AIEOP
ASSOCIAZIONE ITALIANA EMATOLOGIA ONCOLOGIA PEDIATRICA

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13-14 aprile 2026

Insuffcienze Midollari

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IRCCS Istituto Giannina Gaslini-Genova

Disclosures of Name Surname

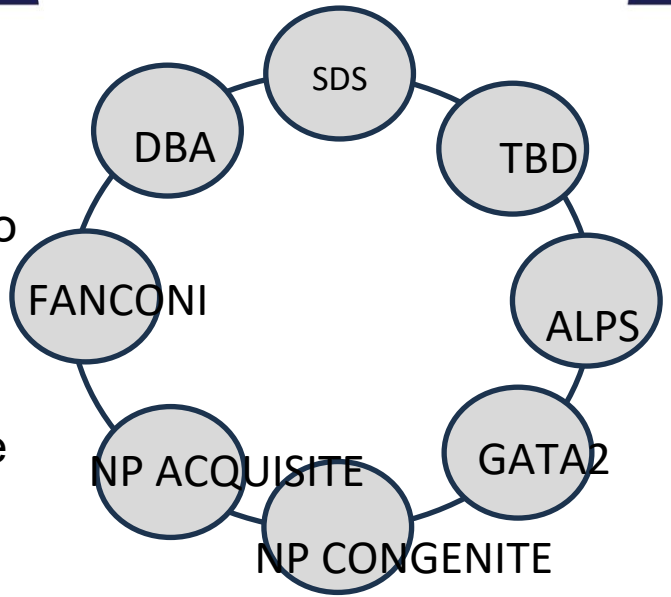
Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
No disclosures							


OBIETTIVI
LAVORI SCIENTIFICI
RESOCONTO
Studi in conclusione
Studi in itinere
NUOVE PROPOSTE
SUPPORTO
monitoraggi
Longitudinali
IMPLEMENTAZIONE
COLLABORAZIONI
Trasversali

OBIETTIVI

Alto il profilo assistenziale/scientifico
Inclusivita'

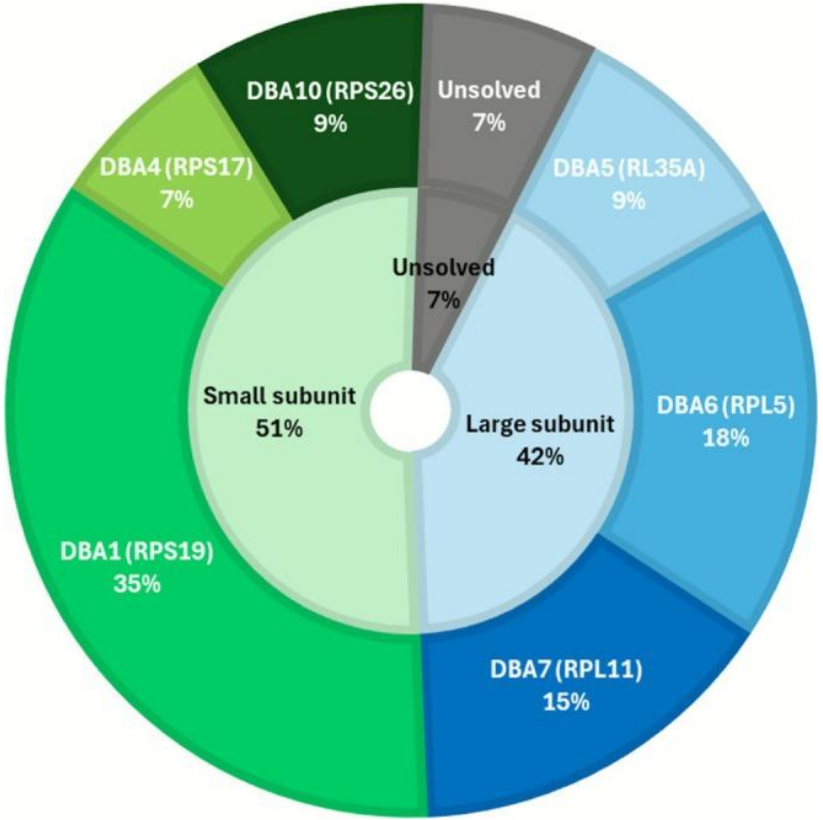
Mantenimento « in salute» dei registri e degli Studi retrospettivi/prospettici



- Piattaforma Redcap
- Comitati etici
- Aggiornamento dati di follow-up

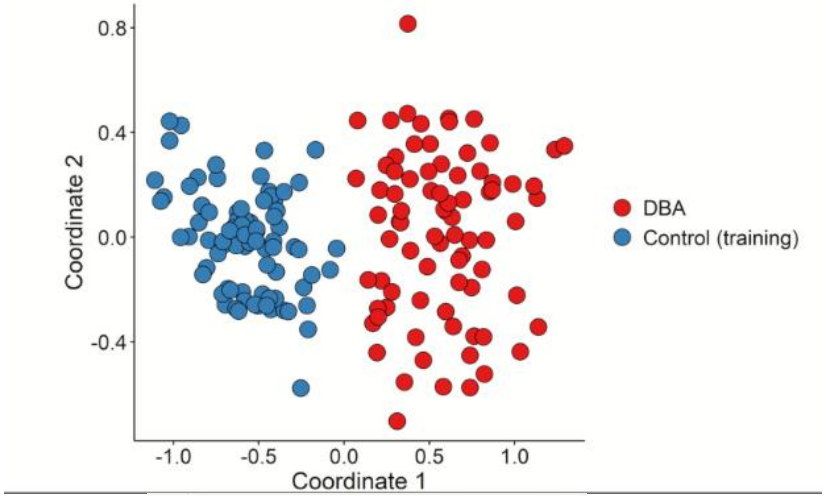
Profilo di metilazione in DBA

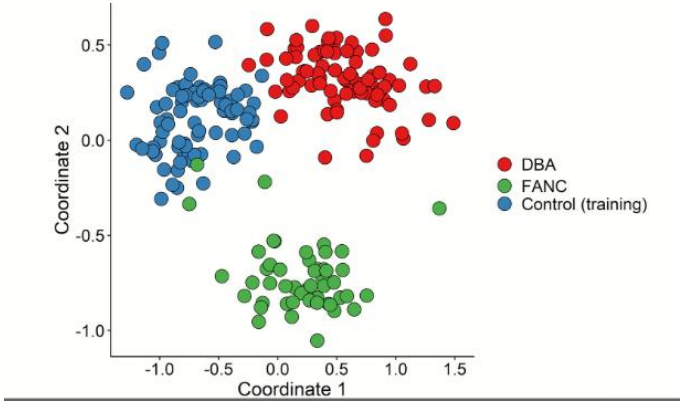
Corte di 80 pazienti
6 orfani di gene

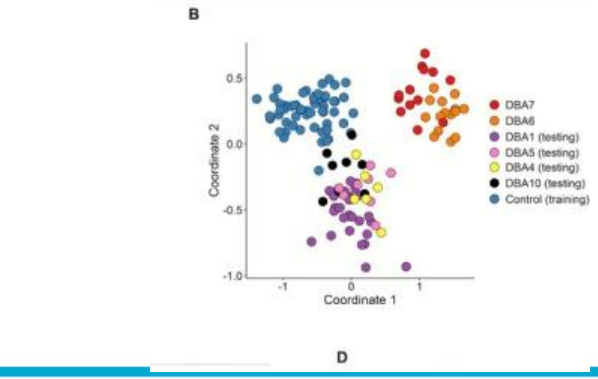


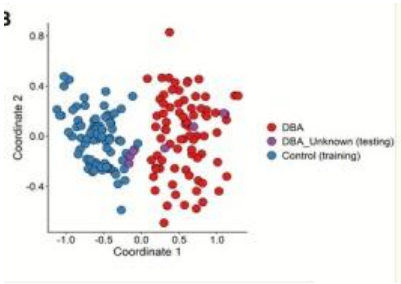
Quarello P AJH 2026

DBA Profilo di metilazione: differenze ed analogie



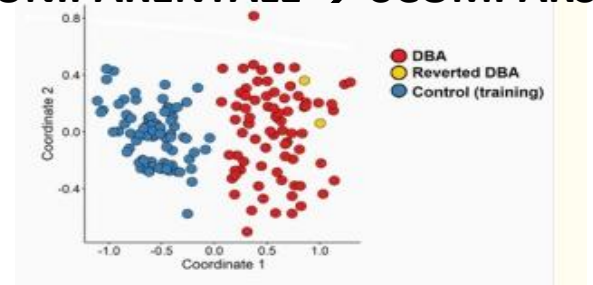






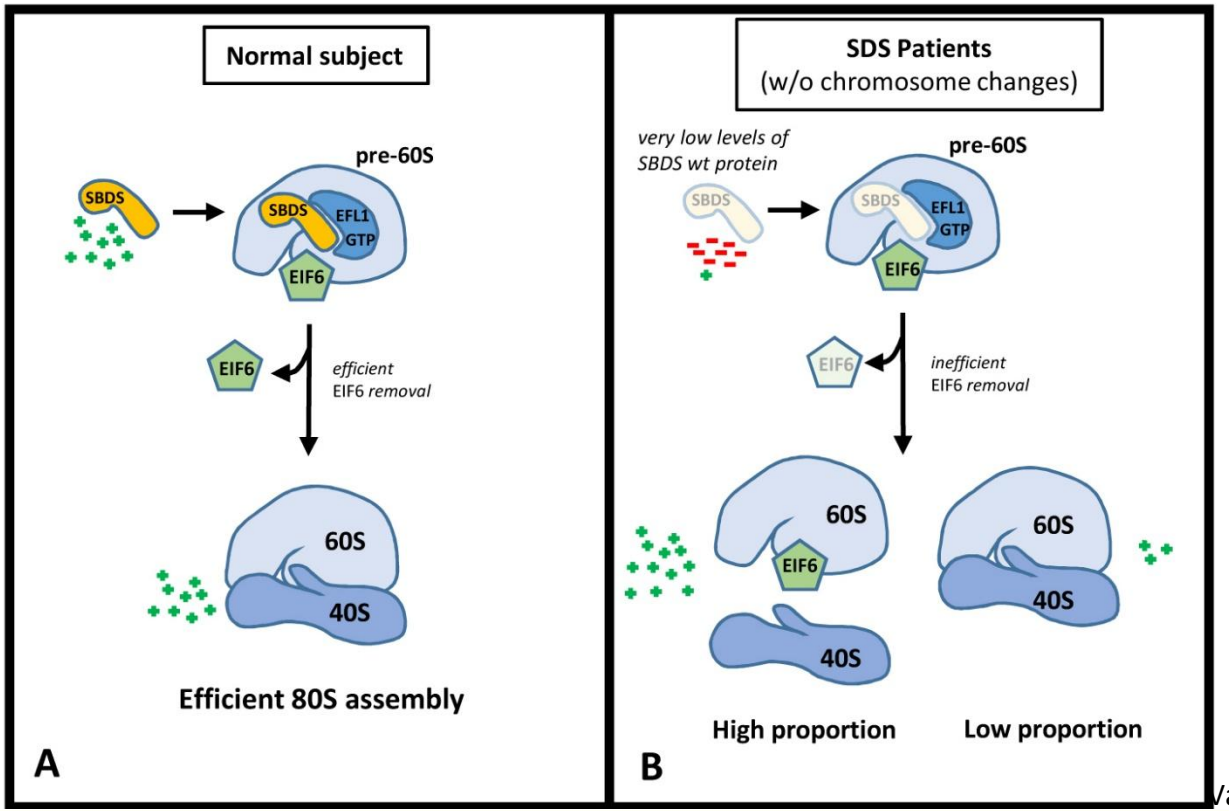
Profilo di metilazione dei soggetti revertiti

DISOMIA UNIPARENTALE → SCOMPARSA della MUTAZIONE



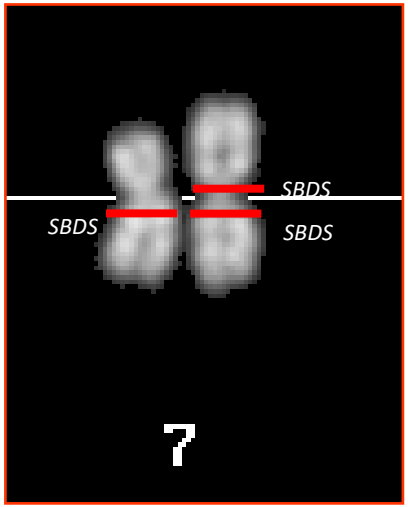
Analisi di metilazione: ruolo nella diagnosi e studio VUS Allargare la corte ed includere anche studio dei familiari .. Estensione ad SDS

Citogenetica in SDS

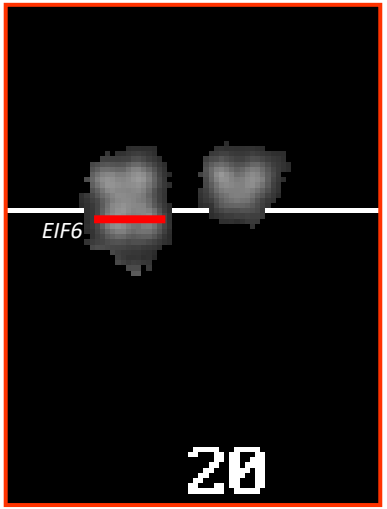


Valli R, submitted EJG

Anomalie cromosomiche (acquisite) più frequenti nel midollo osseo (aggiornamento marzo 2026)



15/107 pazienti (~14%)



24/107 pazienti (~22,5%)

+ 4/107 pazienti entrambe le anomalie! (~4%)
Ci sono poi 3/107 pazienti con LOH di EIF6

Total patients in Italian SDS registry			156
followed up routinely by cytogenetic analysis			**107**
normal karyotype			51
	with single cell chromosome alterations	9	
i(7)(q10)			15
	with other clonal chromosome alterations	2	
	with single cell chromosome alterations	2	
	with CH-LOH in 20q11.22	2	
del(20)(q)			24
	with other clonal chromosome alterations	1	
	with single cell chromosome alterations	2	
i(7)(q10) + del(20)(q)			4
	with CH-LOH in 20q11.22	1	
other clonal chromosome anomalies *			9
chromosome alteration in single cell *			4
Transplanted after MDS/AML/Aplasia evolution			17
With i(7)(q10)			6
	Successful	2	
	Unsuccessful	4	
With del(20)(q)			4
	Successful	4	
	Unsuccessful	0	
With i(7)(q10) + del(20)(q)			1
	Unsuccessful	1	
With only other clonal chromosome anomalies			6
	Successful	5	
	Unsuccessful	1	
Complex karyotype at diagnosis (no HSCT)			1
With only other clonal chromosome anomalies			1

* As the sole anomaly found

Cytogenetics of Shwachman Diamond syndrome: 27 years report of the Italian cohort and review of the literature

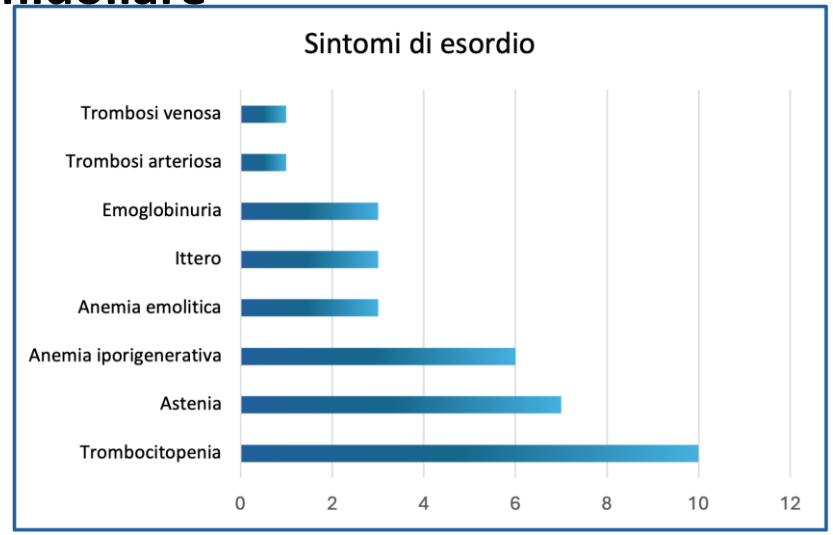
Submission to European Journal of Medical Genetics feb. 2026

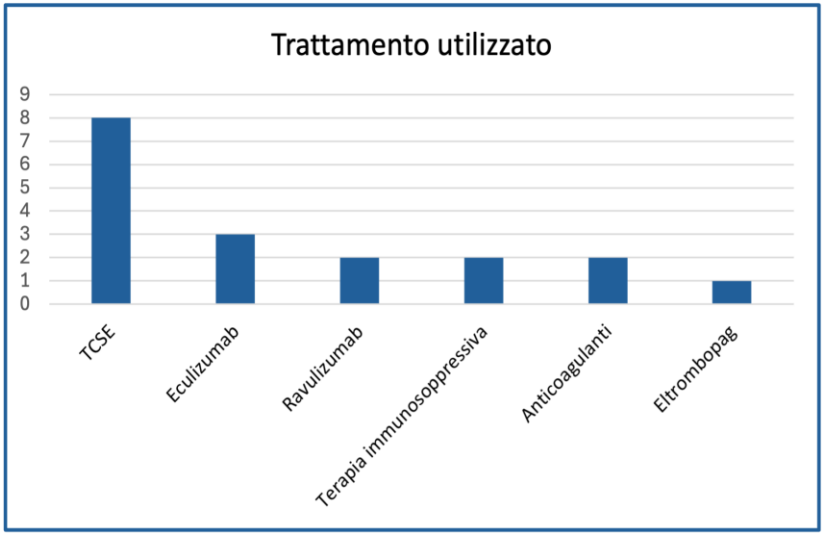
Survey su diagnosi e trattamento PNH nei centri AIEOP

Incidenza annua: 1-5/10^6
Prevalenza: 10-20/10^6
Età di insorgenza: giovani adulti

QUESTIONARIO

16 centri 11 pazienti con PNH. 3 PNH classica/ 8 PNH associata ad aplasia midollare





Patologia rara

Scarsa esperienza con nuovi farmaci

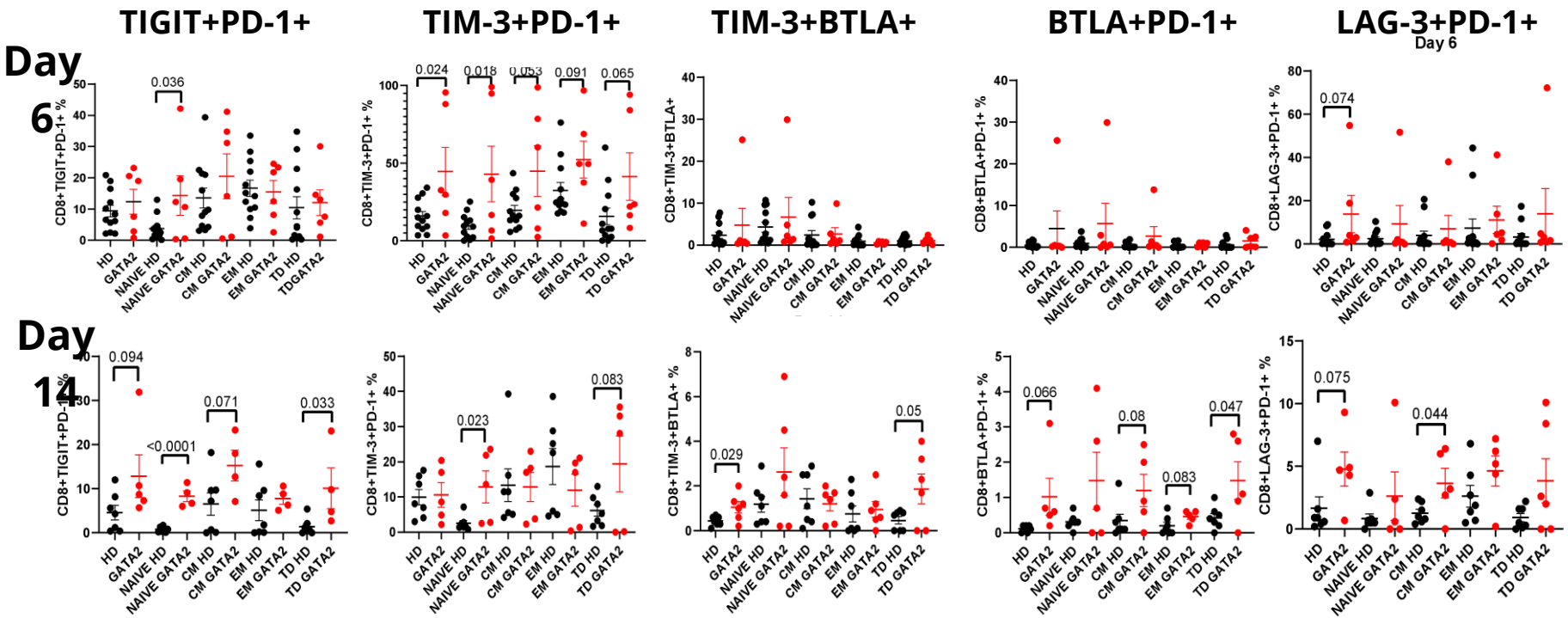
… segnalare nuovi casi …..

elena.turrini3@gmail.com

GATA2

Gennaio 2022 Marzo 2026 → 45 patienti arruolati

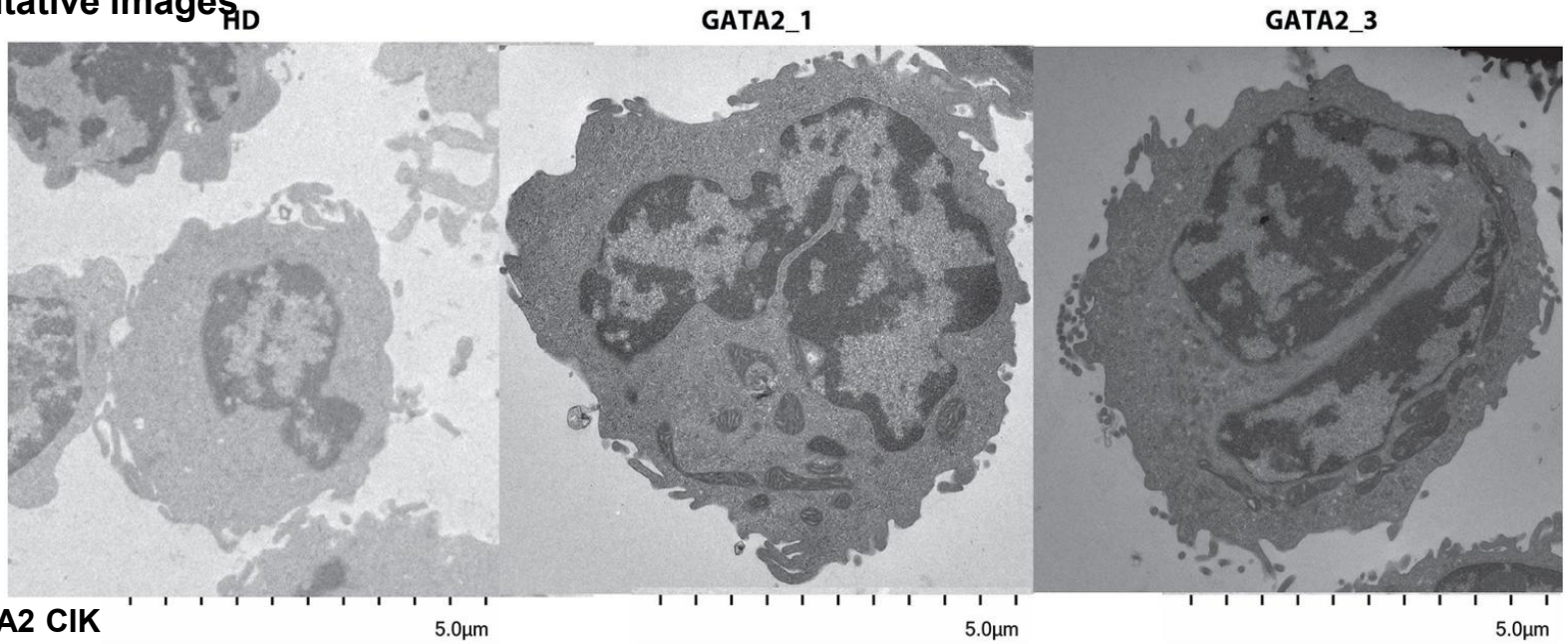
Microbiota in GATA 2
CD8 «esausti» in GATA 2



Exhausted phenotype in CD8+ subsets

Ultrastructure signature of GATA2 CIK

Representative images

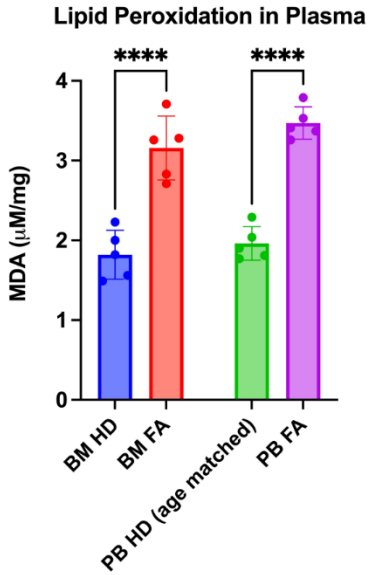


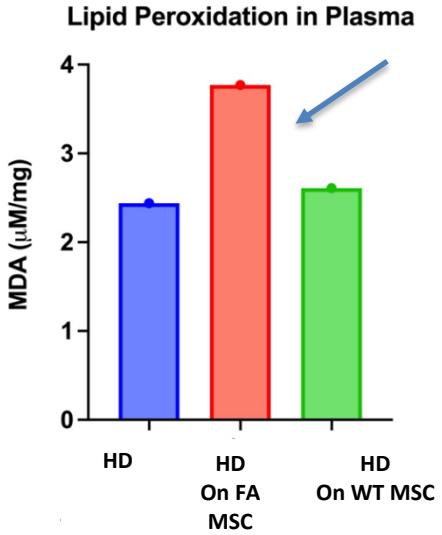
GATA2 CIK
Irregular mitochondria

E' prevista la creazione del registro SAMD9/9L syndrome: l'obiettivo è di costruire una rete nazionale ed una raccolta dati registro per avviare studi funzionali su pazienti affetti

Ruolo della metilazione in FA Post Tmo

In plasma AND BM of FA patients increased oxydative stess





FA- MSC coltured in HD-plasma

After 72 h

Increased lipid peroxidation in HD-plasma

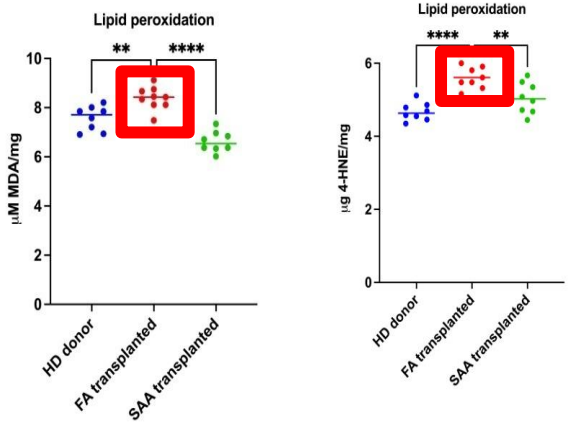
Oxydative stress mediated by BM niche cells

Peripheral Blood mononuclear cells (PB MNCs) from :

- **9 FA transplanted pts and their HD**
- **9 Severe Aplastic Anemia pts after HCT**

All full donor chimerism

> 6 months post HCT

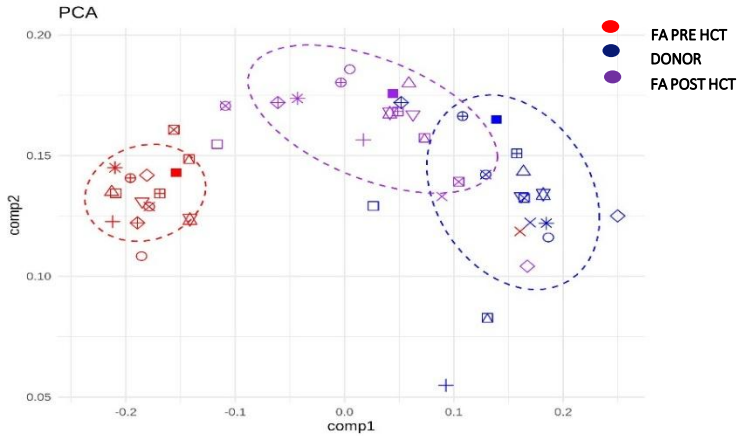


Increased membrane lipid peroxidation

PB MNCs of Healthy donor of FA patients after transplant:

- **Energetically impaired** (ATP/AMP ratio)
- **Enhanced membrane oxidative stress** (Malondialdehyde and 4-Hydroxynonenal) compared to transplanted SAA and HD

16 transplanted FA patients before and after HCT and their HD
Median times since transplant 2.5 years (range 0.1-9.61)



Post HCT profile intermediate between Pre HCT and Donor

Role of epigenetic modification in FA MNC post HCT?

Pagliara et al, Am J Hum Genet 2023

TAKE HOME…BY NOW

- Epigenetic changes in HD cells coming from marrow microenvironment

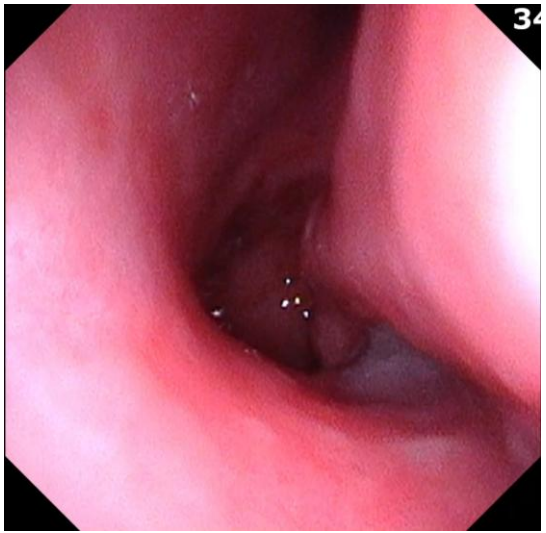
FURTHER STEPS

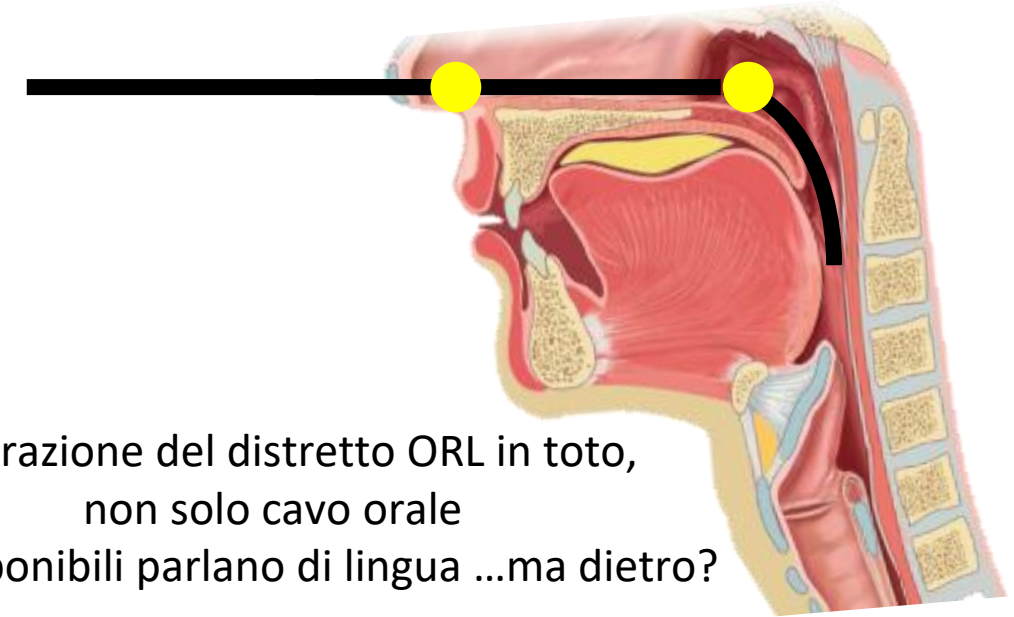
- To investigate the potential impact of post HCT defects on long term outcome of FA patients.

SUPPORTO
monitoraggi
Longitudinali

ORL

BIOENDOSCOPIA





Esplorazione del distretto ORL in toto,
non solo cavo orale
I dati disponibili parlano di lingua …ma dietro?

Choi, J., & Jung, M. (2025). Head and Neck Cancer in Fanconi Anemia: Clinical Challenges and Molecular Insights into a DNA Repair Disorder. Cancers, 17(18), 3046. https://doi.org/10.3390/cancers17183046

BIOENDOSCOPIA

BIO

Magnificazione di caratteristiche tissutali «istologiche»: biopsia ottica

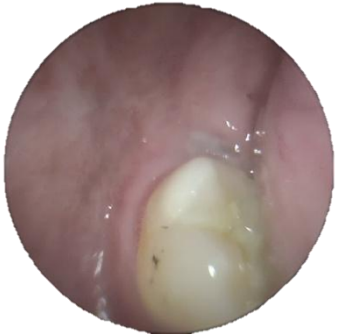
STEP 1

narrow band imaging NBI

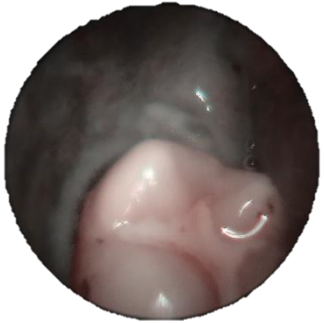
STEP 2

yellow enhancement YE

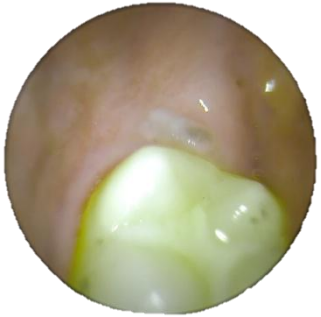
inflammatory mucosa heat map



White light



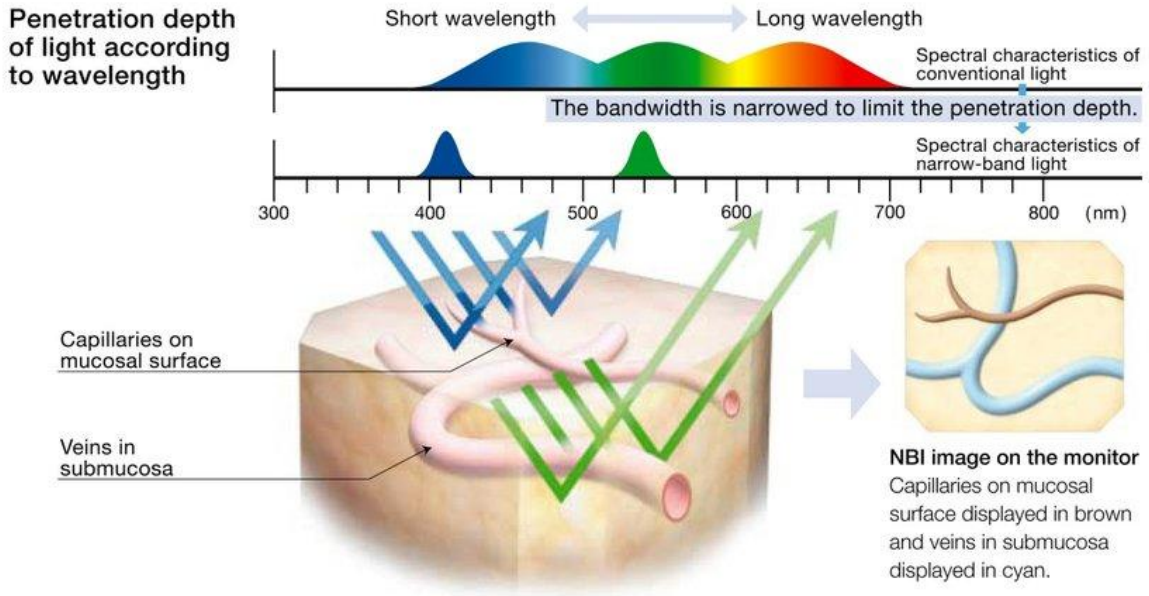
NBI



YE

BIO: Magnificazione di caratteristiche tissutali «istologiche»: biopsia ottica

NBI



Implementazione dati

Inizio studio, raccolta dati ottobre 2024

14 pazienti (8 F, 6 M)

numero visite eseguite: 17

lesioni sospette identificate: 5

Brushing: 5

istologico: 1

tommasocacco@gaslini.org

COLLABORAZIONI trasversali

ALPS.IT.NET

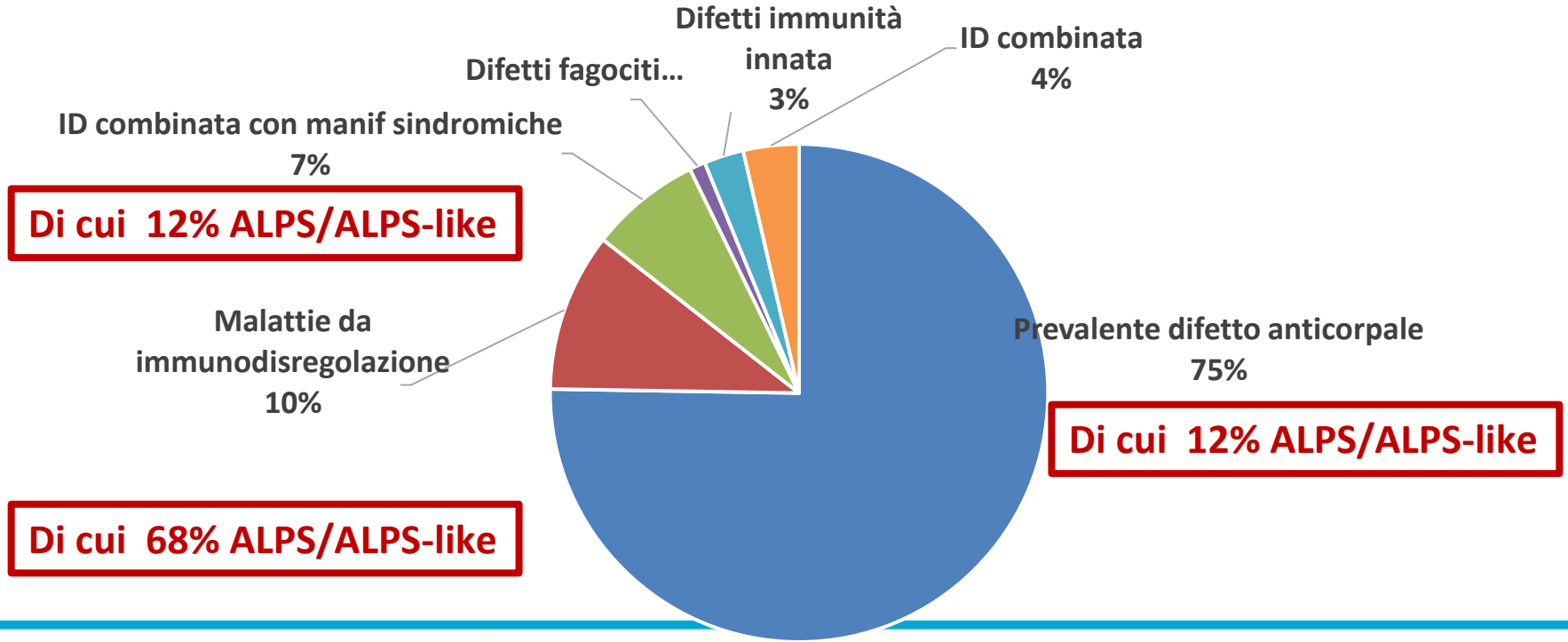
↓

IPINET Immunoreum

Descrivere la prevalenza e il tipo di manifestazioni cliniche reumatologiche in una coorte di pazienti con IEI

RISULTATI aggiornamento marzo2026

23 Centri, 203 pazienti arruolati in 24 mesi



PROSSIMI STEP E TIMELINE

- Completamento studio → **31.03.2026 DATABASE LOCK**
- Analisi statistica per successiva pubblicazione → **APRILE 2026**
- **Sottomissione abstract ESID 2026 - Maastricht**

Giulia Loiacono – Data Manager UOSD Reumatologia e Immunologia pediatrica P.O. «Vito Fazzi» Lecce

immunoreum@gmail.com

PROPOSTE: malformazioni cranio faciali in DBA

Descrizione delle anomalie del sistema nervoso centrale &
Possibili correlazioni con la genetica

Descrizioni sporadiche in letteraturA

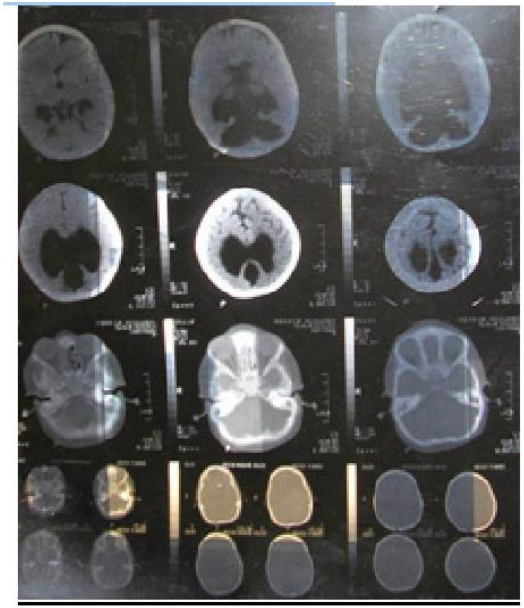


Fig. 1: CT brain shows a corpus callosum

- ✓ Anomalie cranio faciali/ condotto uditivo/ decroso n faciale
- ✓ Difetto del corpo calloso
- ✓ Atrofia corticale / Dilatazione dei ventricoli
- ✓ Compressione midollo allungato
- ✓ Ritardo dello sviluppo/Ritardo mentale

Tominaga, Hum Genome Var 2019

Rabah and Nermine, Egypt J Medical Human Genetics, 2010, Roberti, Front Genet 2018,

Condivisione dati Radiologici

- Invio di Immagini con Wetransfer al seguente indirizzo: renzo.manara@unipd.it
- Invio di CD (o lastre) a:

  Prof Renzo Manara,

  Neuroradiologia c/o Azienda Ospedaliera Universitaria di Padova

  via Giustiniani 2, 35128, Padova

Timeline

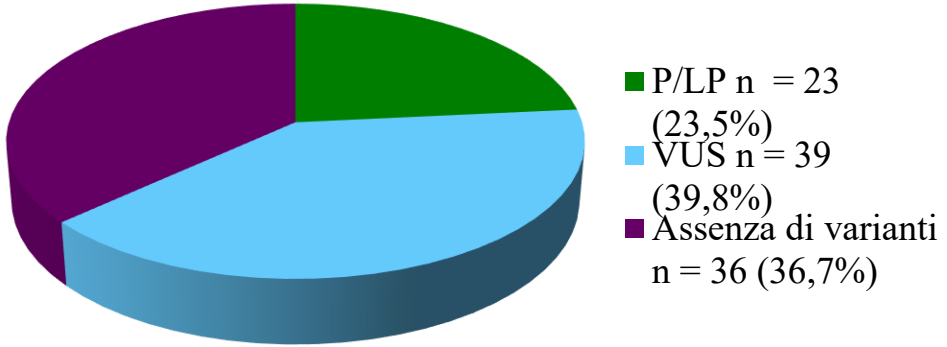
- Periodo di arruolamento e Raccolta Dati: Febbraio - Settembre 2026
- Analisi dati: Ottobre 2026 - Gennaio 2027
- Stesura Report e Manoscritto: Febbraio - Aprile 2027

NUOVE PROPOSTE

Significato delle VUS nei telomeri

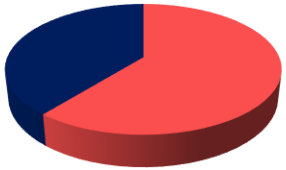
- **98 pazienti pediatrici e adulti**
- Unità Ematologia Gaslini: **gennaio 1989 - dicembre 2025**
- Criteri di inclusione “genetici”: portatori di varianti **P/LP**, **VUS** geni TBD-relati e pazienti **senza varianti genetiche ma con lunghezza telomerica < 10° percentile per età**.

Distribuzione delle classi di variante



Genetica e analisi della lunghezza dei telomeri

Pazienti con varianti P/LP

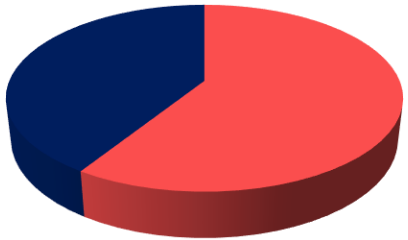


Geni core n = 14

Geni core:
TERT n = 5
TINF2 n = 4
DKC1 n = 3
TERC n = 2

Geni accessori:
PARN n = 4
RTEL1 n = 4
WRAP53 n = 1

Pazienti con VUS

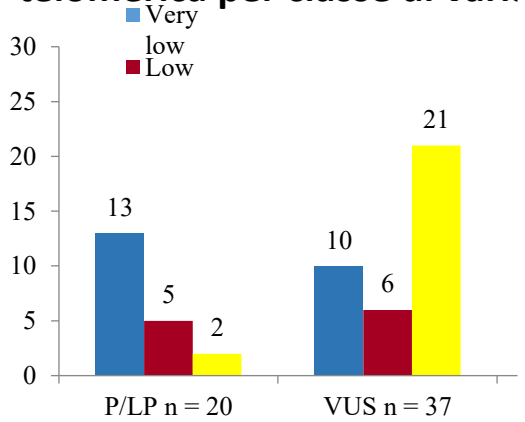


Geni core n = 23 Geni accessori n = 16

Geni core:
TINF2 n = 9
TERT n = 8
ACD n = 4
TERC n = 1
POT1 n = 1

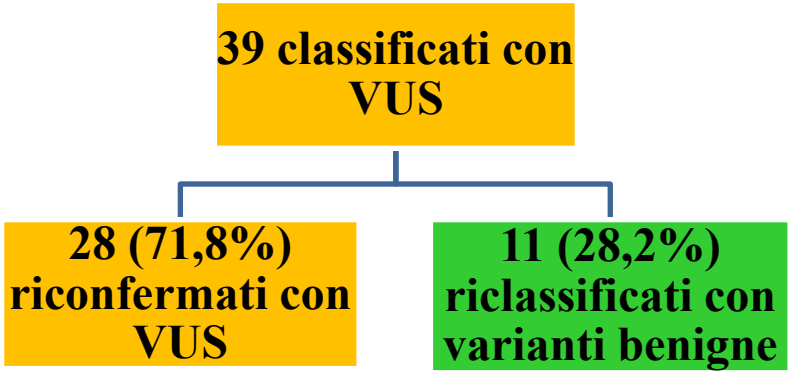
Geni accessori:
RTEL1 n = 10
PARN n = 4
CTC1 n = 1
NAF1 n = 1

Distribuzione della lunghezza telomerica per classe di variante



p = 0,001

Focus sulle VUS: la riclassificazione nel tempo



- **Lunghezza telomerica:**

30% pazienti con VUS confermate: TL < 10° percentile
10% paziente con variante benigna: TL < 10° percentile
p = 0,05

- **Manifestazioni extraematologiche note:**

50% pazienti con VUS confermate
0% con varianti benigne
p = 0,003

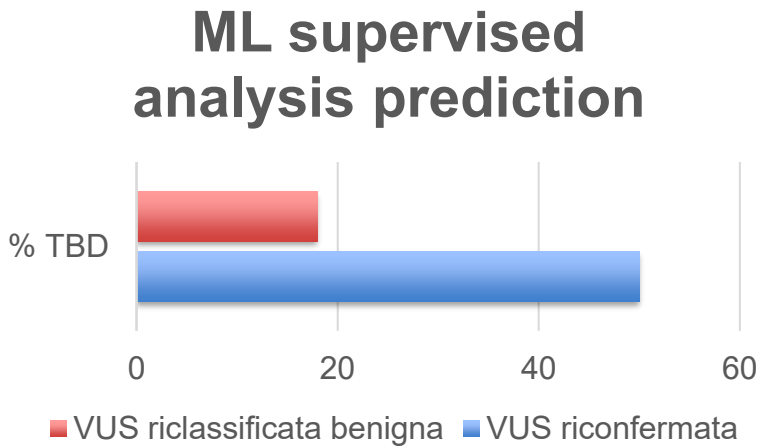
- **Manifestazioni ematologiche:**

75% pazienti con VUS confermate
72% pazienti con varianti benigne
p = ns

- **Citopenia e short TL**

54% pazienti con VUS confermate
9% pazienti con varianti benigne
p = 0,08

VUS e machine learning



p=0.08, Odds ratio= 4.5

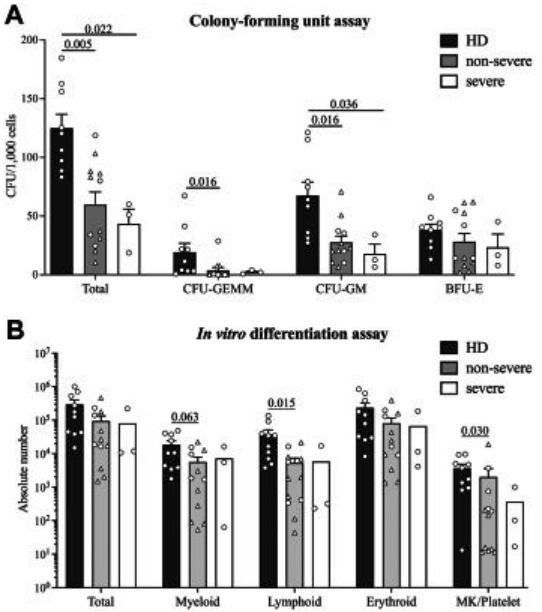
lucaarcuri@gaslini.org
erikamassaccesi@gaslini.org

Received: 12 February 2025 | Accepted: 5 October 2025
DOI: 10.1002/hem3.70272
HemaSphere eha
ARTICLE

Application of machine learning in the diagnostic work-up of telomere biology disorders

Estensione studio DADA2

RICERCA FINALIZZATA GASLINI /SAN RAFFAELE

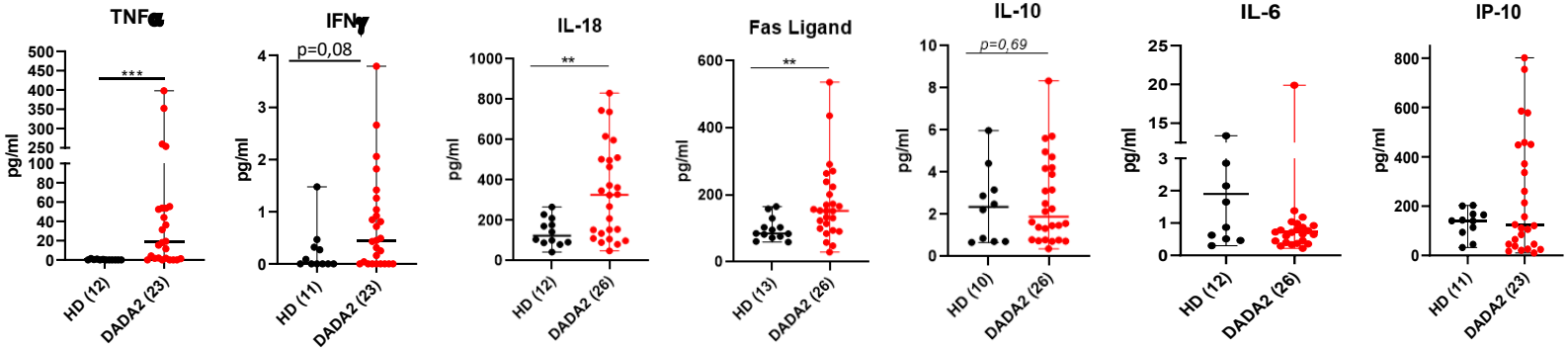


18 patients

Autoimmune cytopenias and bone marrow failure (61 %)

Bulte' D, J Allerg Clin Immunol 2025

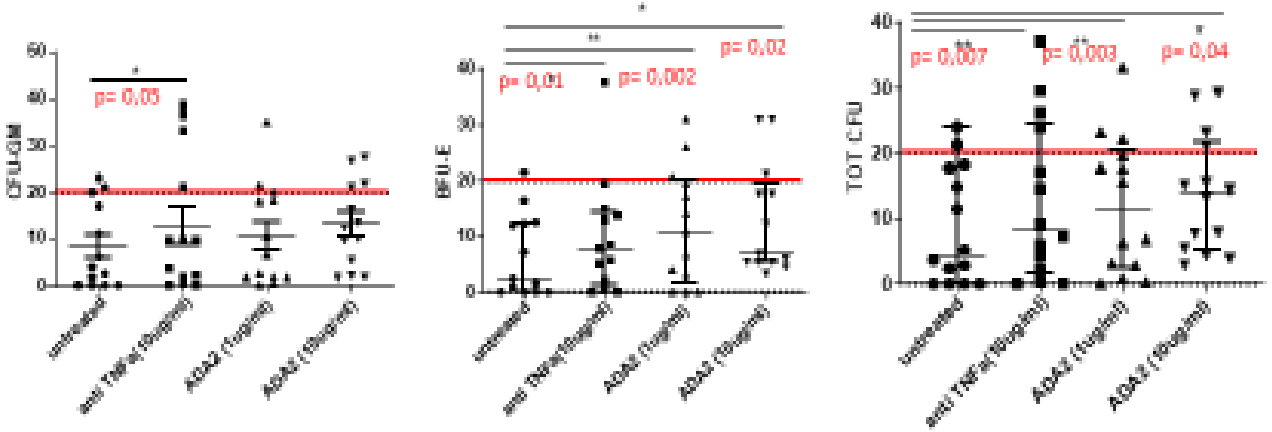
DADA2 patients → Increased pro-inflammatory cytokines in PB



Lupia M. , Schena F. manuscript in preparation

Treatment with anti-TNFα, human recombinant ADA2, or Eltrombopag. BFU-E (Burst-Forming UnitErythroid) and CFU-GM (Colony-Forming Unit-Granulocyte Macrophage)

CFU-GM BFU-E Total

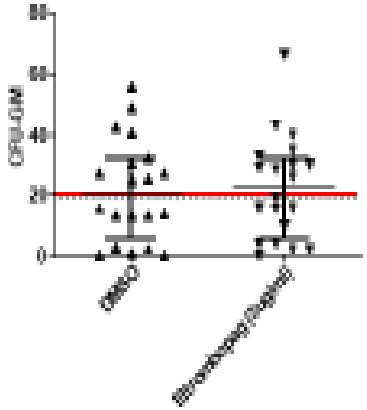


Lupia M. , Schena F. manuscript in preparation

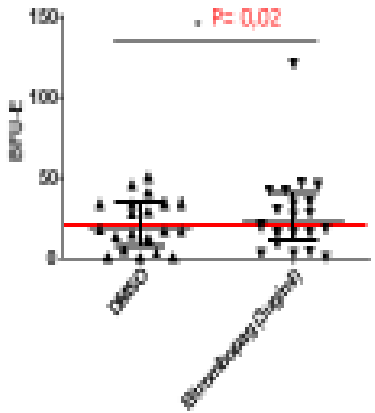
✓ *Anti-TNFa stimulates CFU-GM and BFU-E growth*

+ *Eltrombopag*

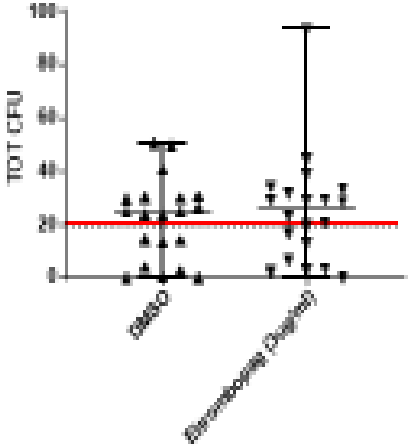
CFU-GM



BFU-E



Total



Eltrombopag stimulates BFU-E growth

Lupia M. , Schena F. manuscript in preparation

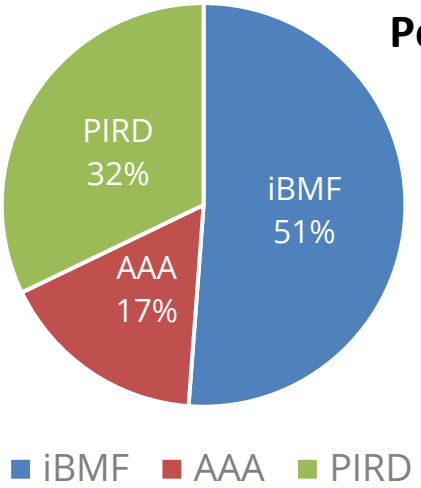
Ematopoiesi clonale in insufficienze midollari congenite

Characteristic of the cohort

Sept 24-Dec25

117 samples of 84 pts iBMF/PIRD patients (females 52%,
age at first analysis 19.9y;range 1.5-53y)-14/84 serial testing

Marrow (79%)

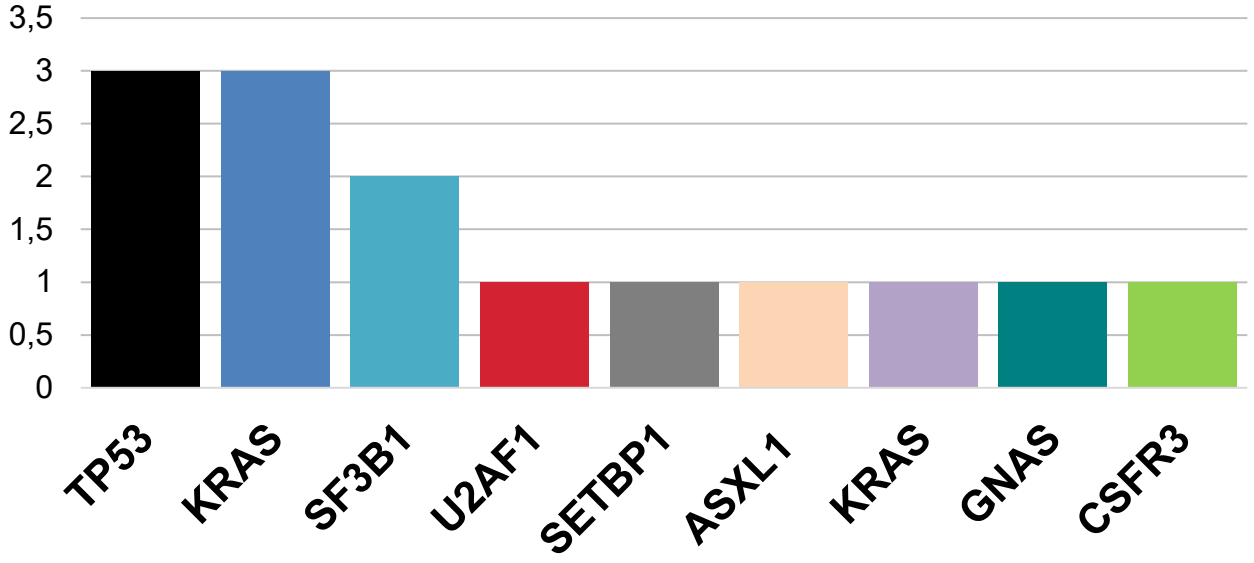


Peripheral Blood (21%)

13 Severe Congenital Neutropenia
11 Fanconi Anemia
9 Telomere Biology Disorders
4 Swachman Diamond Syndrome
4 Blackfan-Diamond Syndrome
5 Congenital Thrombocytopenia

Frequency of LP/P variants

Nine/84 patients (11%) carried somatic pathogenic or likely pathogenic variants



SOMATIC VARIANTS in disease groups

CH was more common in iBMF 14% than, AAA in 7% or PIRD 7%

ENLARGED COLLECTION

SHARED PANELS

INPUT DATA in REDCAP according to the DISEASE

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IMPLEMENTAZIONE

Neutropenie Long Lasting Late Onset

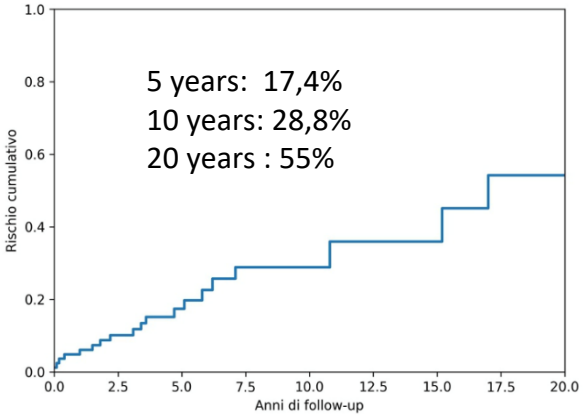
85 patients, 46 females (54%), median age at examination **14.5 years** (range 0.4-55 years) affected with **LO/LL neutropenia**

from January 2005 to June 2024

Neutropenia at DX : **mild 34% moderate 38% and severe** in **28%**

Severe infections 10%

Autoimmunity



<<	CD19/NK/CD8
>>	B Transitional ($CD27^{-}CD10^{+}CD38^{++}$)
<<	CD27+IgD-IgM- (B Memory Switched)
>>	CD27-IgD-CD21low (DN2 B cells)
>>	CD27-CD10+-CD38+-IgD+CD21low
<<	T helper naïve ($CD4^{+}CD45RA^{+}CD27^{+}$)
>>	T helper central memory ($CD4^{+}CD45RA^{-}CD27^{+}$)
<<	T cytotoxic naïve ($CD8^{+}CD45RA^{+}CD27^{+}$)
>>	T cytotoxic central memory ($CD8^{+}CD45RA^{-}CD27^{+}$)
<<	T regulatory ($CD3^{+}CD4^{+}CD25^{\wedge}bright^{+}CD45RA^{-}$)

Fioredda F AJH 2024,

Genetic profile
NGS panel 160 genes (BFM/IEI)

Analyzed 70/85 available samples

At least 1 variant in 28/70 (40%)

Pathogenic/ Likely pathogenic (9 pt) 14%

CARD11
TNFRSF13B
FASL

Pathogenic and likely pathogenic variants:

PT 1	TNFRSF13B	c.204 dup	p.Leu69 *
PT 2	TNFRSF13B	c.579C>A	p.Cys193Ter
PT 3	TNFRSF13B	c.260T>A	p.Ile87Asn
PT 4	CARD 11	c.3G>A	p.Met1Ile
PT 5	TNFRSF13B	c.542C>A	p.Ala181Glu
PT 6	CARD11	c.1316C>T	p.Ser439Phe
PT 7	FASL	del 1>4	del 1>4
PT 8	TNFRSF13B	C:431C>G	p.Ser144*
PT 9	TNFRSF13B	c.310T>C	p.Cys104 Arg

- **TNFRSF13B:** mutations in 6 patients (frameshift, nonsense, missenso)
- **CARD11:** mutations in 2 patients
- **FASL:** deletion in 1 patient

DATA COLLECTION

Currently available data : **971** patients with neutropenia

- AIN **524** (of wich **254** non remitting) in follow-up 80
- IN **226** (of wich **139** non remitting) in follow-up 40

Red CAP migration

WORK PLAN

Enlargement of the cohort involving also adults patients:

- Genetic data
- Immunological data
- Autoimmunity

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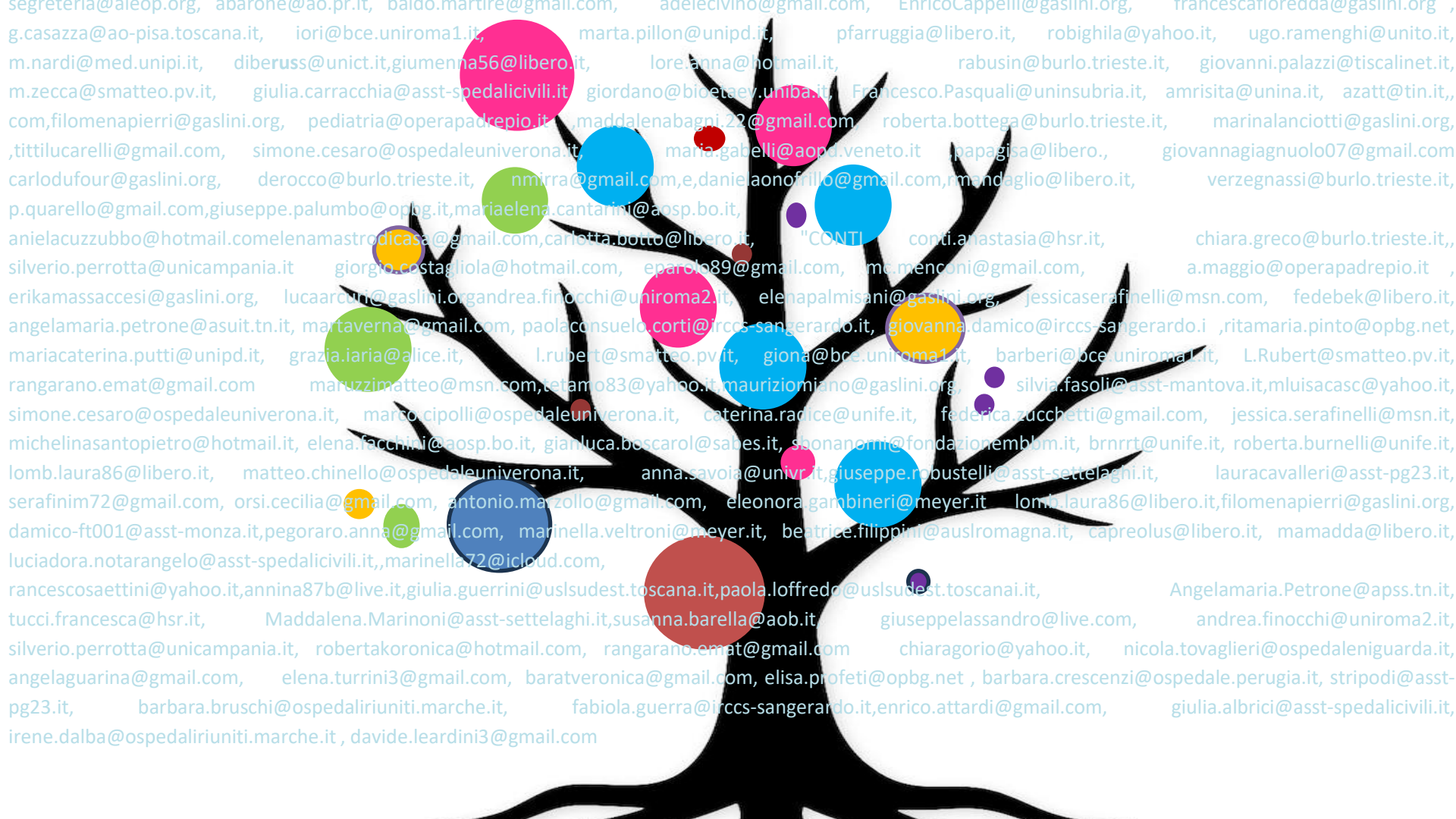
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