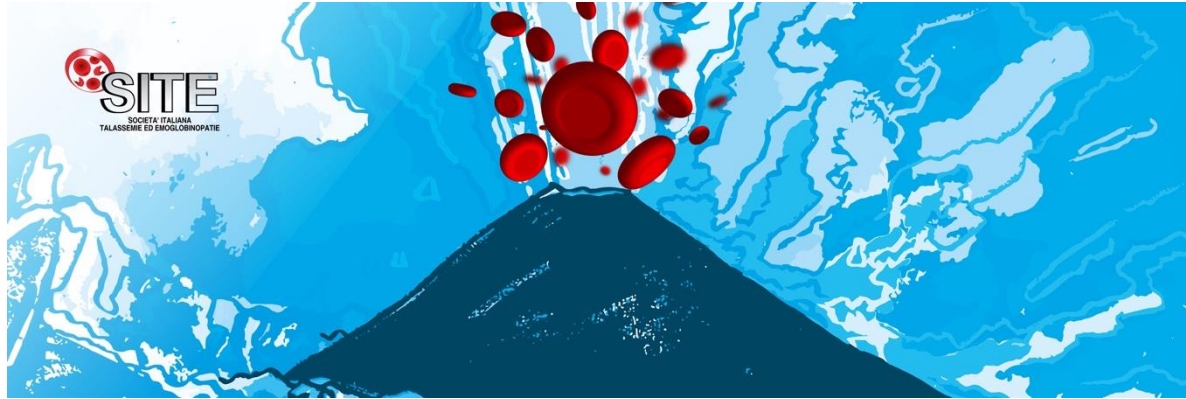




β -Talassemia Major da disordine acquisito dell'imprinting genomico

Dott.ssa Giorgia Mandrile
SSD Microcitemie – Malattie Rare Ematologiche
Dipartimento di Scienze Cliniche e Biologiche
Universita' degli Studi di Torino
AOU San Luigi Gonzaga – Orbassano

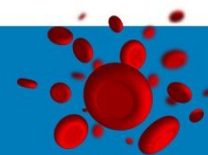
2023 - 2027
**DIPARTIMENTO
DI ECCELLENZA**
Ministero dell'Università e della Ricerca



**UNIVERSITÀ
DI TORINO**

Disclosures

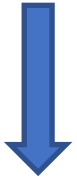
Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Amylam	x					x	
Novo Nordisk						x	



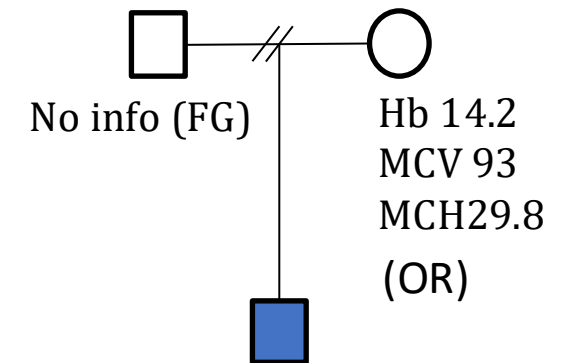
Il Caso Clinico



- 46 aa
- Controlli ematochimici occasionali (cambio medico curante) :
iperferritinemia (1882,5 ng/ml), sideremia 241 mcg/dl, transferrina non eseguita



- Consulenza GEL: verosimile talassemia + epatopatia di ndd (emosiderosi?)
- Milza 21 cm
- Consulenza ematologica → invio al Centro



Evoluzione del quadro clinico

età	Hb	MCV	MCH	RDW (%)	PLT	G.B.	Bili tot	AST	AL T	GGT	LDH
20y	12	62.9	21.3		330	6,12		21	20	13	
27y	11.8	70	23	17	434	8,9		24	18	11	
33y	10,1	67	21		377	5,0	4,6 (dir 0,33)	22	22	12	
37y	10,6	70	23		415	5,9		43	77	14	
39y	10,2	70	23		362	5,3		32	37	13	
44y	9,1	74,6	21,6	23,5	292	5,70			68	14	
45y	9,6	74,5	21,7	23,6	213	5,42	7,1 (dir 0,45)	77	99	17	
45y	8,9	74	23		259	5,63	4,99 (dir 0,4)	70	84	16	669
45y	9,2	73	23		292	5,25	6,42 (dir n.d. emolisi)	71	80	17	851
46y	9,2	73,4	23	27,8	242	5,68	8,1 (dir 0,47)	51	37	16	451
48y	9,2	73,4	22,5	21,4	300	5,94					

Ac folico 3,5ng/ml
B12 491 pg/ml

Ac folico 4 ng/ml
B12 430 pg/ml

Reticolociti 3,44%, 138000/mcl - 4,15%, 170000/mcl

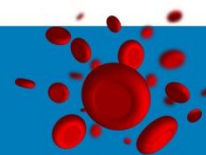
HbA2 3,4%
HbF 39,8% } HPLC

FERRO 224 mcg/dl
FERRITINA 1417 ng/ml
TRANSFERRINA 191 mg/dl
Saturazione 82%

Aptoglobina indosabile
Coombs diretto e indiretto negativi

HbA2 3,5%
HbF 45,1% } capillare

LIC 14,7 mg/g dw



Evoluzione del quadro clinico

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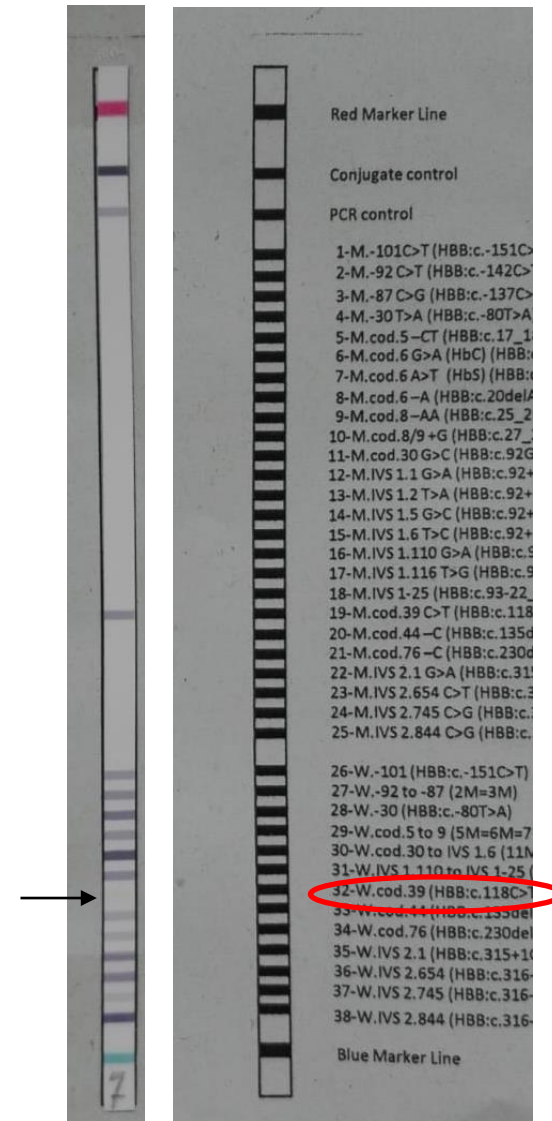
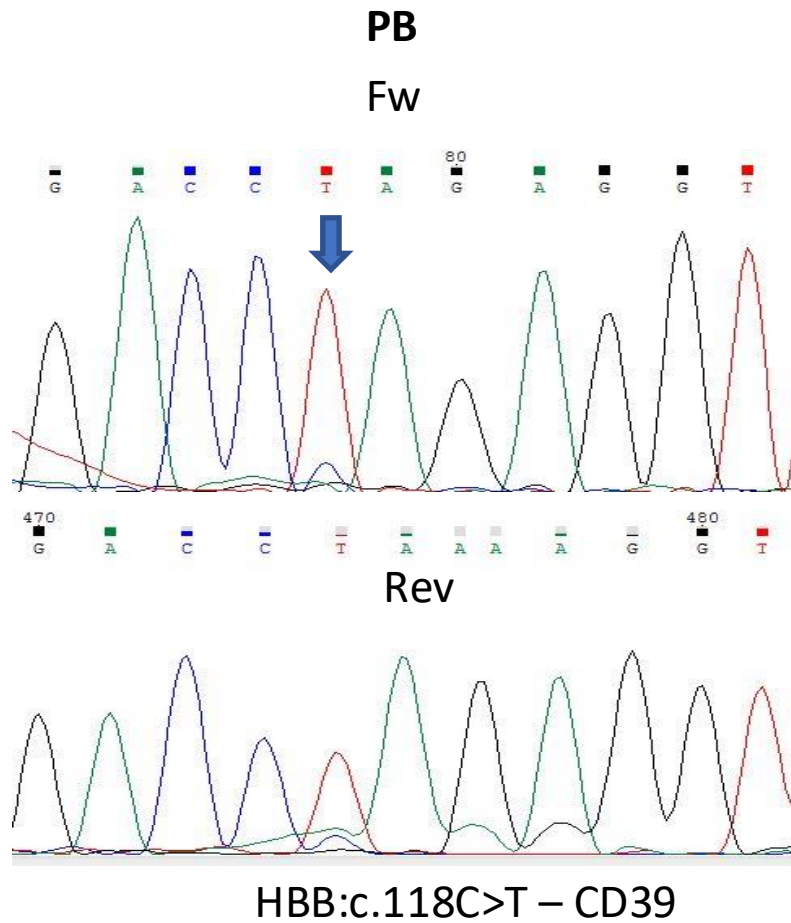
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TRANSFERRINA 191 mg/dl
Saturazione 82%

Aptoglobina indosab
Coombs diretto
LIC 14,7 mg/g dw

NTDT??

L'analisi genetica

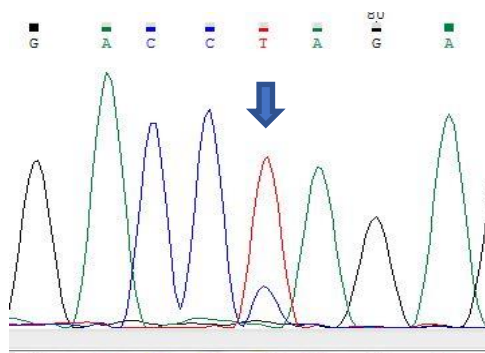


Reverse dot blot
Nuclear Laser Medicine
Beta globin strip assay

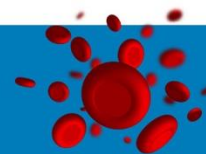
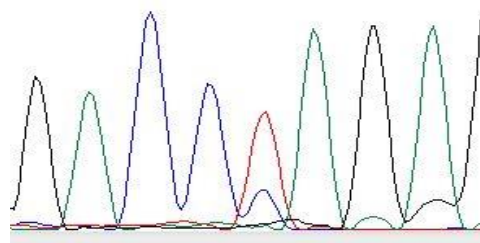
L'analisi genetica

Buccal swab

Fw



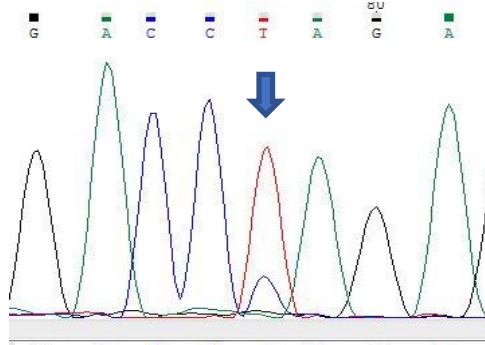
Rev



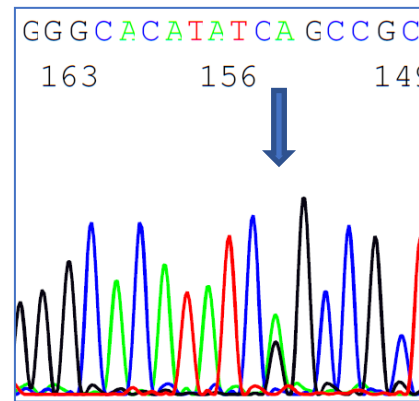
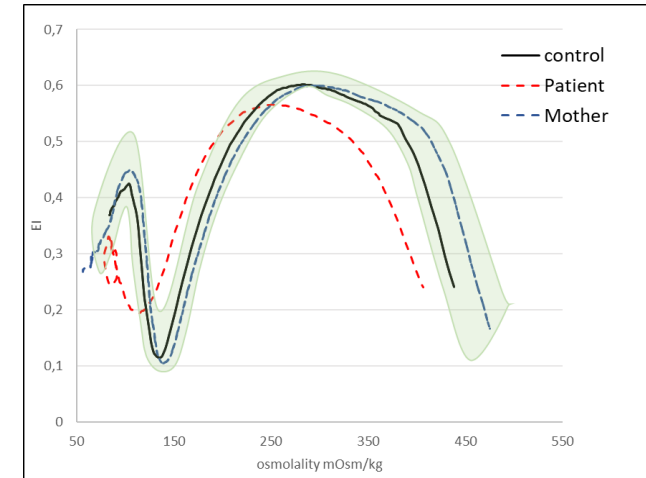
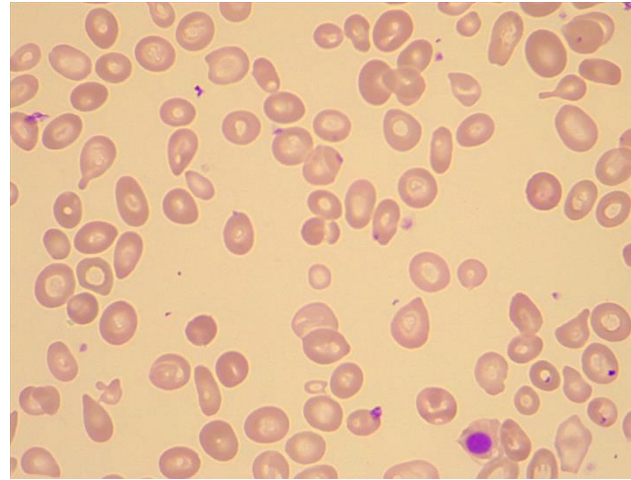
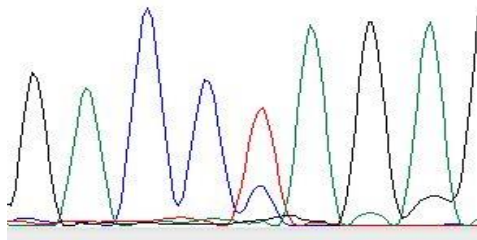
Analisi genetica e morfologica

Buccal swab

Fw

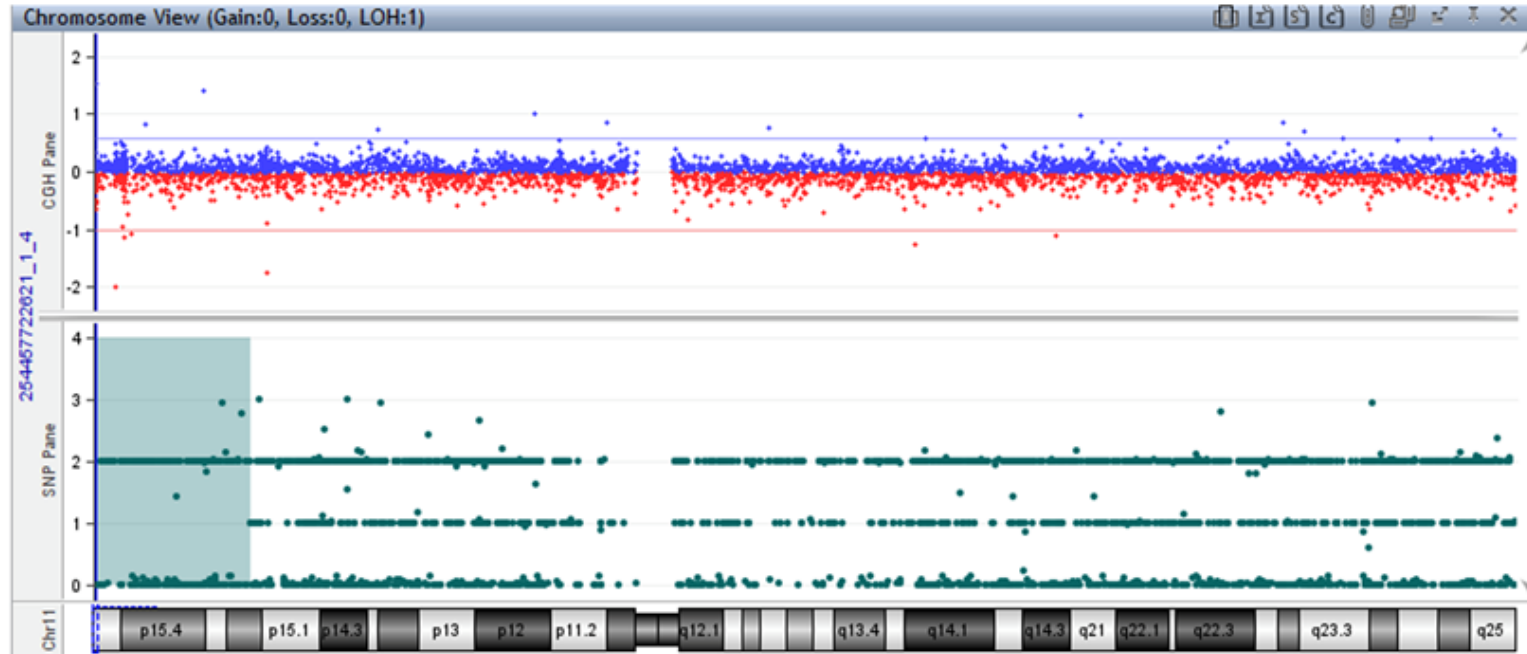


Rev



PIEZO1 c.5819G>A (p.Arg1940Gln)

SNParray su DNA midollare



14.7 Mb pUPD 11p15.2-11p15.5

American Journal of Hematology, 2026; Mandrile et al 0:1-6 10.1002/ajh.70177

Disomia Uniparentale Paterna 11 p15



Sindrome di Beckwith Wiedemann



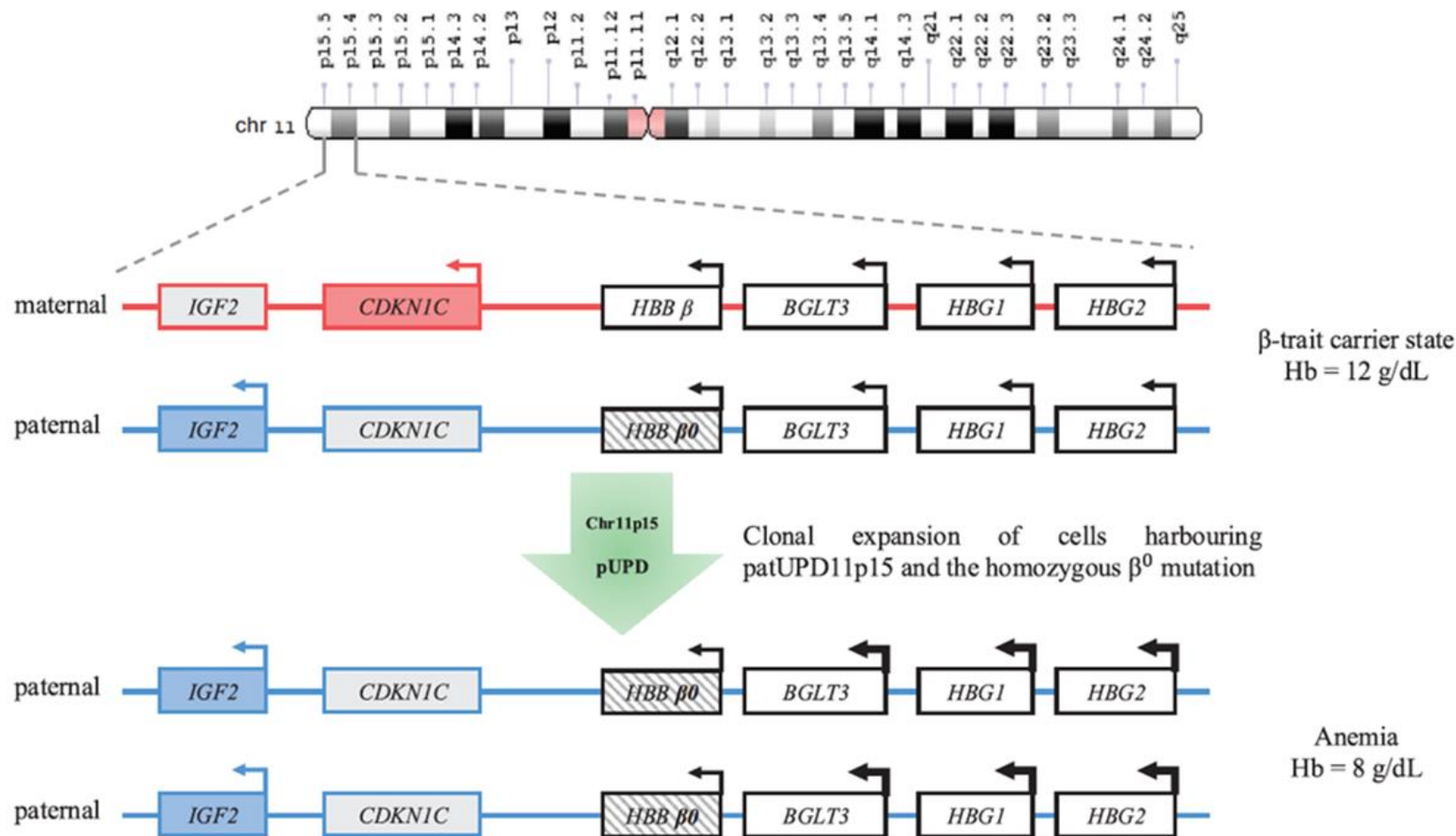
Macroglossia



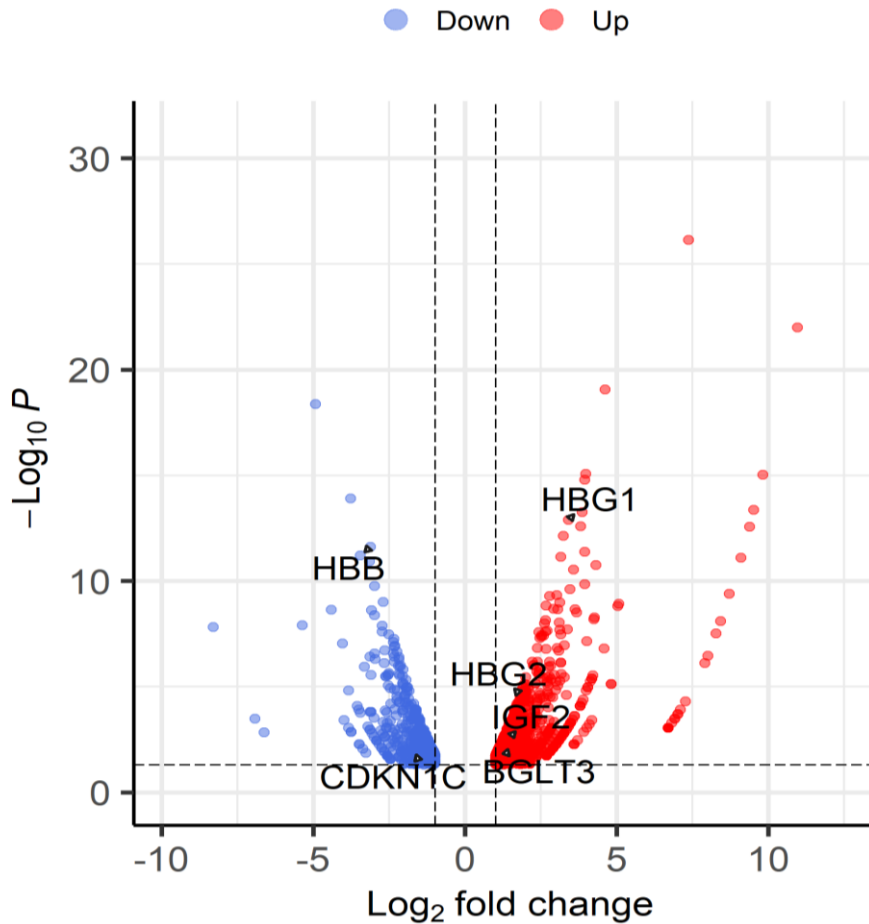
Umbilical hernia



Omphalocele

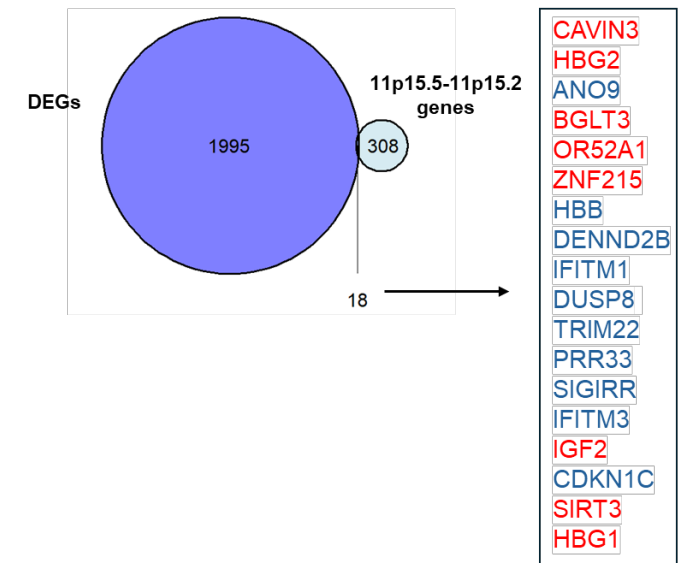


La Dimostrazione del meccanismo molecolare

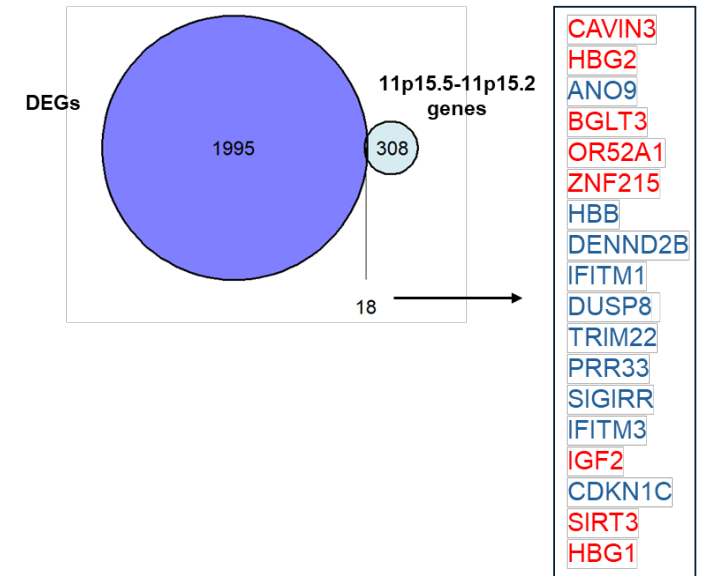
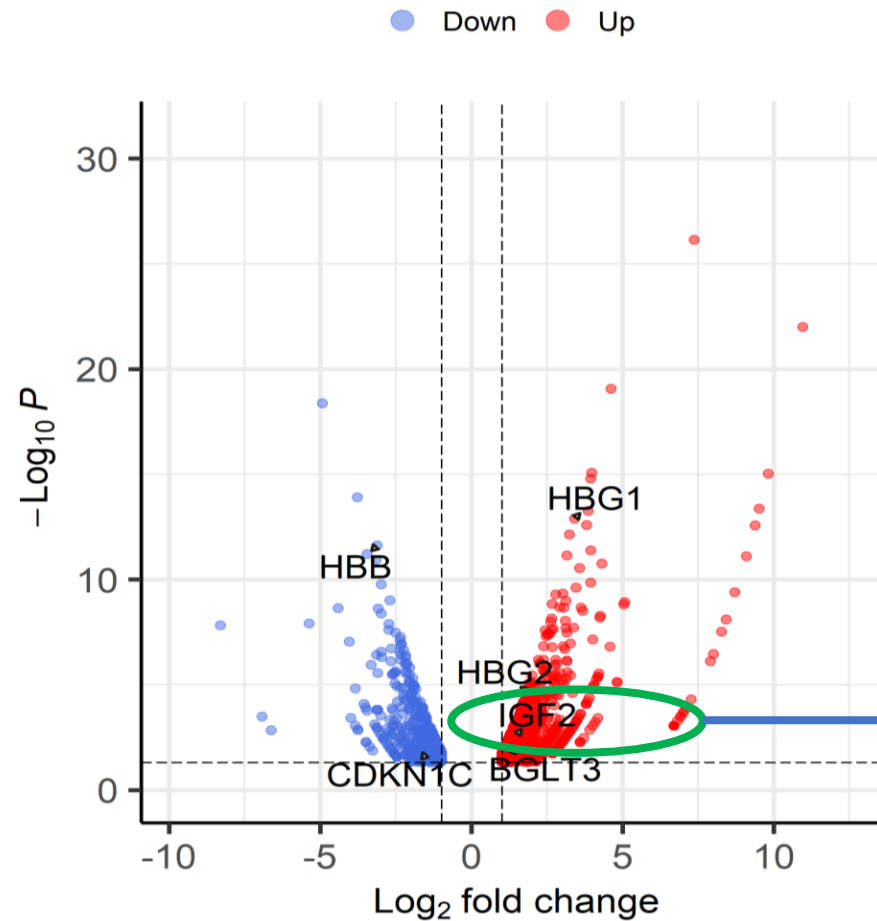


RNAseq su midollo:

- Assente espressione di HBB
- Incremento dell'espressione di IGF2, HBG1, HBG2

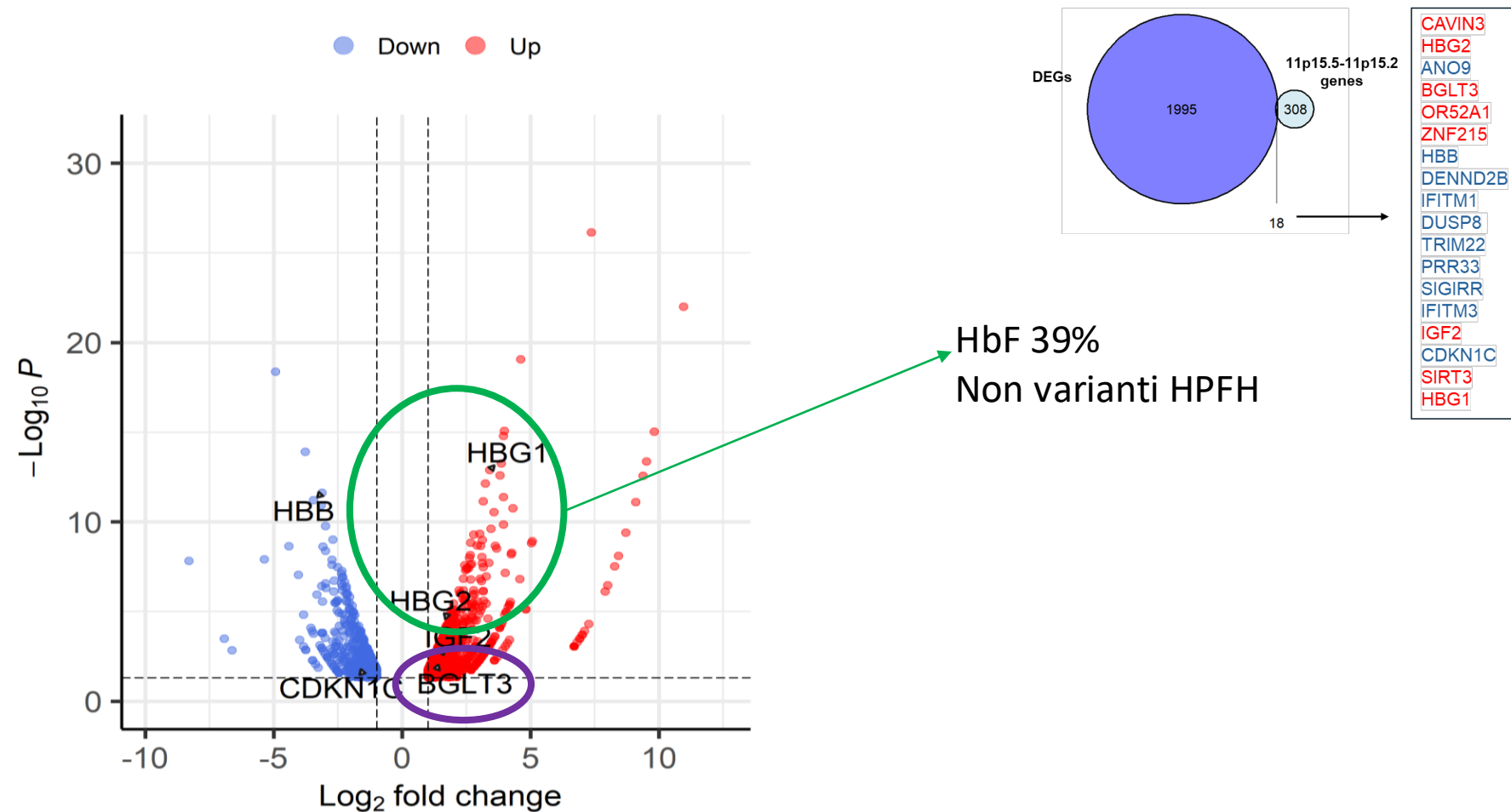


La Dimostrazione del Meccansimo Molecolare

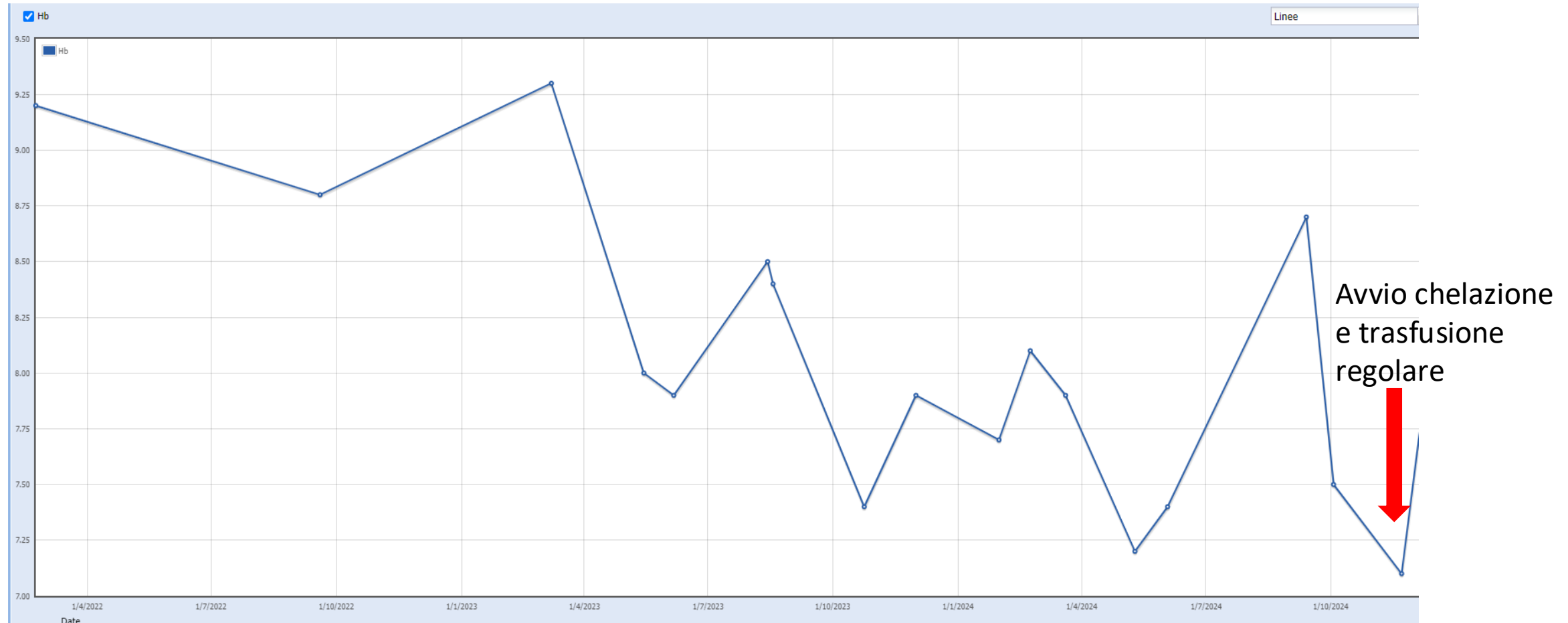


Espansione clonale del clone
11pUPD con HBB mutato

La Dimostrazione del Meccanismo Molecolare



L'evoluzione clinica

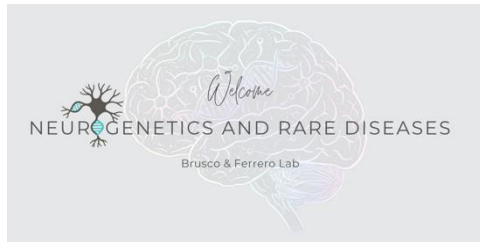


Ringraziamenti

Microcitemie e Malattie Rare Ematologiche

AOU San Luigi Gonzaga

Teresa Ceglie -Carmen Gaglioti – Daniela Giachino Giorgia Mandrile Francesca Mete - Francesco Porta- Vincenzo Voi - Neha Kargutkar



Molecular Biotechnology Center –

University of Torino

Alfredo Brusco – Simona Cardaropoli - Slavica Traikova
Silvia Carestiato - Chiara Pullano – Federico Rondot –



Genetica Università della Campania

Andrea Riccio – Flavia Cerrato





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