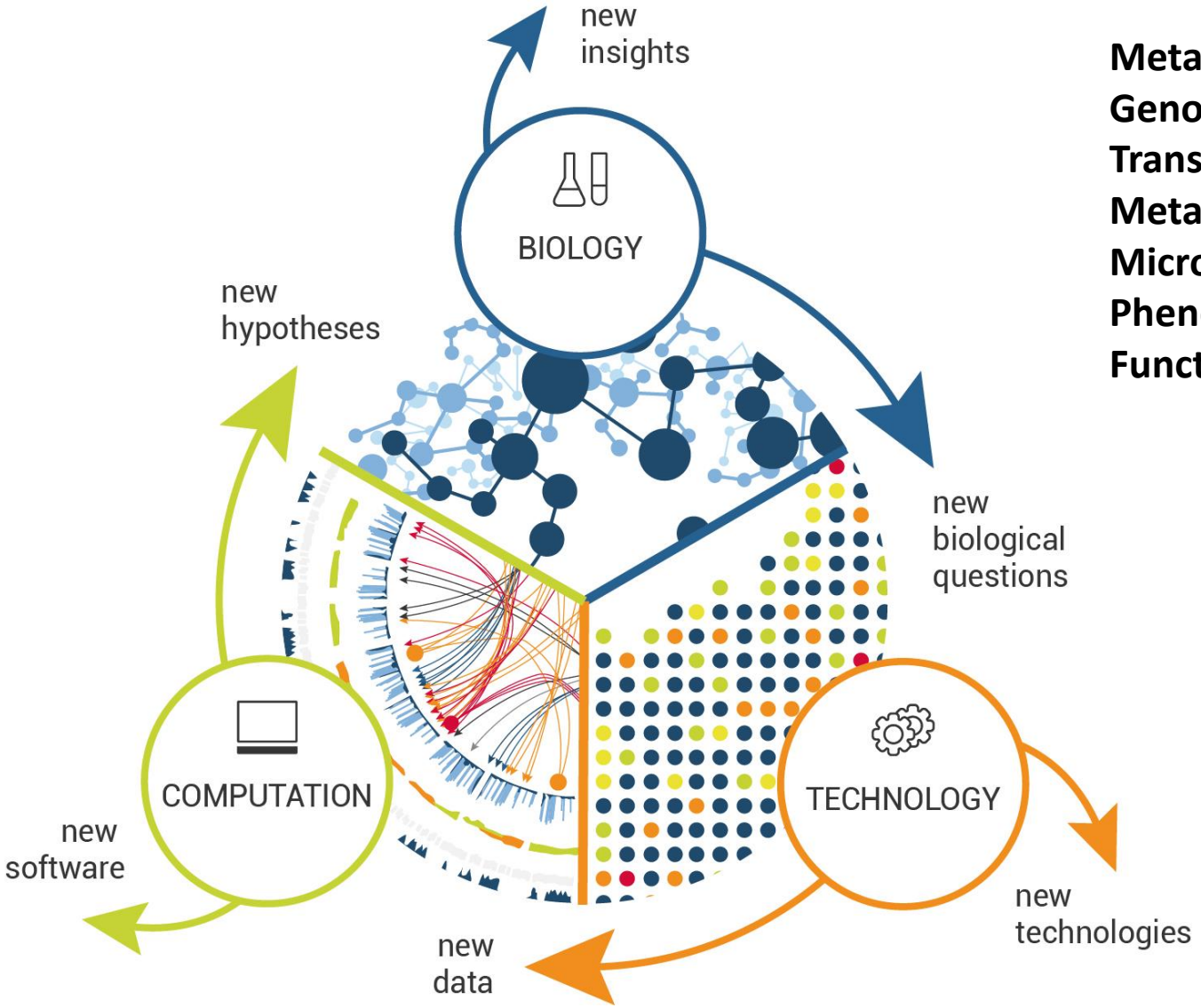
[c]Glasgow Coma Scale scores range from 3–15; higher score indicates better neurological function.

A population-based cohort to identify factors that contribute to inter-individual variability in immune responses



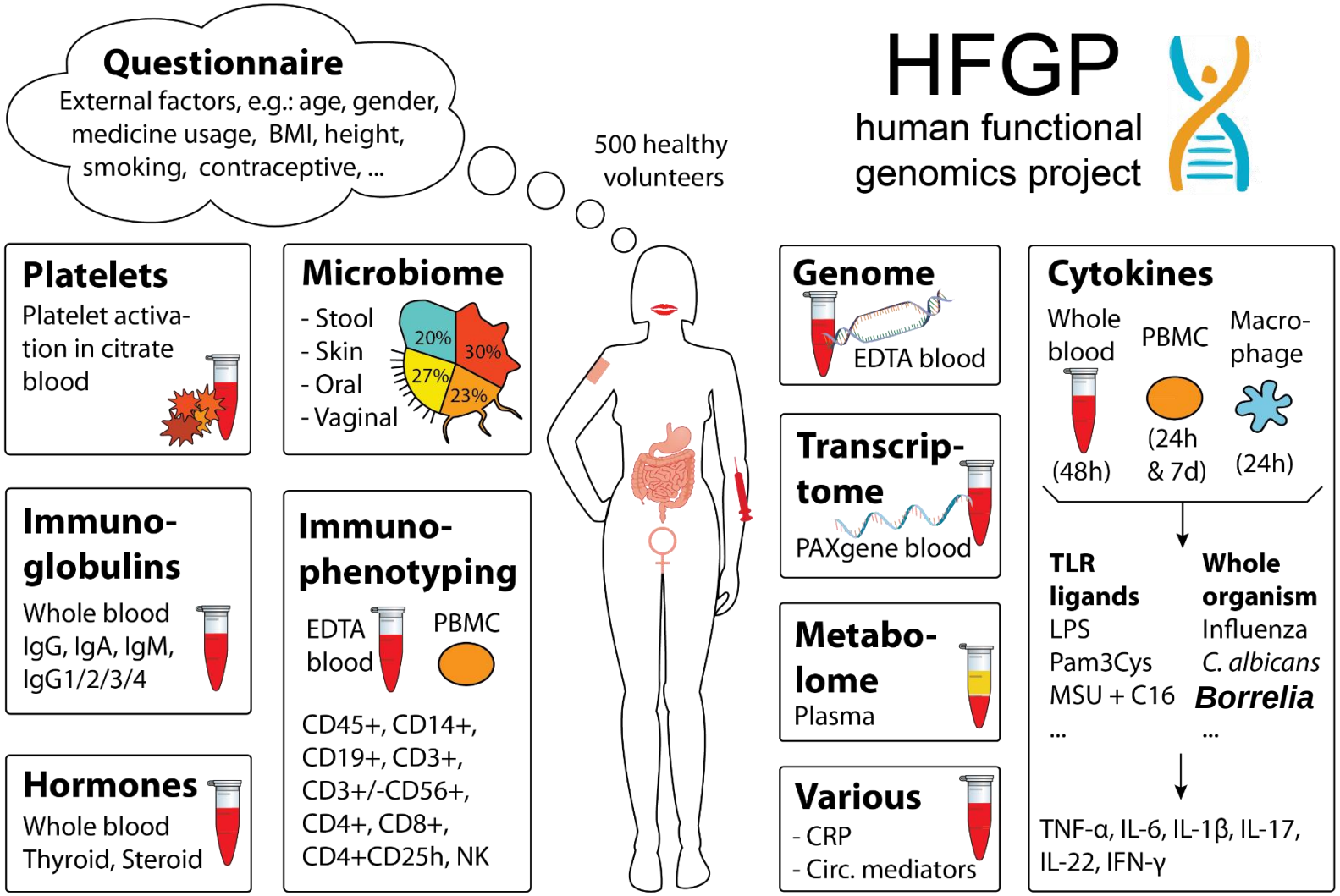
ter Horst R et al., ***Cell*** (2016)
Schirmer M et al., ***Cell*** (2016)
Li Y et al., ***Cell*** (2016)

Romanian data sepsis functional validation



Metadata
Genome
Transcriptome
Metabolome
Microbiome
Phenotypical
Functional

immunological data



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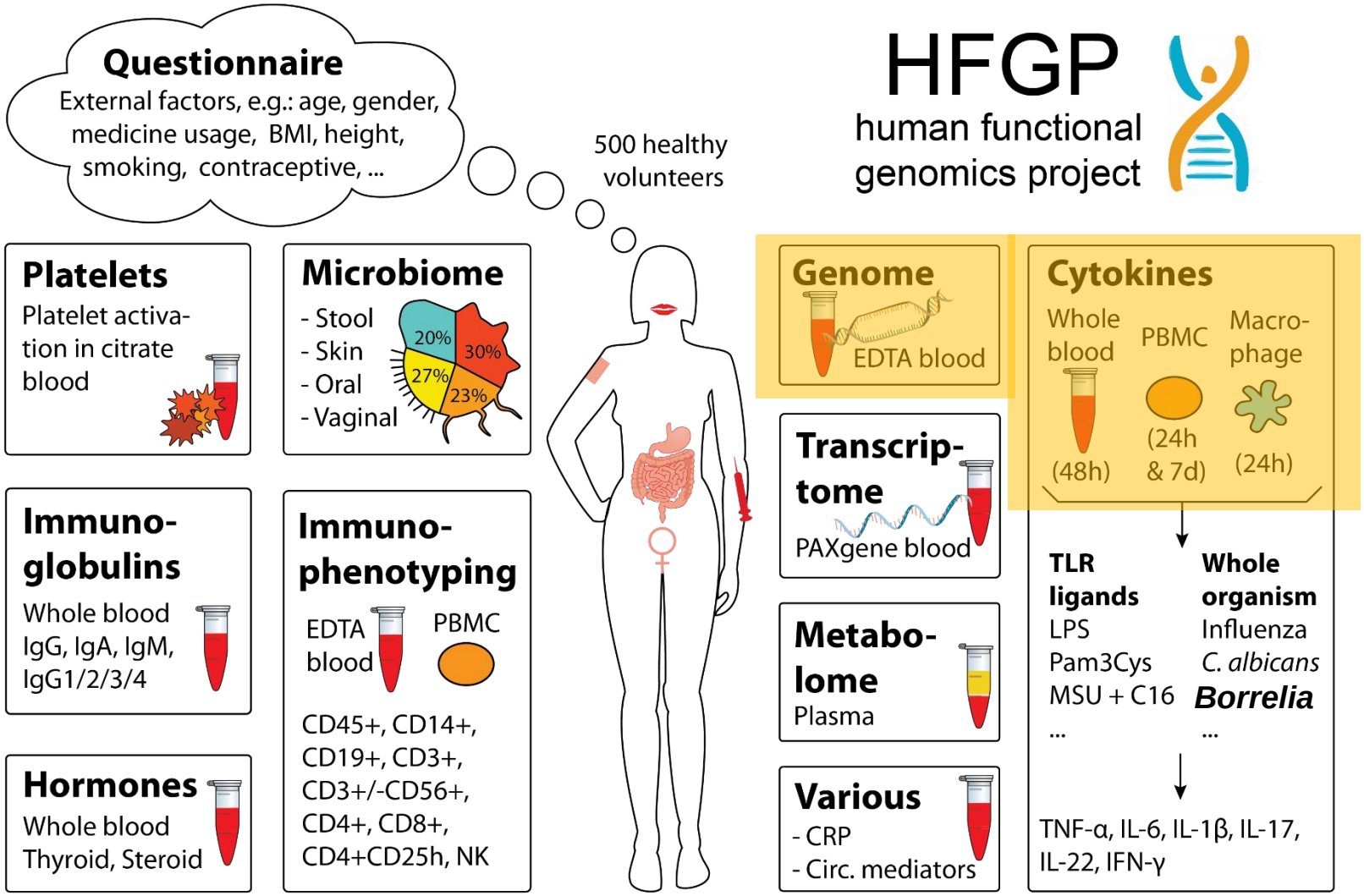

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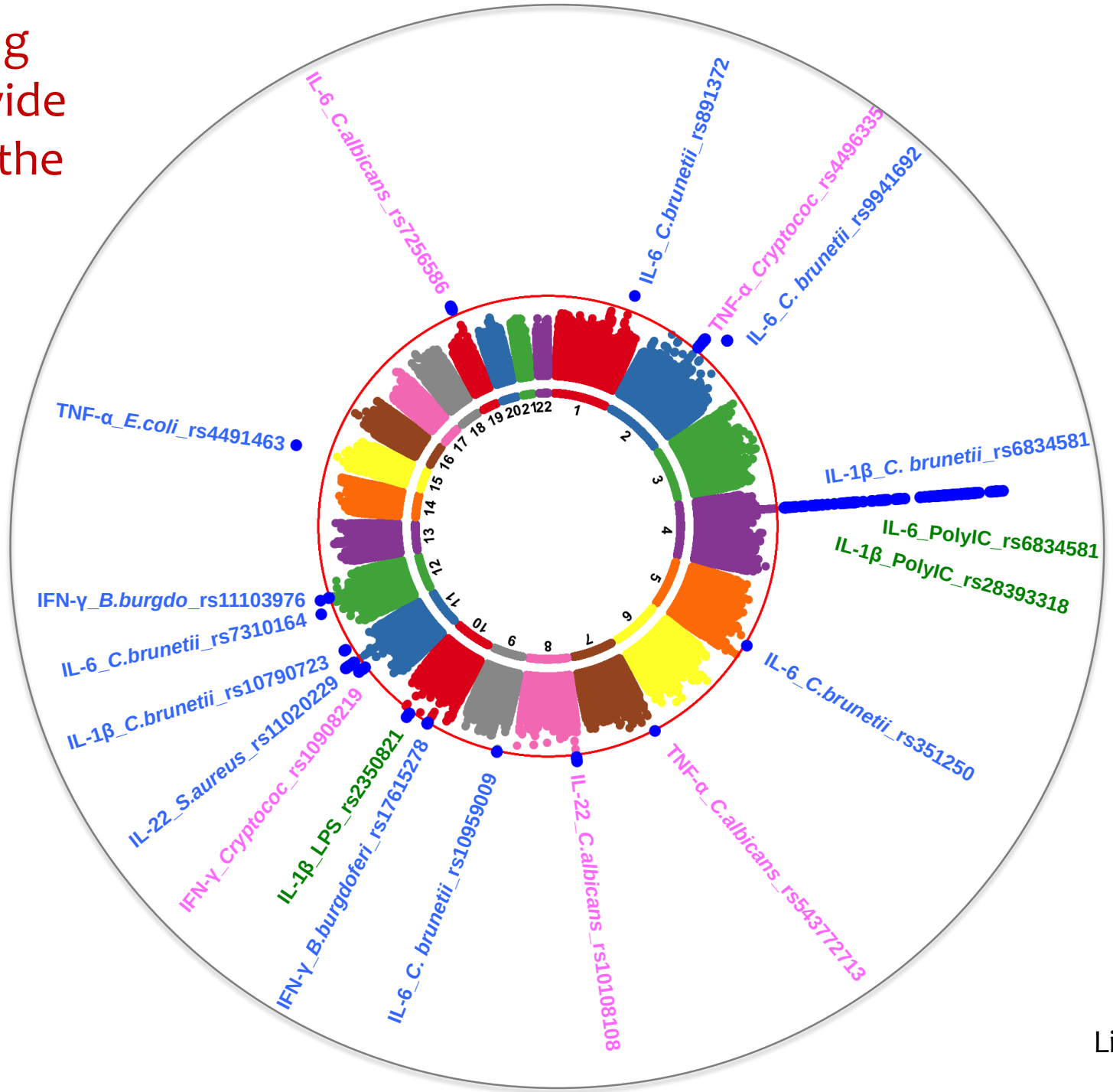
Cytokine QTL mapping identified 17 genome-wide cQTLs – *trans* effect in the Dutch population

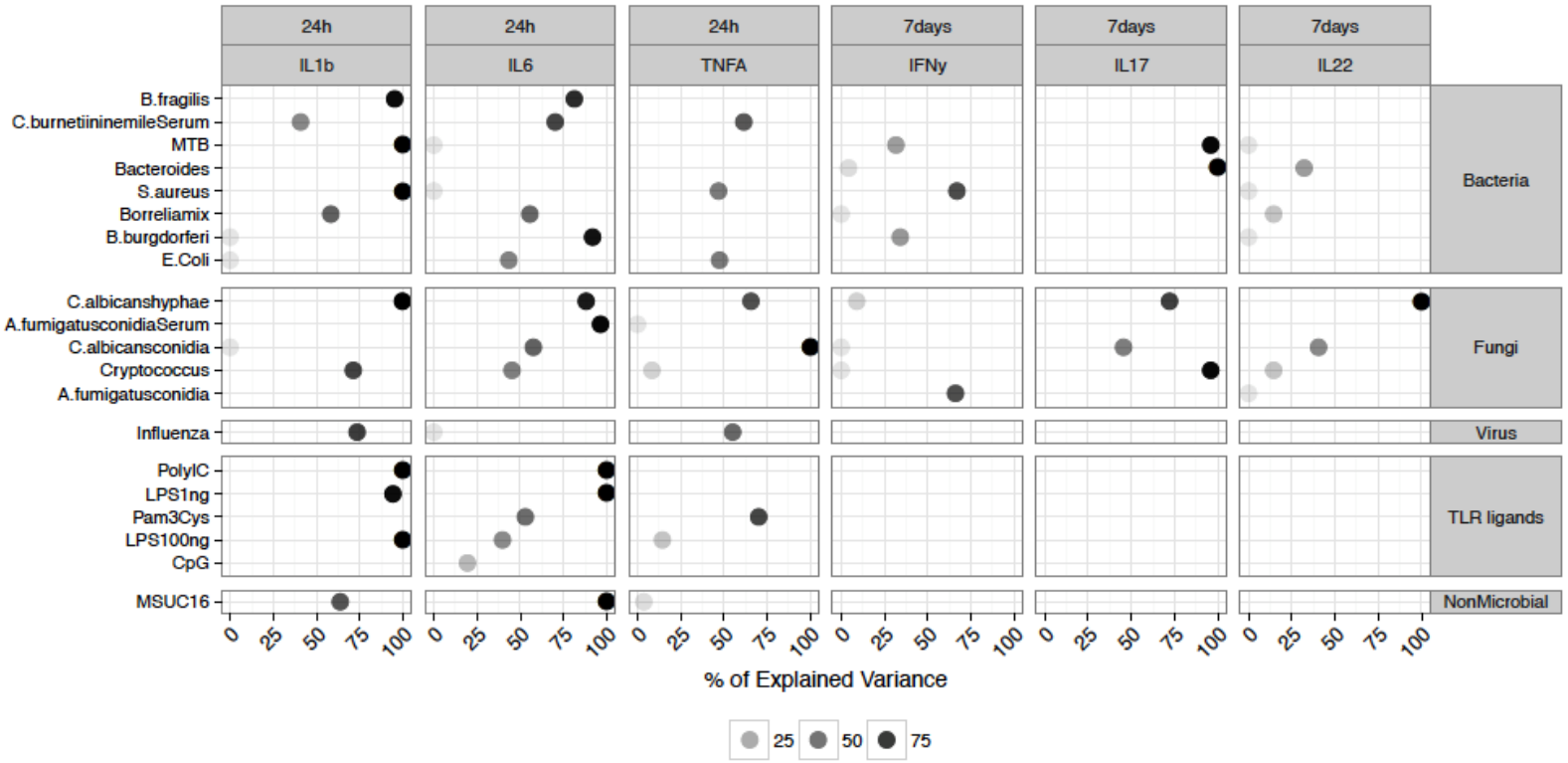


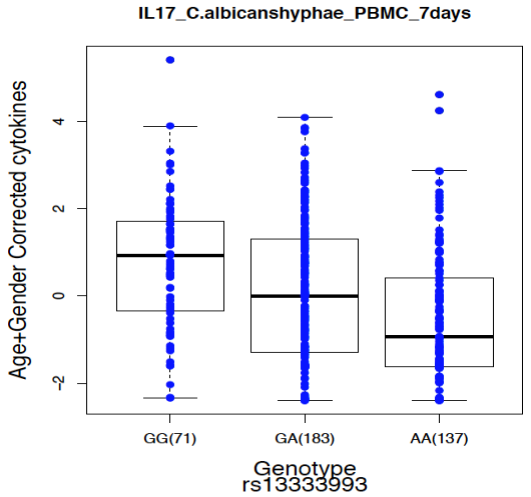
Blue = bacterial
Pink = fungal
Green = other

Major cQTL on chromosome 4

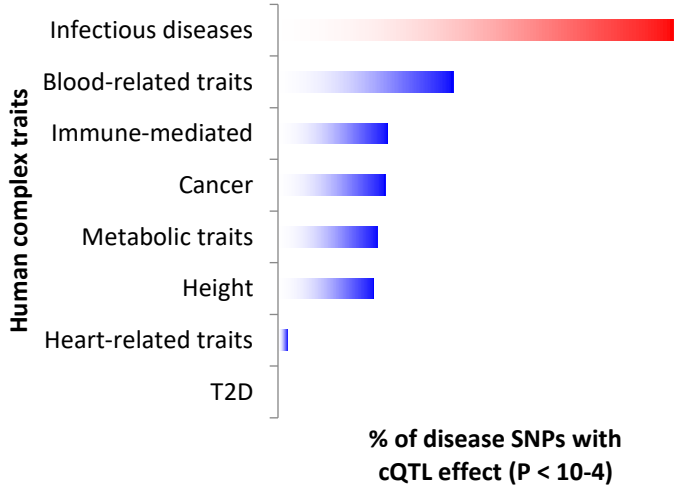
Li Y et al., ***Cell*** (2016)

Genetic variation explains part of the cytokine variability (corrected for age, gender and cell counts)



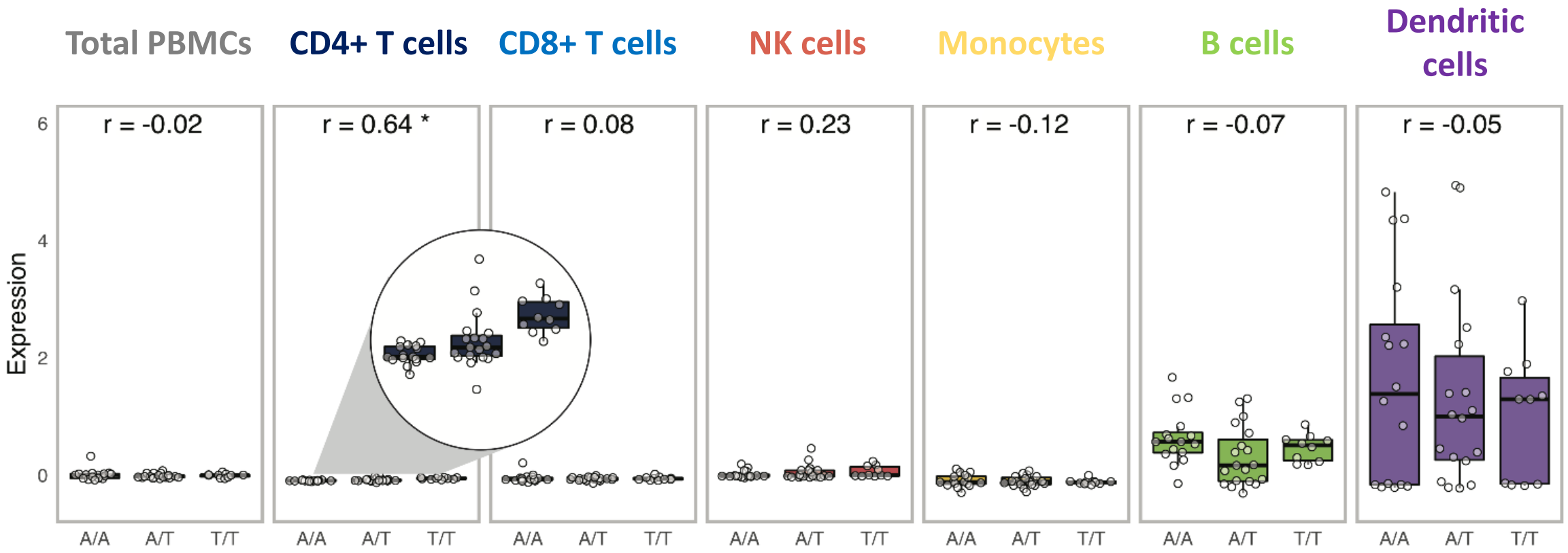


Cytokine QTLs overlap with SNPs associated with human diseases



Li Y et al, ***Cell*** (2016)

Identifying cell-type and context-dependent QTLs may help in explaining susceptibility

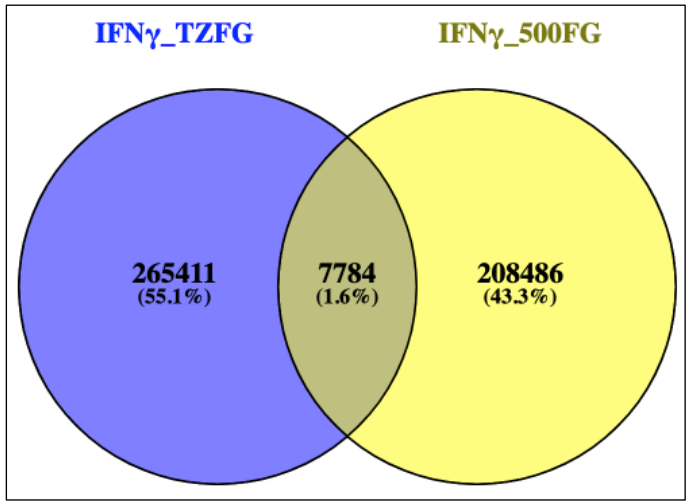


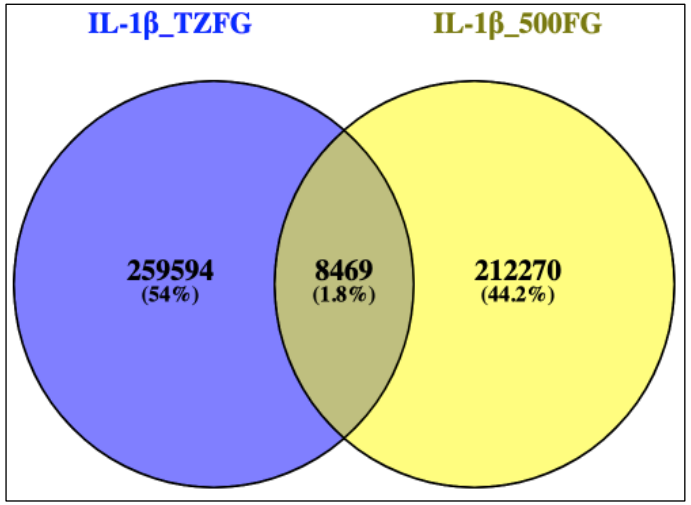
TSPAN13 & rs2272245

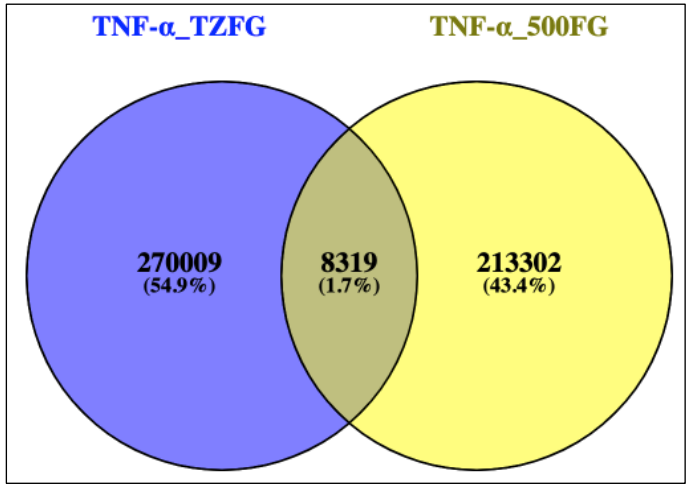
Van der Wijst *et al*, *Nature Genetics* 2018

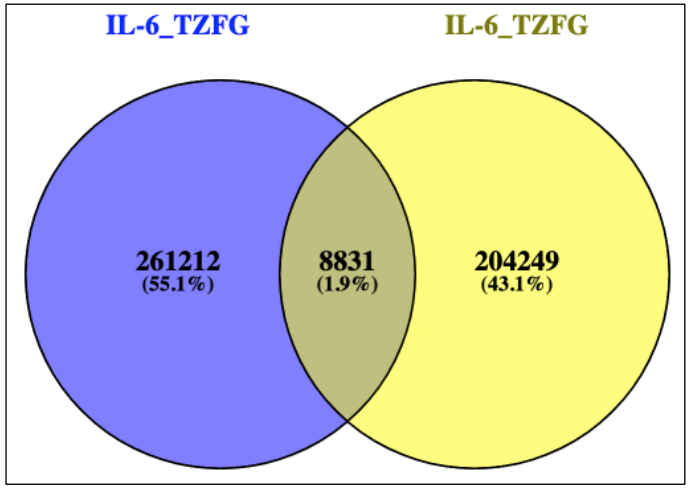
Limited overlap between cytokine QTLs identified in Tanzanian (TZFG) and European dataset (500FG)

Stimulations	Cytokines				
	IFN-γ	TNF-α	IL-10	IL-1β	IL-6
LPS	●	●		●	●
Poly:IC			X		
C.albicans	●	●	X	●	●
E.coli					
S.pneumoniae					
S.aureus	●	●	X	●	●
C.burnetii					
S.typhi					
S.enteritidis					
M.tuberculosis					

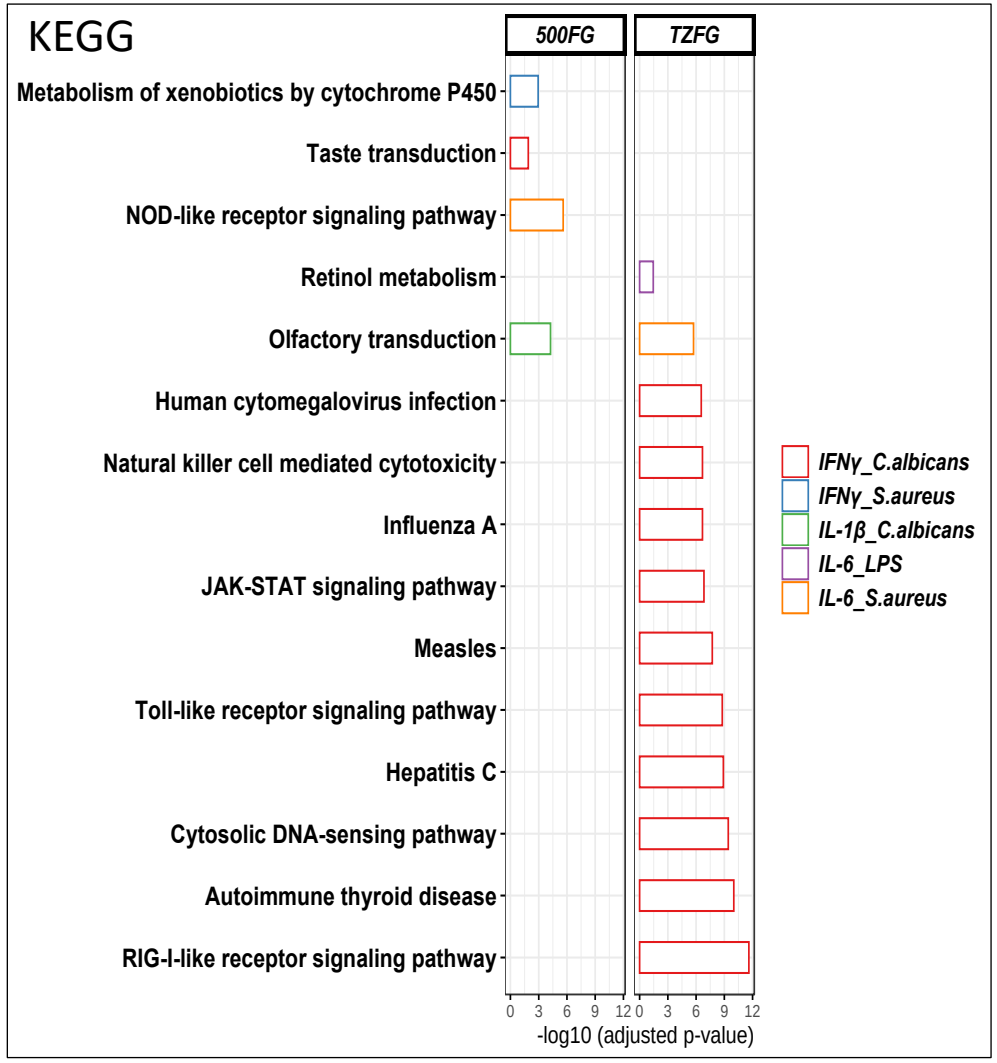


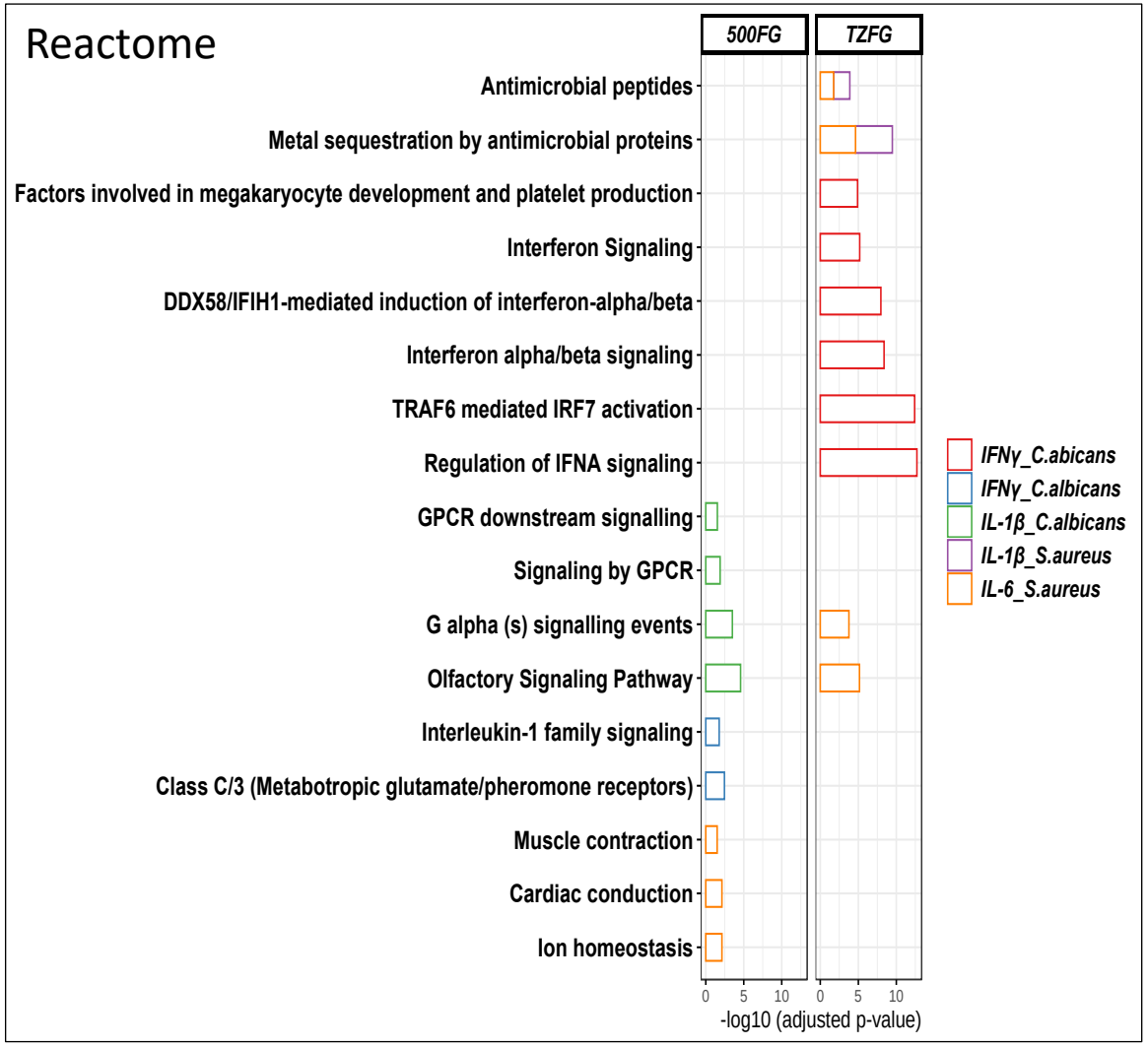




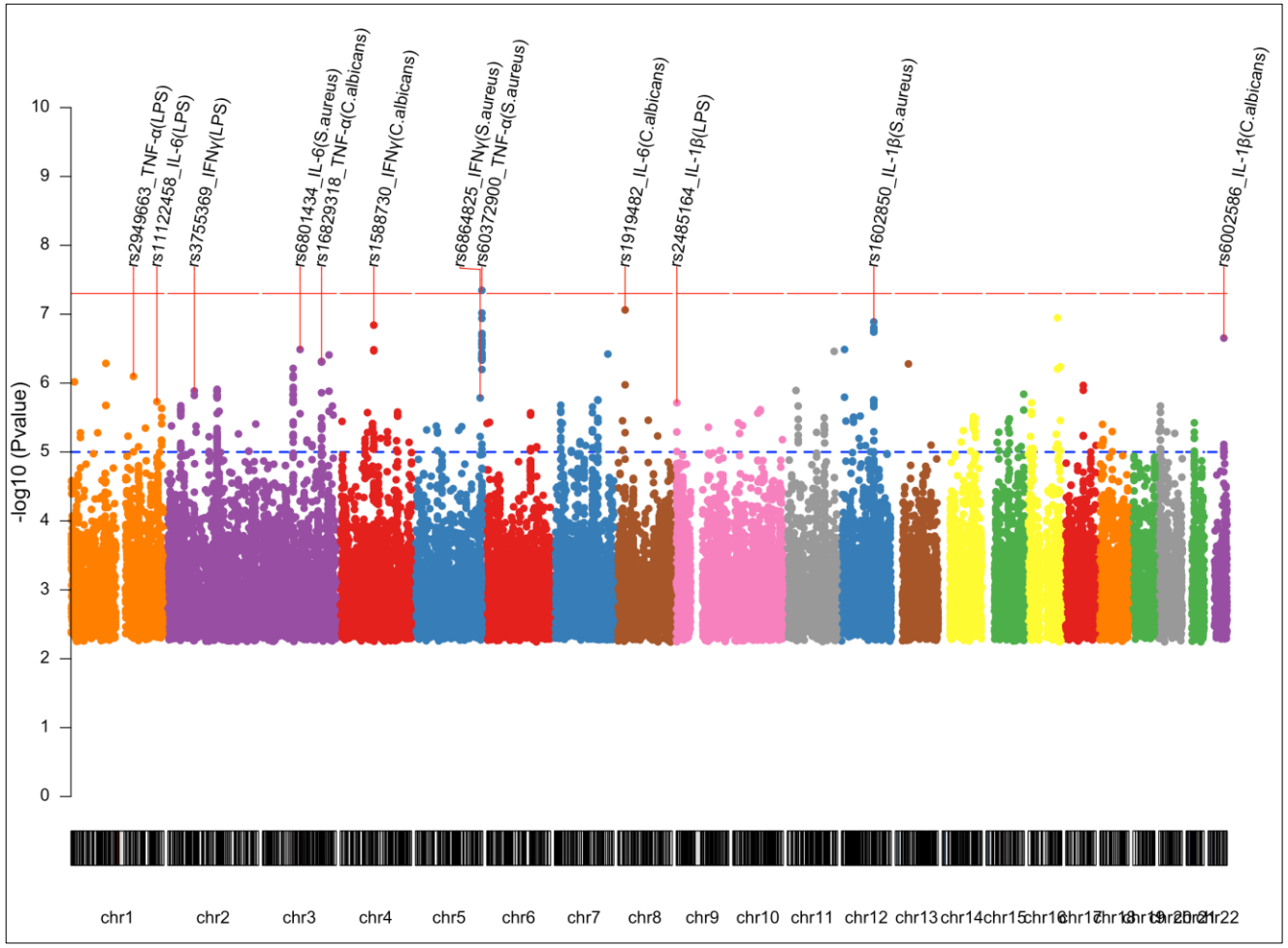


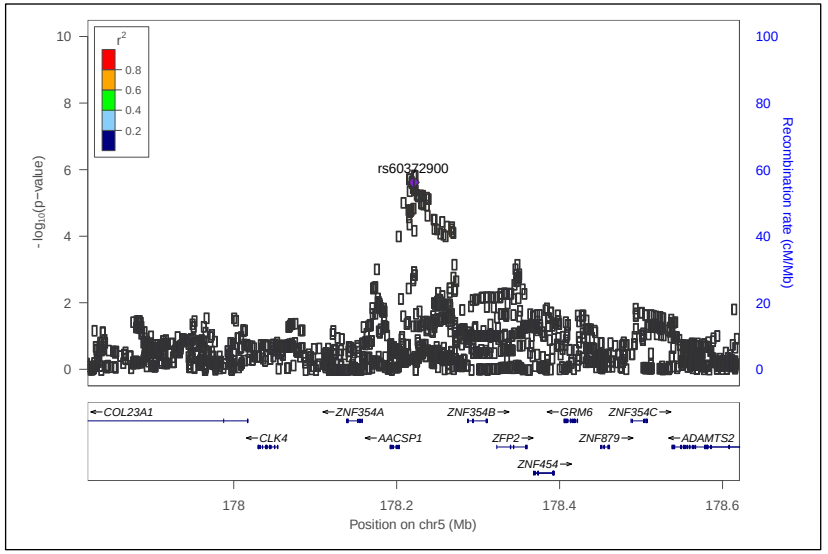
Distinct enriched pathways for Tanzania (TZFG) and European (500FG) cytokine QTLs

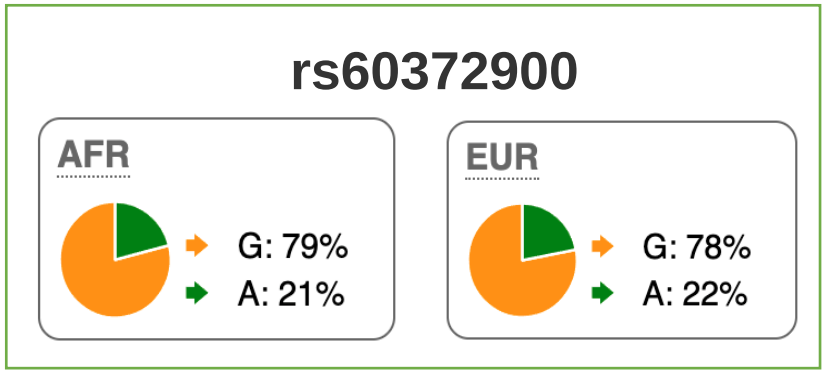


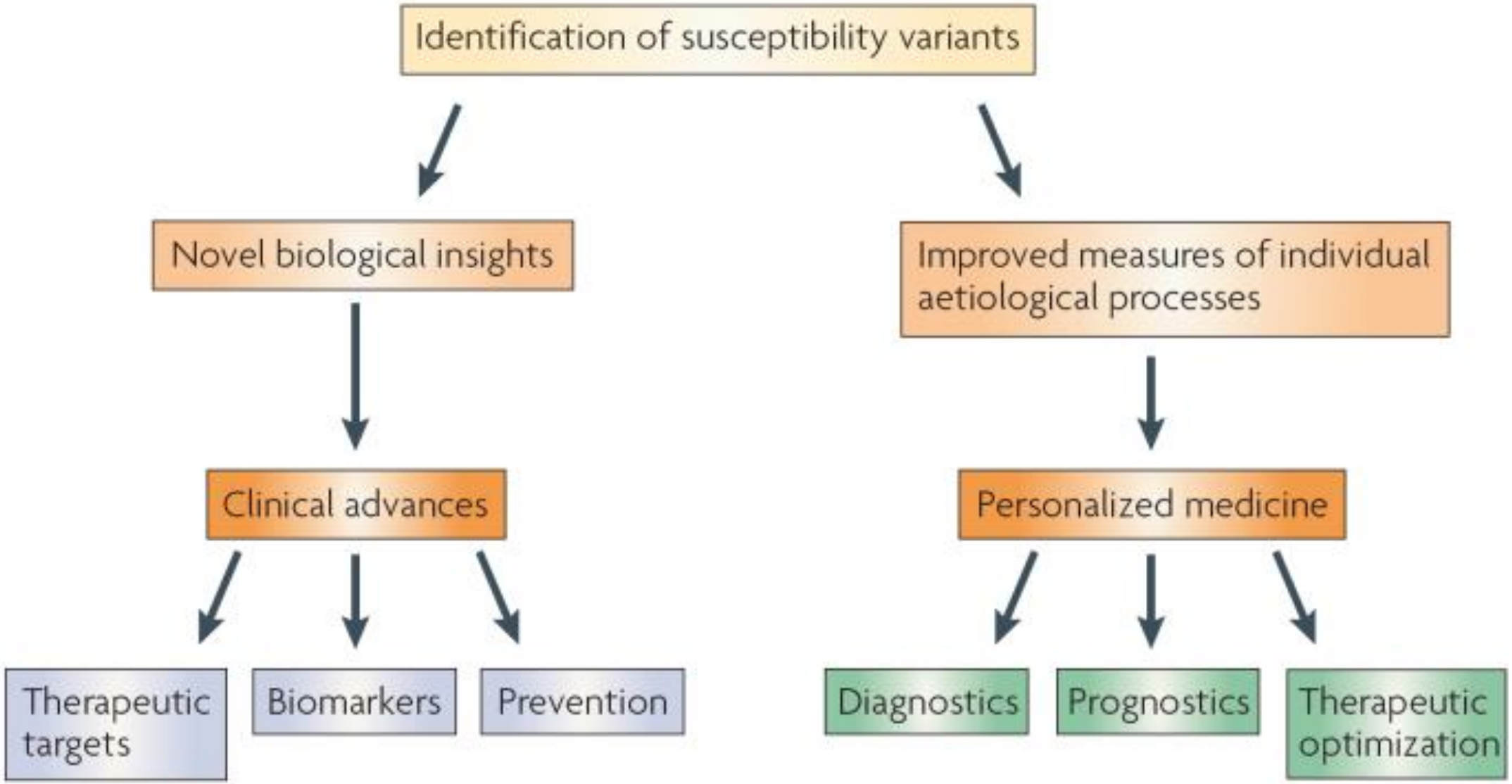


Meta-analysis of cytokine QTLs identified in Tanzanian and European dataset

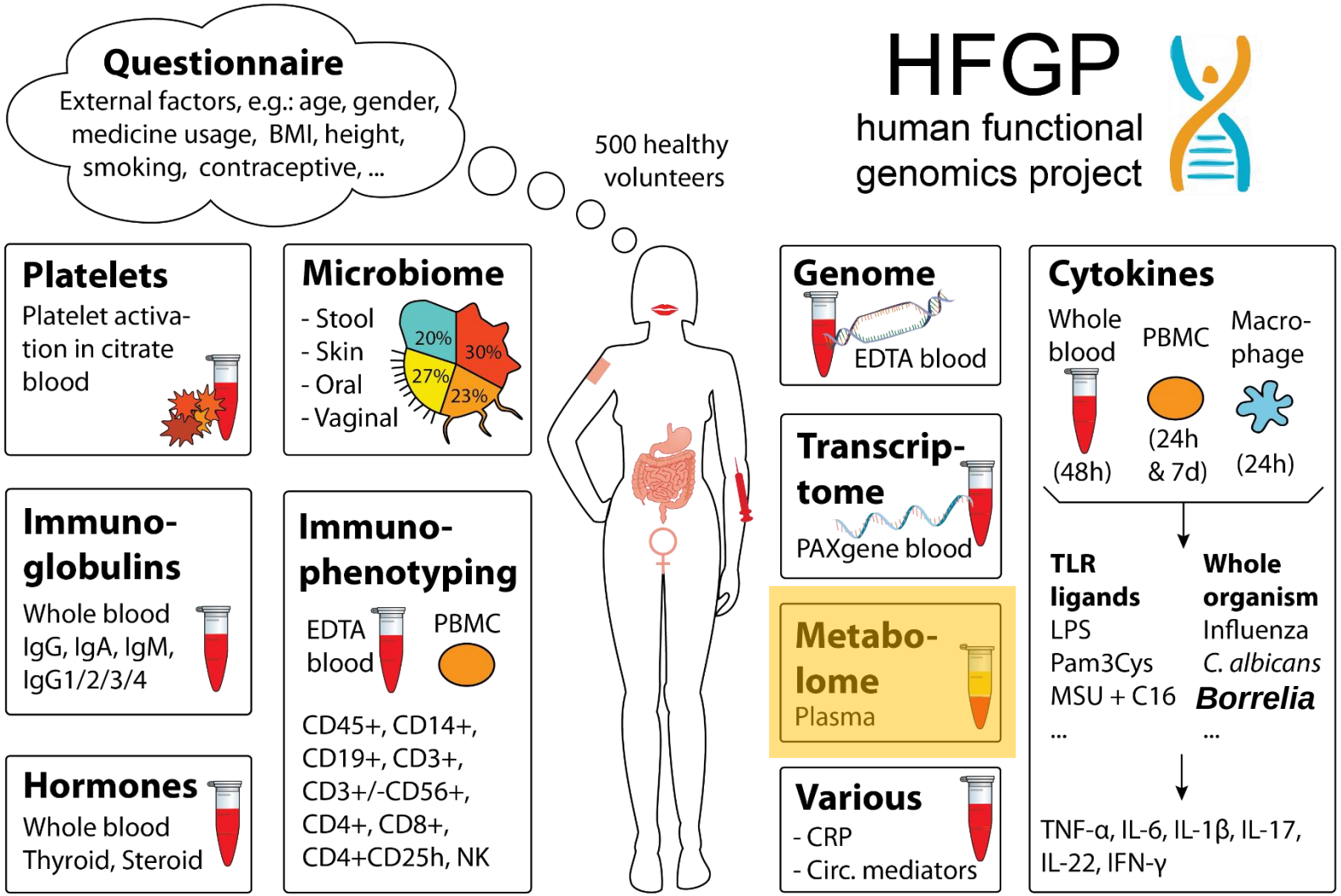








McCarthy, M. et al.. Nature Reviews Genetics 9, 366 (2008)



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Schirmer M, , Smeekens S, et al, Cell. 2016 Nov 3;167(4):1125-1136

RESEARCH Open Access

Characterization of sepsis inflammatory endotypes using circulatory proteins in patients with severe infection: a prospective cohort study

Isis Ricaño-Ponce[1*†], Anca-Lelia Riza[1,2,3†], Aline H. de Nooijer[1†], Andrei Pirvu[2,3], Stefania Dorobantu[2,3], Adina Dragos[2,3], Ioana Streata[2,3], Mihaela Roskanovic[4,5], Inge Grondman[1], Florentina Dumitrescu[4,5], Vinod Kumar[1,6], Mihai G. Netea[1,7] and Mihai Ioana[2,3]

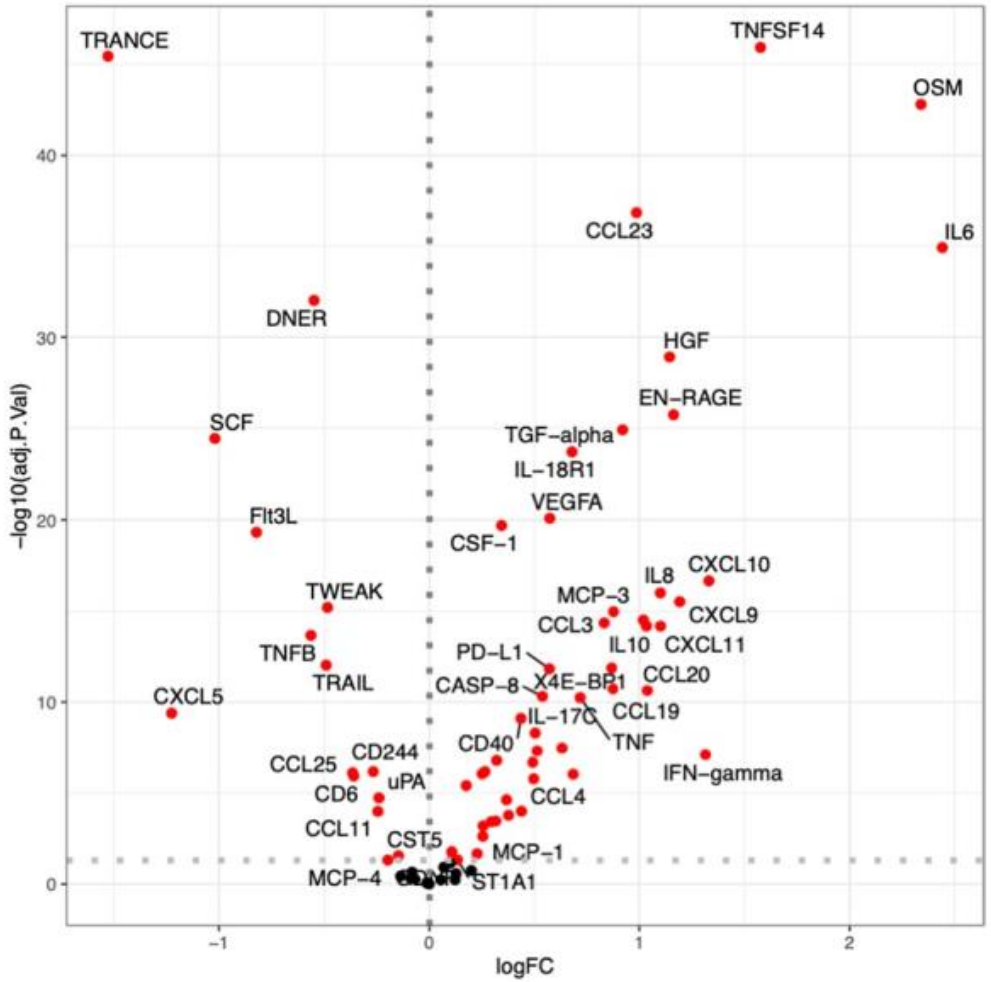


Fig. 1 Comparison of circulatory inflammation proteins in patients with severe infection. Volcano plot with the comparison of 75 circulating proteins between patients and controls. Significant changes are depicted in red. Benjamini–Hochberg method was used to correct for multiple testing. Significance was defined as adjusted p values < 0.05. Age, sex and BMI were used as covariates in the analysis. *logFC* logarithm of the fold change

Characterization of sepsis inflammatory endotypes using circulatory proteins in patients with severe infection: a prospective cohort study

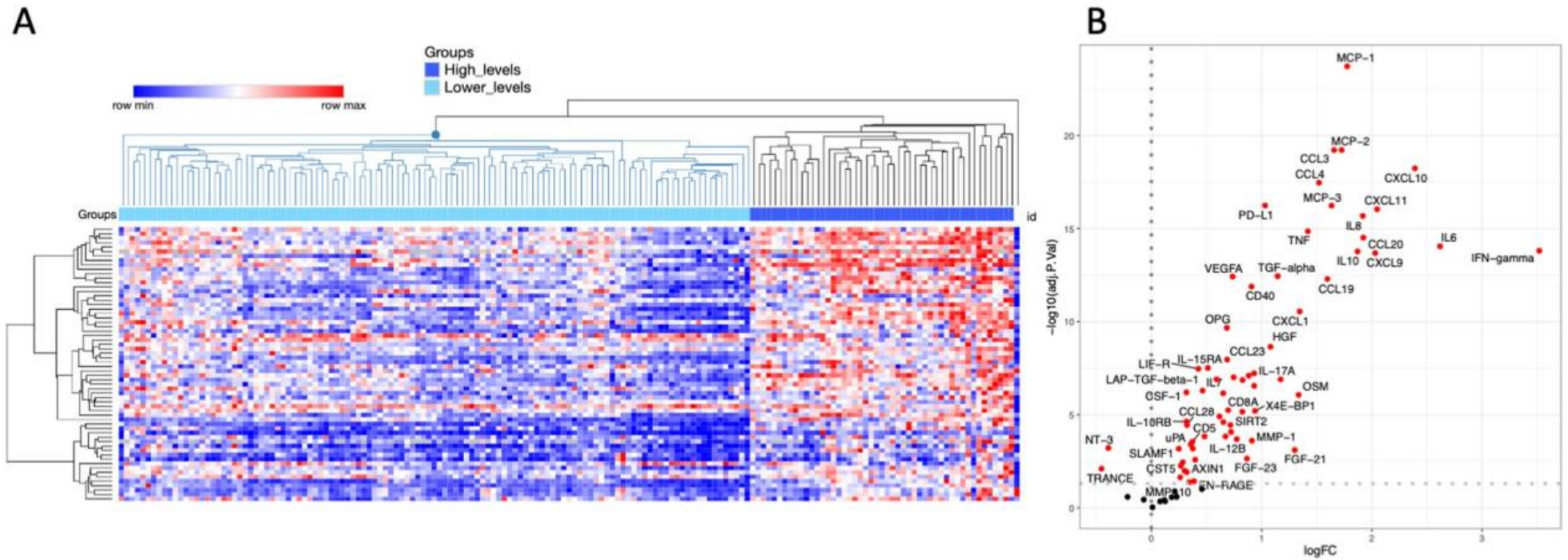
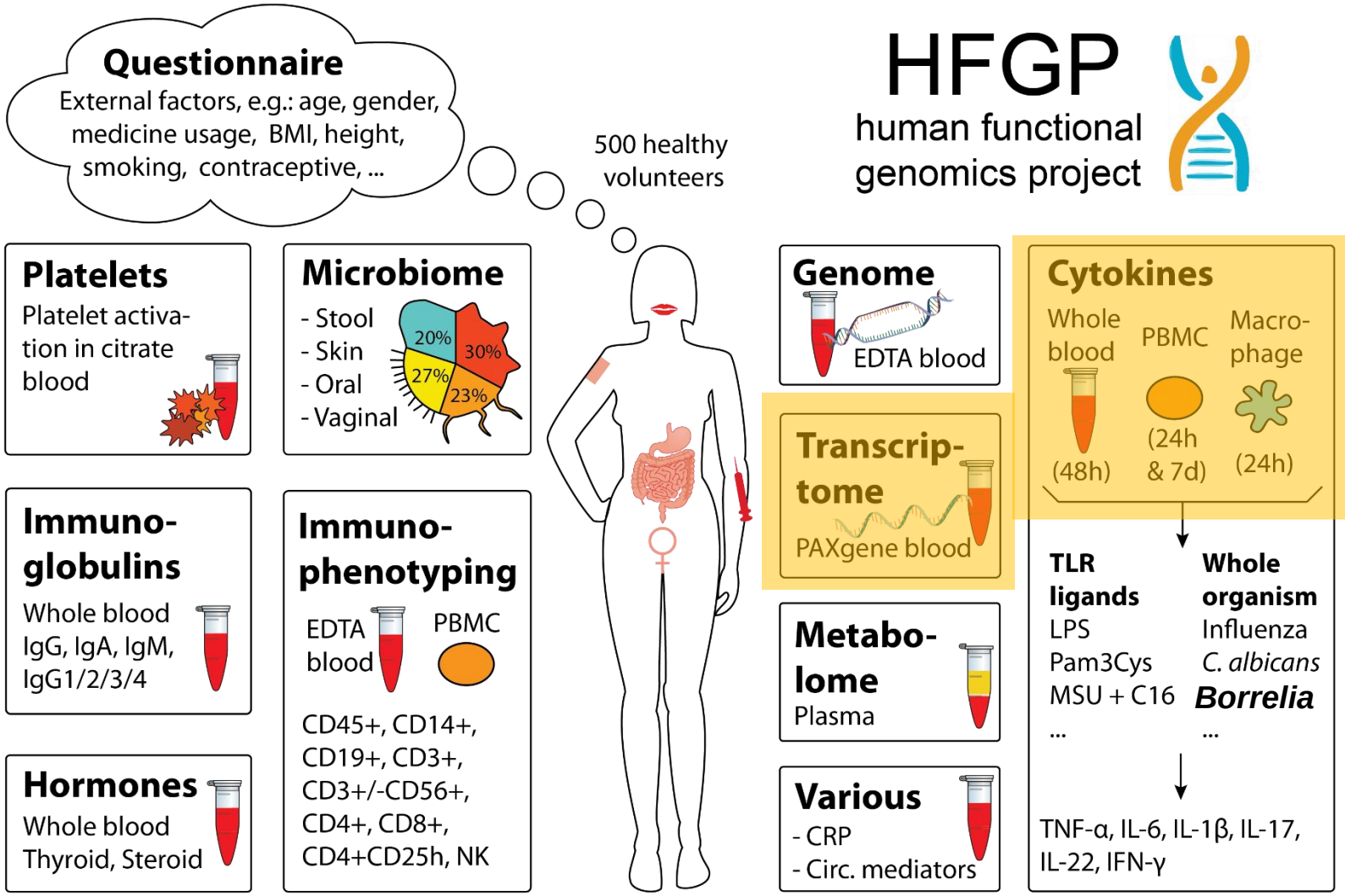


Fig. 2 Characterization of inflammatory endotypes. **A** Hierarchical clustering of patients based on 62 proteins. **B** volcano plot of 75 circulating proteins comparing both endotypes. The 65 significantly differentially expressed proteins are highlighted in red (adjusted p values < 0.5). Age, sex and BMI were included as covariates in the analysis



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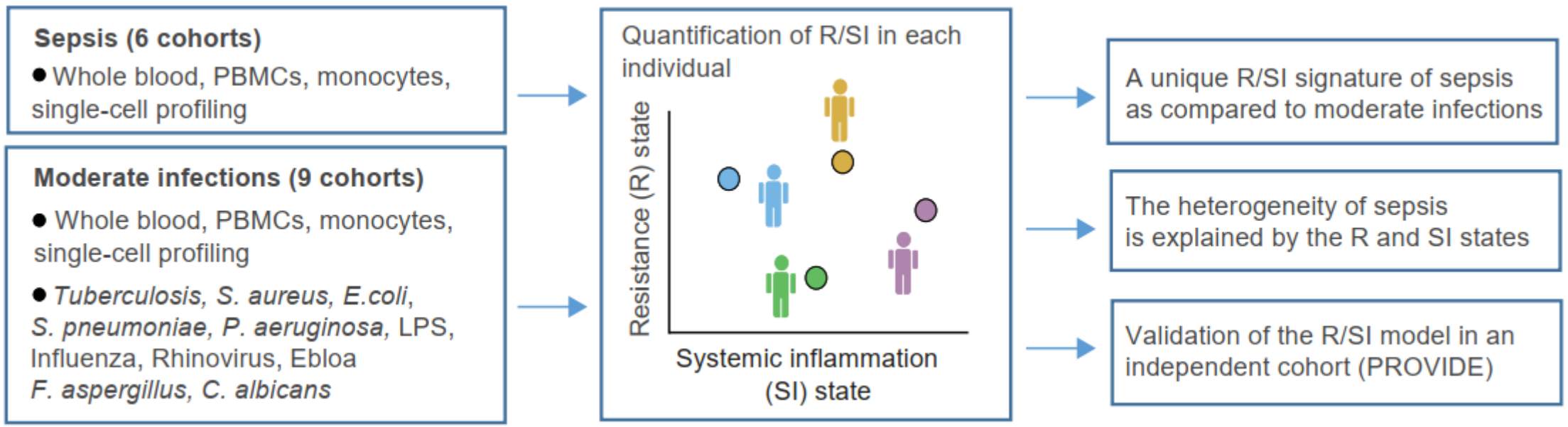
Sepsis pathogenesis and outcome is shaped by the balance between systemic inflammation and the antimicrobial response

A unified framework of sepsis-associated immune dysfunctions

Authors and affiliations
Rachel Brandes-Leibovitz[1,*], Anca Riza[2,3*], Gal Yankovitz[1], Andrei Pirvu[2,3], Stefania Dorobantu[2,3], Adina Dragos[2,3], Ioana Streata[2,3], Mihaela Roskanovic[4,5], Isis Ricano-Ponce[7], Aline de Nooijer[7], Florentina Dumitrescu[4,5], Nikolaos Antonakos[6], Eleni Antoniadou[7], George Dimopoulos[8], Ioannis Koutsodimitropoulos[9], Theano Kontopoulou[10], Dimitra Markopoulou[11], Eleni Aimoniotou[12], Apostolos Komnos[13], George N. Dalekos[14], Mihai Ioana[2,3], Evangelos J. Giamarellos-Bourboulis[6,15], Irit Gat-Viks[1, ¶,#], Mihai G. Netea[2,16,17, ¶,#]



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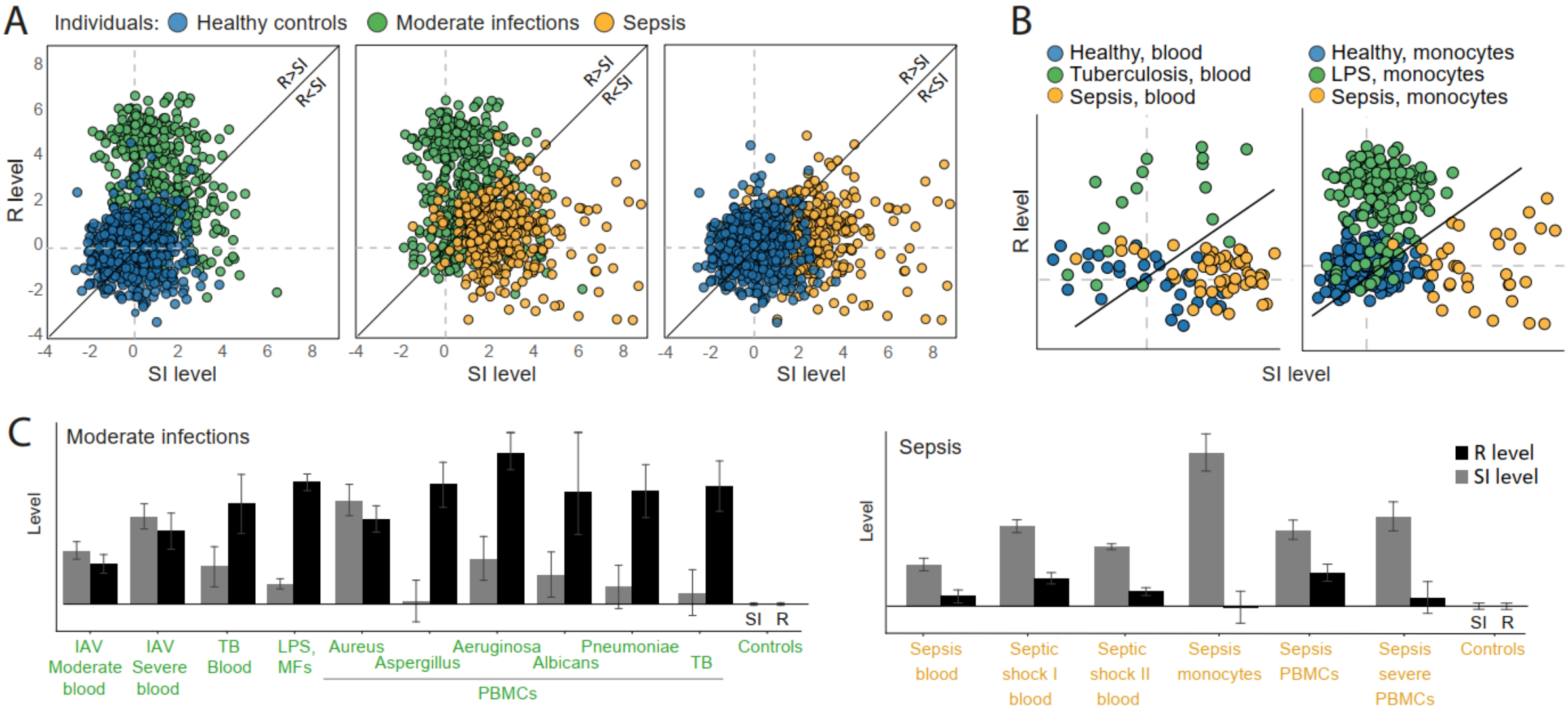

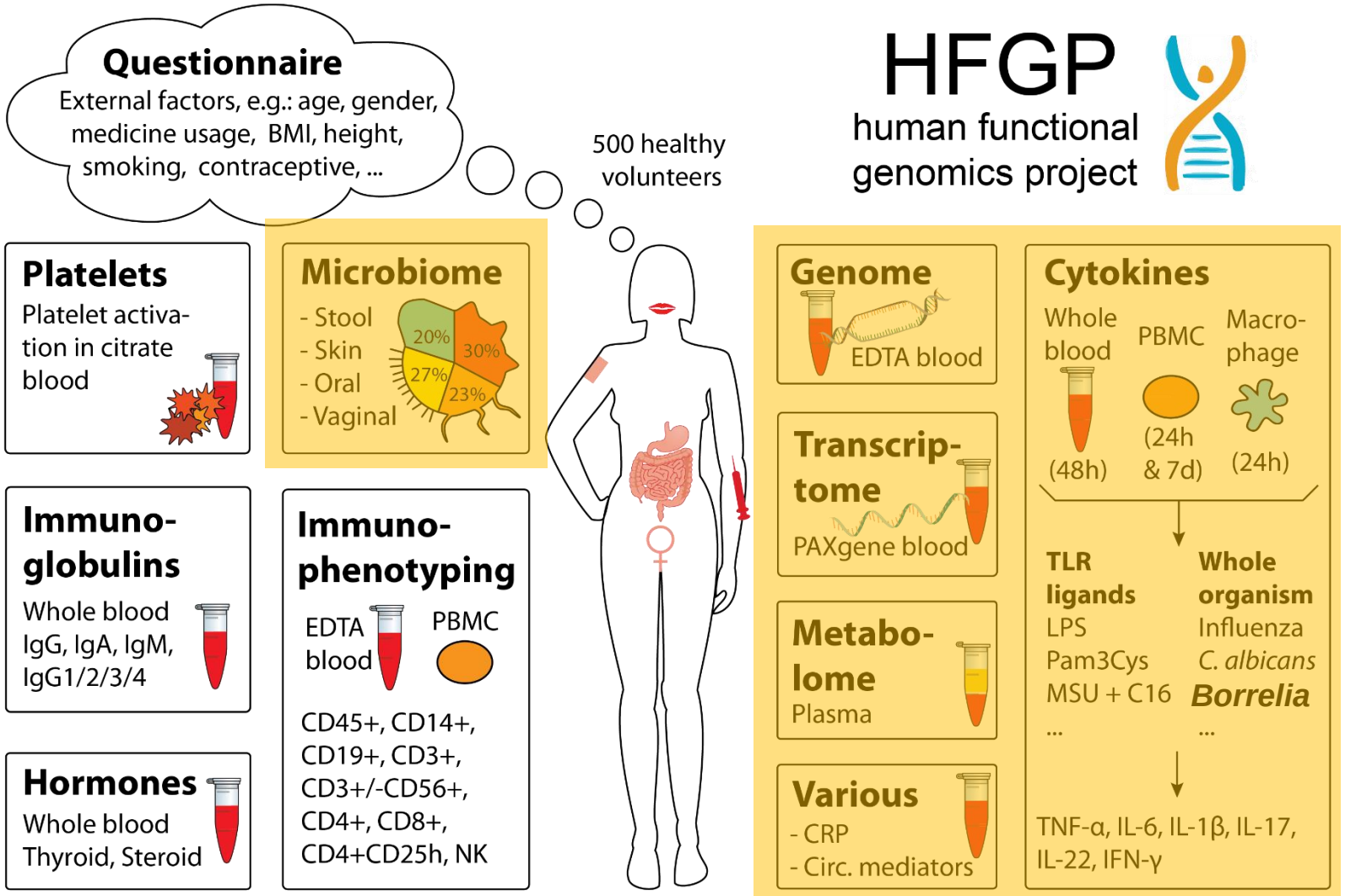

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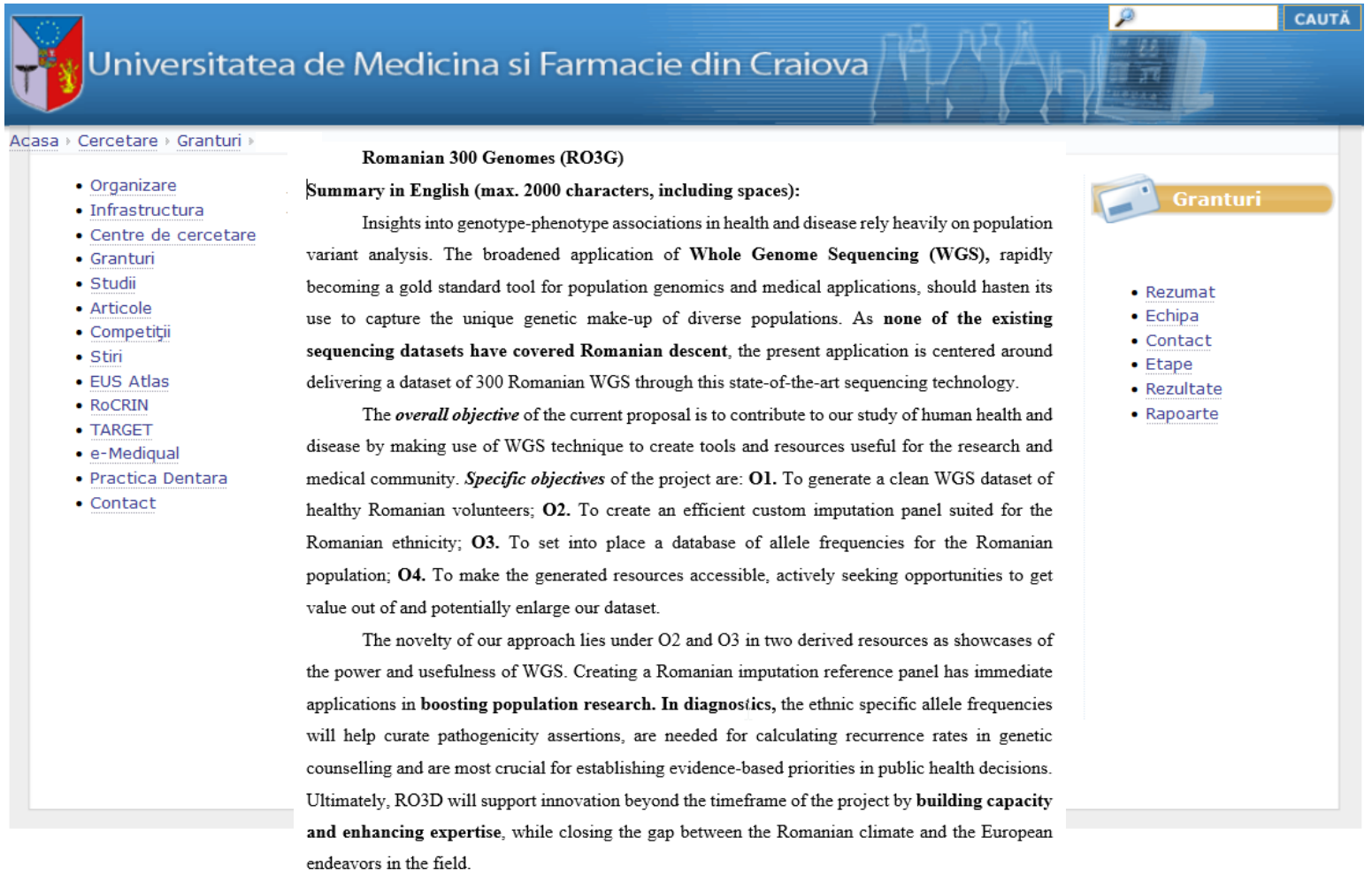
Romania's National Recovery and Resilience Plan

Pillar III. Smart, sustainable and inclusive growth, including economic cohesion, jobs, productivity, competitiveness, research, development, and innovation, and a well-functioning internal market with strong small and medium-sized enterprises (SMEs)

Component C9. SUPPORT FOR THE PRIVATE SECTOR, RESEARCH, DEVELOPMENT AND INNOVATION

"I8. Development of a program to attract highly specialised human resources from abroad in research, development and innovation activities"



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Romanian 300 Genomes (RO3G)

Summary in English (max. 2000 characters, including spaces):

Insights into genotype-phenotype associations in health and disease rely heavily on population variant analysis. The broadened application of **Whole Genome Sequencing (WGS),** rapidly becoming a gold standard tool for population genomics and medical applications, should hasten its use to capture the unique genetic make-up of diverse populations. As **none of the existing sequencing datasets have covered Romanian descent**, the present application is centered around delivering a dataset of 300 Romanian WGS through this state-of-the-art sequencing technology.

The ***overall objective*** of the current proposal is to contribute to our study of human health and disease by making use of WGS technique to create tools and resources useful for the research and medical community. ***Specific objectives*** of the project are: **O1.** To generate a clean WGS dataset of healthy Romanian volunteers; **O2.** To create an efficient custom imputation panel suited for the Romanian ethnicity; **O3.** To set into place a database of allele frequencies for the Romanian population; **O4.** To make the generated resources accessible, actively seeking opportunities to get value out of and potentially enlarge our dataset.

The novelty of our approach lies under O2 and O3 in two derived resources as showcases of the power and usefulness of WGS. Creating a Romanian imputation reference panel has immediate applications in **boosting population research. In diagnostics,** the ethnic specific allele frequencies will help curate pathogenicity assertions, are needed for calculating recurrence rates in genetic counselling and are most crucial for establishing evidence-based priorities in public health decisions. Ultimately, RO3D will support innovation beyond the timeframe of the project by **building capacity and enhancing expertise**, while closing the gap between the Romanian climate and the European endeavors in the field.

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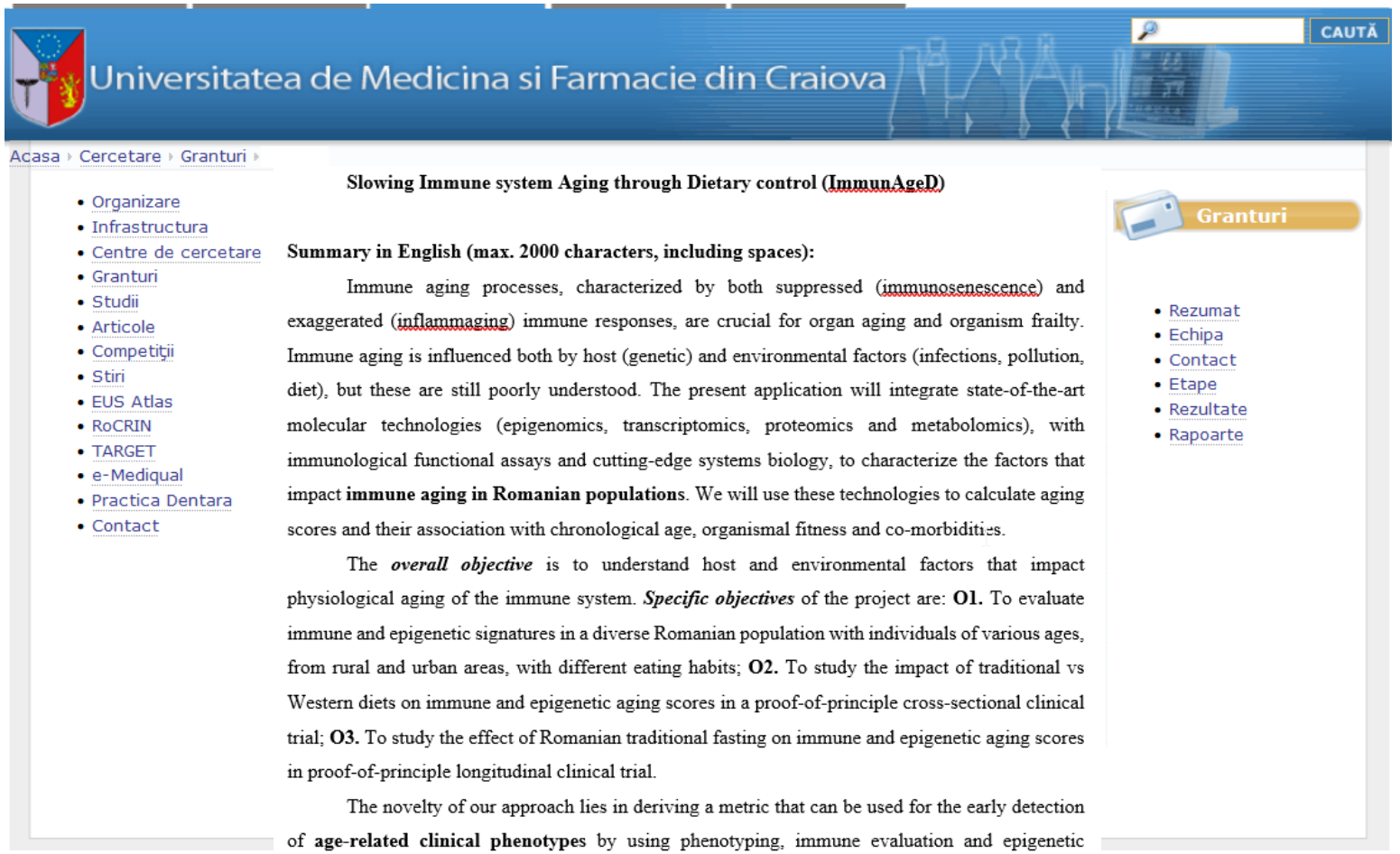

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Slowing Immune system Aging through Dietary control (ImmunAgeD)

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- Rezultate
- Rapoarte

Summary in English (max. 2000 characters, including spaces):

Immune aging processes, characterized by both suppressed (immunosenescence) and exaggerated (inflammaging) immune responses, are crucial for organ aging and organism frailty. Immune aging is influenced both by host (genetic) and environmental factors (infections, pollution, diet), but these are still poorly understood. The present application will integrate state-of-the-art molecular technologies (epigenomics, transcriptomics, proteomics and metabolomics), with immunological functional assays and cutting-edge systems biology, to characterize the factors that impact **immune aging in Romanian populations**. We will use these technologies to calculate aging scores and their association with chronological age, organismal fitness and co-morbidities.

The ***overall objective*** is to understand host and environmental factors that impact physiological aging of the immune system. ***Specific objectives*** of the project are: **O1.** To evaluate immune and epigenetic signatures in a diverse Romanian population with individuals of various ages, from rural and urban areas, with different eating habits; **O2.** To study the impact of traditional vs Western diets on immune and epigenetic aging scores in a proof-of-principle cross-sectional clinical trial; **O3.** To study the effect of Romanian traditional fasting on immune and epigenetic aging scores in proof-of-principle longitudinal clinical trial.

The novelty of our approach lies in deriving a metric that can be used for the early detection of **age-related clinical phenotypes** by using phenotyping, immune evaluation and epigenetic methylation clock, as well as the potential for **intervention** through understanding the role of dietary interventions. This study will also allow to assess the role of important societal changes as the Romanian population transitions from a traditional to a Western-type diet and lifestyle.

Radboud UMC

Reinout van Crevel; Mihai Netea

Vinod Kumar

…

Indonesia – UNPAD

Bachti Alisjahbana

Rovina Ruslami

….

Partner Universities

Craiova University of Medicine and Pharmacy

Mihai Ioana

Ioana Streata

Florentina Dumitrescu

Andrei Pirvu

Stefania Dorobantu

Adina Dragos

…

anca.crgm@gmail.com

TANDEM

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GENOMICĂ FUNCȚIONALĂ ÎN INFECȚII SEVERE

HFGP

human functional genomics project

anca.crgm@gmail.com