



2ND meeting of the European Research Consortium on ITP

NEW INSIGHTS INTO IMMUNE
THROMBOCYTOPENIA

Paris Crowne Plaza Paris République

April 23-24, 2026



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CIRCULATING CD8 T CELLS AS A POTENTIAL BIOMARKER OF NON-RESPONSE TO RITUXIMAB IN ITP

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Disclosures


Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
None							

Immune Thrombocytopenia (ITP)

Rare autoimmune disease characterised by isolated thrombocytopenia (<100 G/L)

Chronicity occurring in 70% of adult cases

The main risk is spontaneous haemorrhage, which can be life-threatening

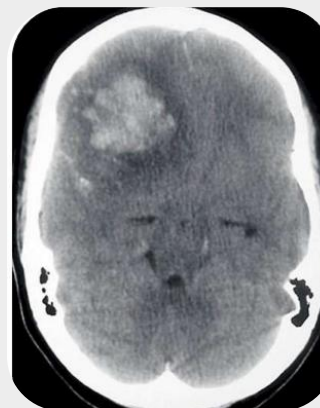
 Rapid administration of effective treatment is a major factor in patient survival



Bruising and purpura



Intrabuccal blood blister

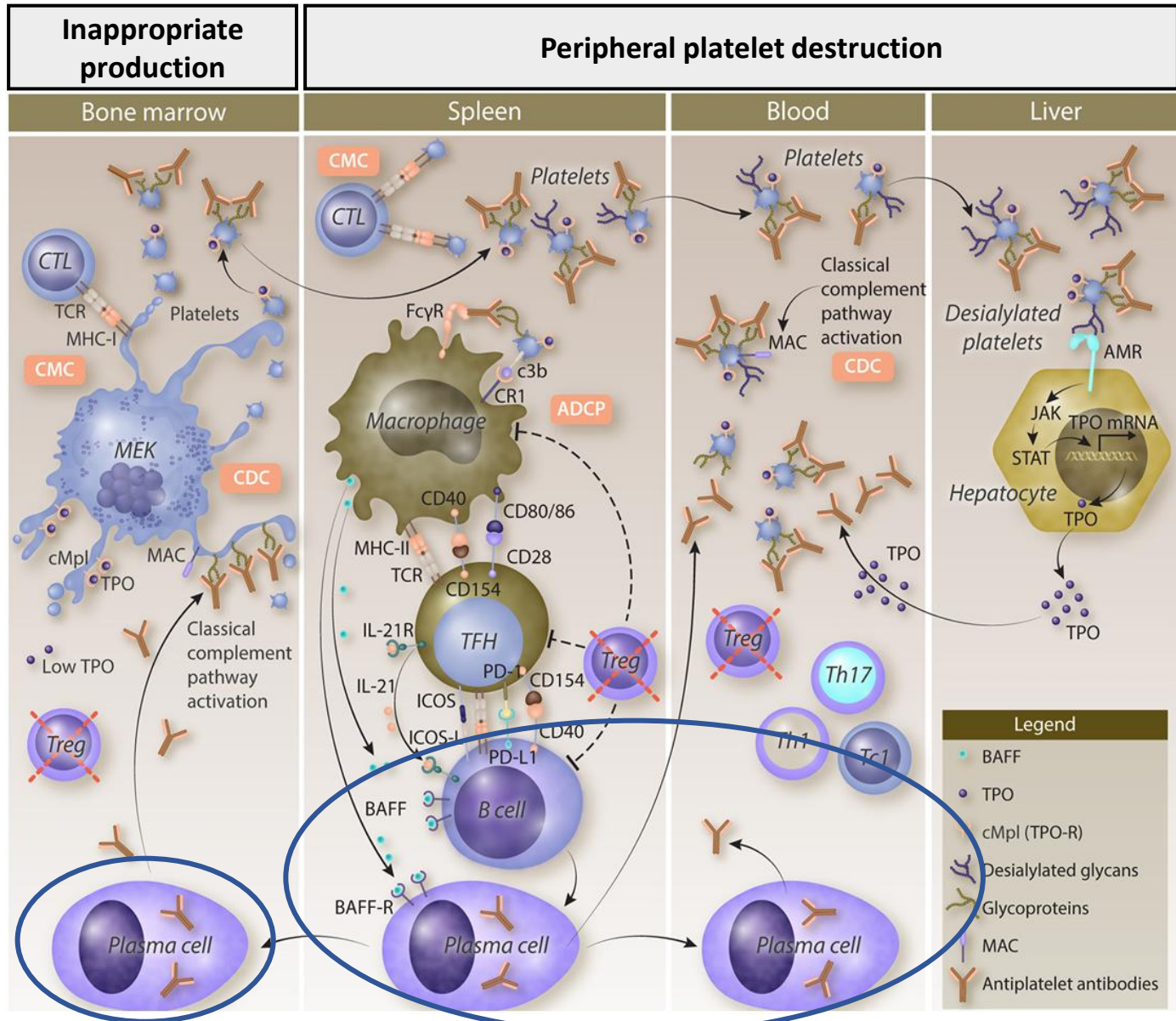


Intracerebral
hemorrhage



Epistaxis

Pathogenesis of ITP



Complement dependent cytotoxicity (CDC)

Th1/Th17 polarisation of CD4 T cells
 CD4 T regulatory deficit
 Amplification of B cell activation by TFH

Humoral immune response:
B cells activation and antiplatelet antibody production

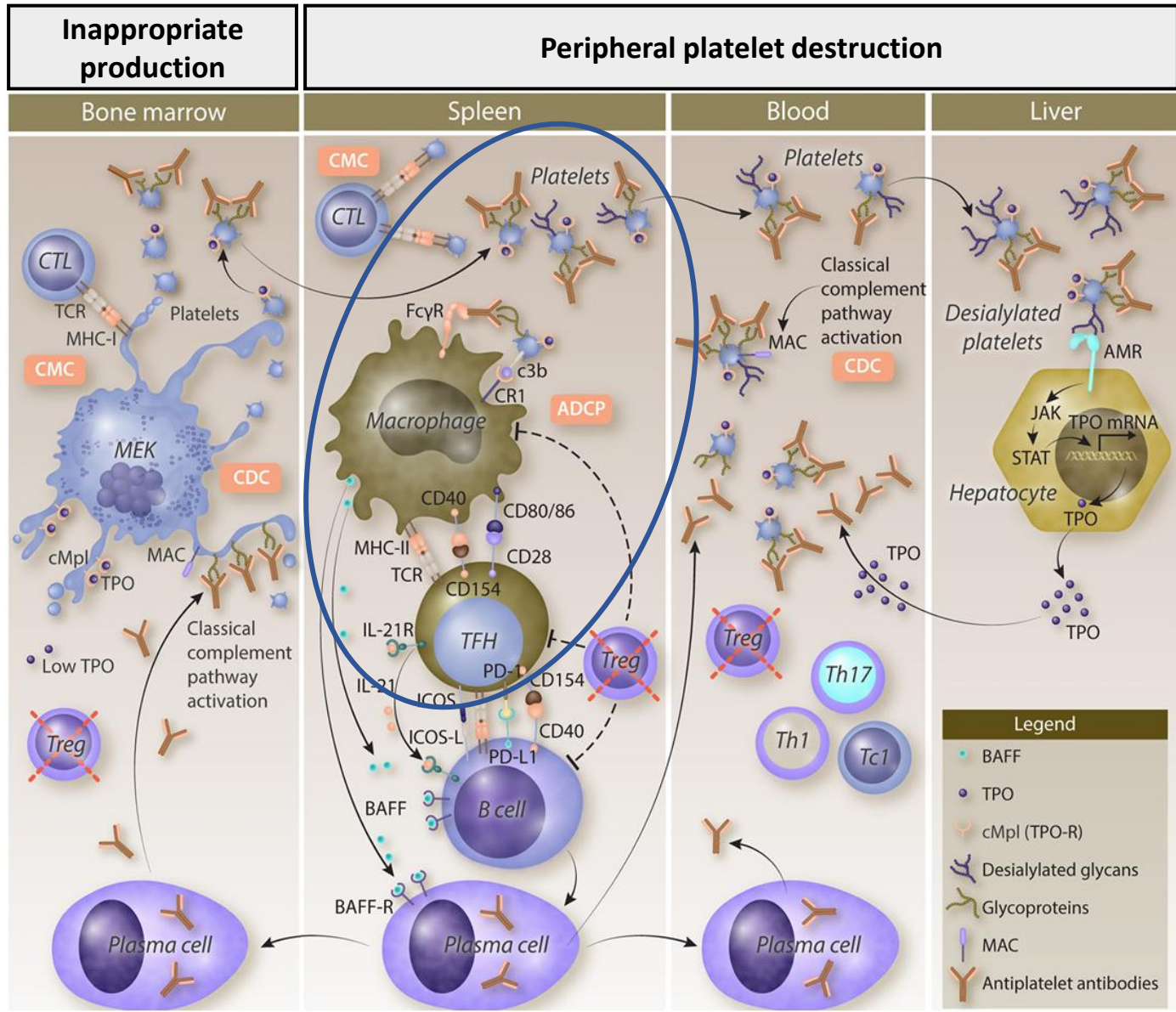
Cellular cytotoxicity by CD8 T cells

Phagocytosis by splenic macrophages
 Antigen presentation

Inappropriate TPO level

Audia et al., Hemasphere, 2021

Pathogenesis of ITP



Cellular cytotoxicity by CD8 T cells

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Complement dependent cytotoxicity (CDC)

Th1/Th17 polarisation of CD4 T cells

CD4 T regulatory deficit

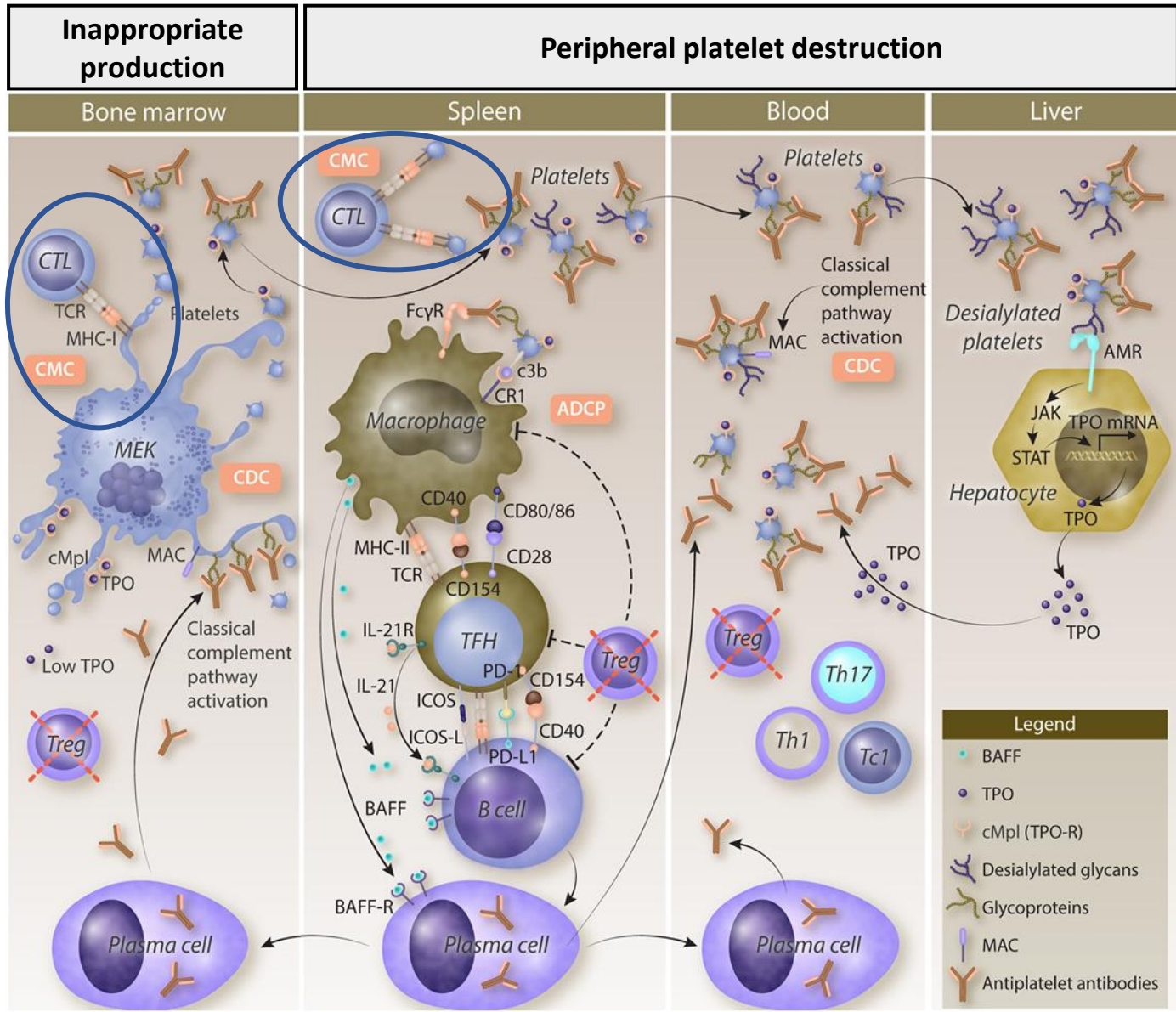
Amplification of B cell activation by TFH

Humoral immune response:

B cells activation and antiplatelet antibody production

Audia et al., Hemasphere, 2021

Pathogenesis of ITP



Cellular cytotoxicity by CD8 T cells

Phagocytosis by splenic macrophages

Antigen presentation

Inappropriate TPO level

Complement dependent cytotoxicity (CDC)

Th1/Th17 polarisation of CD4 T cells

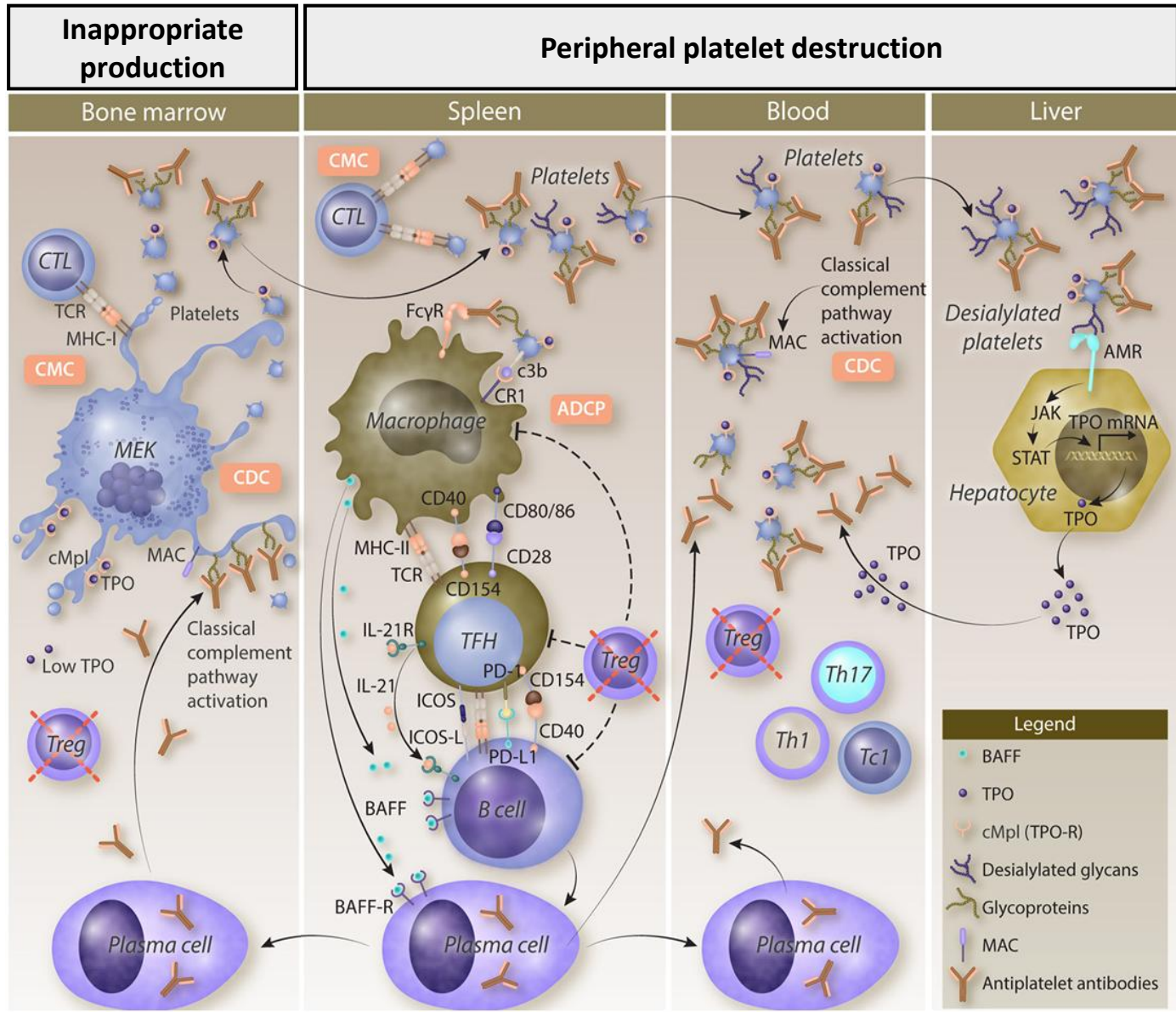
CD4 T regulatory deficit

Amplification of B cell activation by TFH

Humoral immune response:

B cells activation and antiplatelet antibody production

Treatment of ITP



Cellular cytotoxicity by CD8 T cells

Phagocytosis by splenic macrophages

Antigen presentation

Thrombopoietin receptor agonist

Complement dependent cytotoxicity (CDC)

Th1/Th17 polarisation of CD4 T cells

CD4 T regulatory deficit

Amplification of B cell activation by TFH

Humoral immune response

Rituximab

antiplatelet antibody production

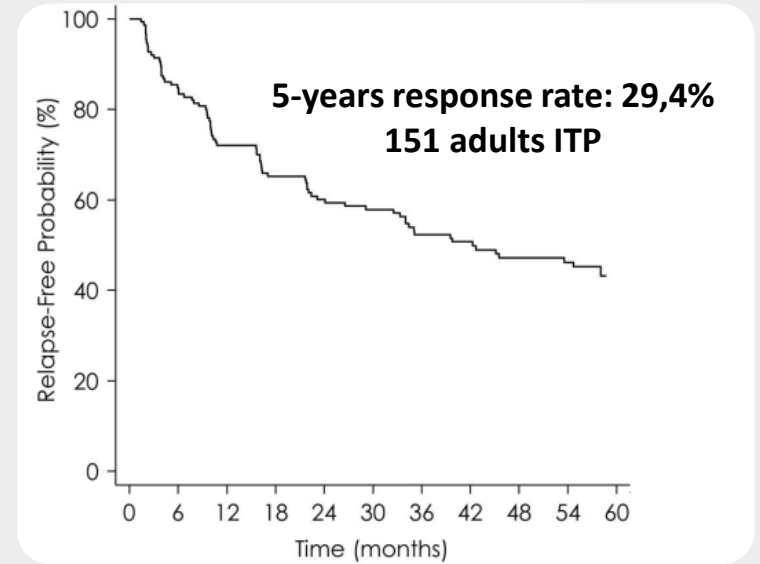
Audia et al., Hemasphere, 2021

Rituximab efficacy

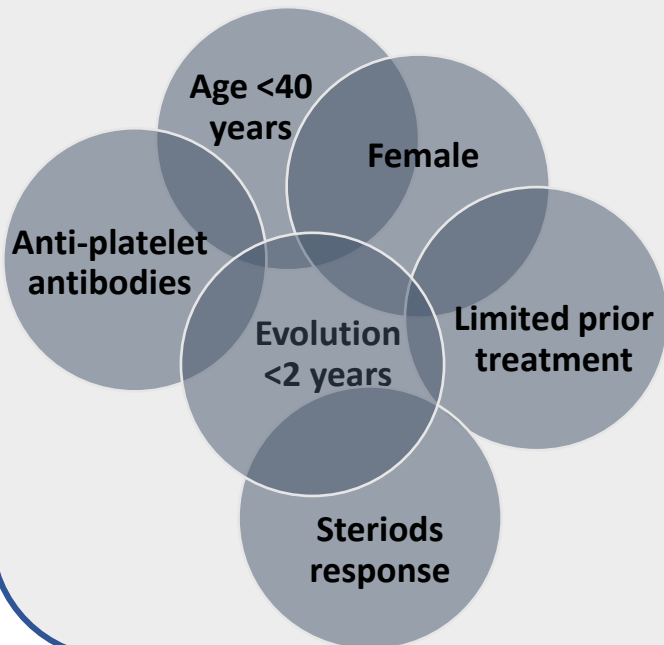


The long-term therapeutic response is variable:

- **60% at 1 year but 30% at 5 years for rituximab**



Deshayes *et al.*, AJH, 2021



No predictive factors of response to rituximab have been identified

- Treatments are used sequentially

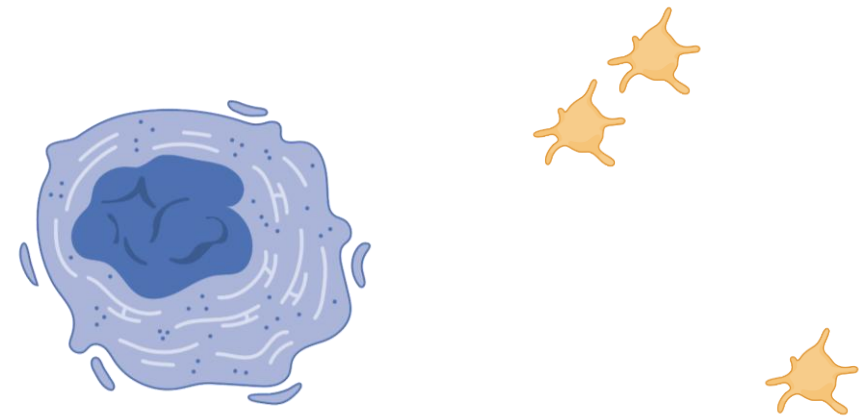
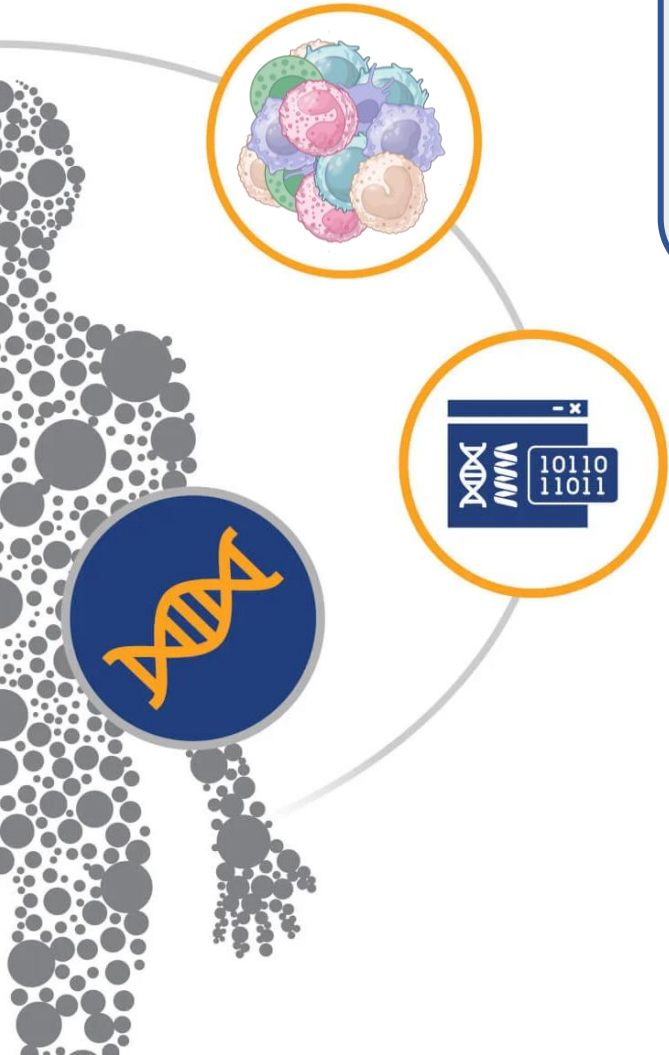


Hypothesis :

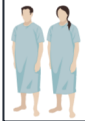
Variable response rates may reflect the involvement of different pathophysiological pathways at the individual level

Objective

To identify immune signatures associated with long-term response to rituximab, we analyzed baseline immune profiles in adult patients with ITP.

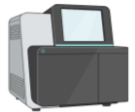


Method



PBMC before rituximab
4R vs 4NR

Long-term response was
assessed at 5 years



scRNA-seq

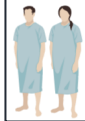
Quantitative analysis
Signaling pathways
Trajectory analysis

Matched on
age, sex, duration of
evolution, prior treatment

Patient characteristics for scRNA-seq analysis

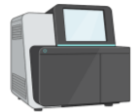
Patient	Age (years)	Sex	Type of ITP	Stage of ITP	ITP duration (months)	Treatment received <4 weeks before sampling	Platelet count at sampling (G/L)	Platelet count at 5 years or first relapse post RTX (G/L)	Response to RTX at 5 years
R1	75	Male	Primary	Chronic	84	None	14	185	Complete Response
NR1	74	Male	Primary	Chronic	60	None	11	7	Non-response
R2	61	Female	Primary	Persistent	6	None	17	188	Complete Response
NR2	56	Female	Primary	Chronic	20	None	20	12	Non-response
R3	25	Female	Primary	Persistent	4	None	35	252	Complete Response
NR3	33	Female	Primary	Persistent	4	None	16	17	Non-response
R4	57	Male	Primary	Newly Diagnosed	2	None	15	110	Complete Response
NR4	81	Male	Primary	Persistent	6	None	1	16	Non-response

Method



PBMC before rituximab
4R vs 4NR

Long-term response was
assessed at 5 years



scRNA-seq

Quantitative analysis
Signaling pathways
Trajectory analysis



PBMC before rituximab
20R vs 18NR

Long-term response was
assessed at 5 years



Multiparameter
cytometry

Cellular phenotyping
Cytokines production

Patient characteristics for cytometry analysis

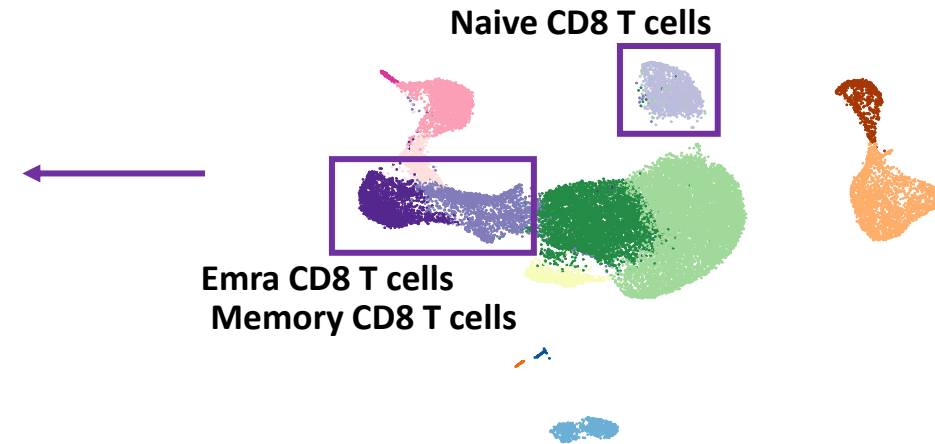
	Responders n=20		Non-responders n=18		<i>p-value</i>
Age (years)	58	[45-69]	64	[45-75]	0.61*
Gender					
Men	11	55%	9	50%	0.99**
Women	9	45%	9	50%	
Platelets at sampling (x10 ⁹ /L)	21	[10-35]	14	[5-27]	0.28*
Duration if ITP evolution (months)	12.5	[4-111]	42	[4-60]	0.89*
ITP course					
Newly diagnosed (<3 months)	4	20%	4	22.2%	0.99**
Persistent (3-12 months)	5	25%	3	16.7%	0.7**
Chronic (>12 months)	11	55%	11	61.1%	0.75**
Type of ITP					
Primary	13	65%	15	83.3%	0.28**
Secondary [†]	7	35%	3	16.7%	

[†]Secondary ITP: 6 Evans syndrome and 1 antiphospholipid syndrome for responders, 2 systemic lupus and 1 antiphospholipid syndrome for non-responders.
Data reported as median [1st quartile-3rd quartile] or number with %. *Mann-Whitney test, **Fisher's exact test.
ITP = Immune thrombocytopenia; IVIg = Intravenous immunoglobulin; TPO = Thrombopoietin.

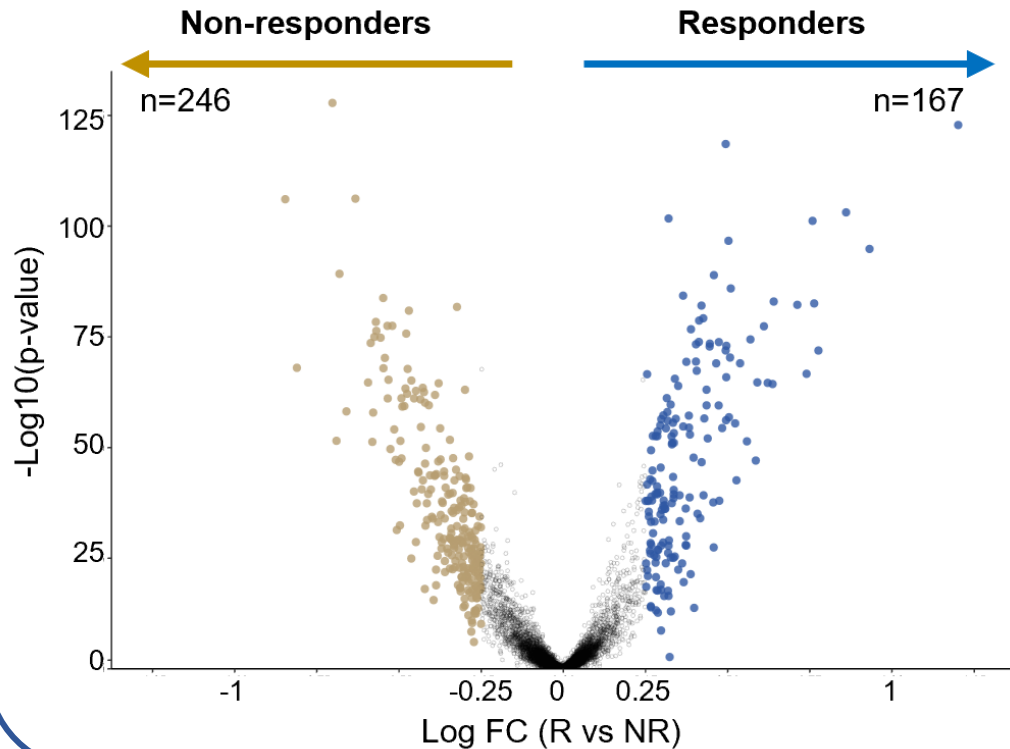
scRNA-seq CD8 T cell analysis

CD8 T cell in non-responders appear to:
- Exhibit increased activation
- Produce higher levels of cytokines (notably IFN- γ)

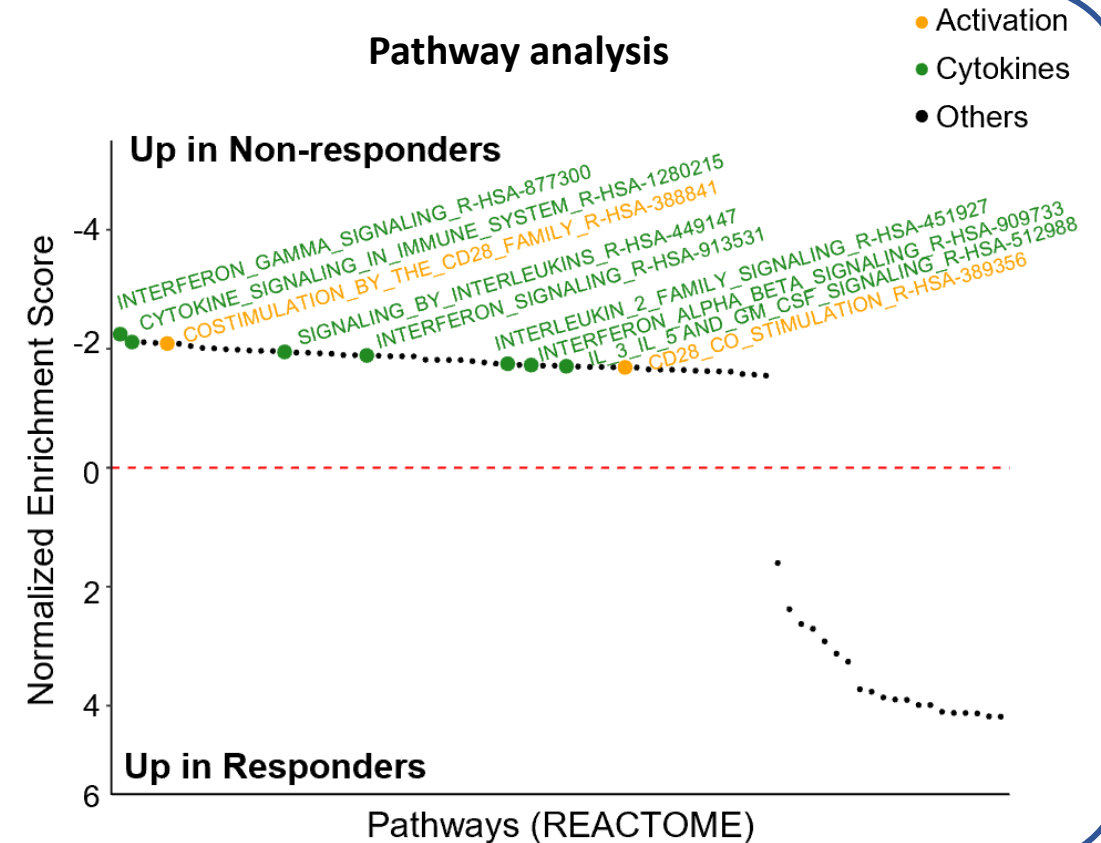
CD8 T cell
reintegration



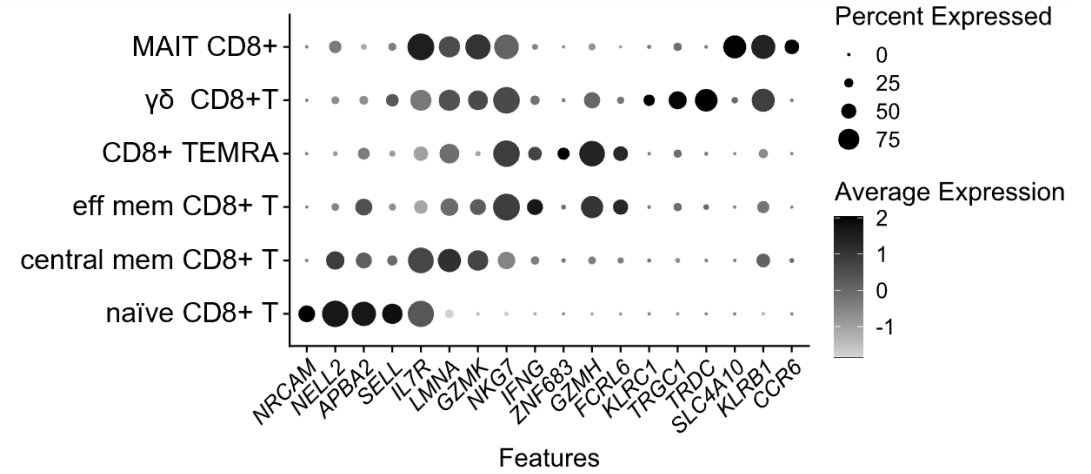
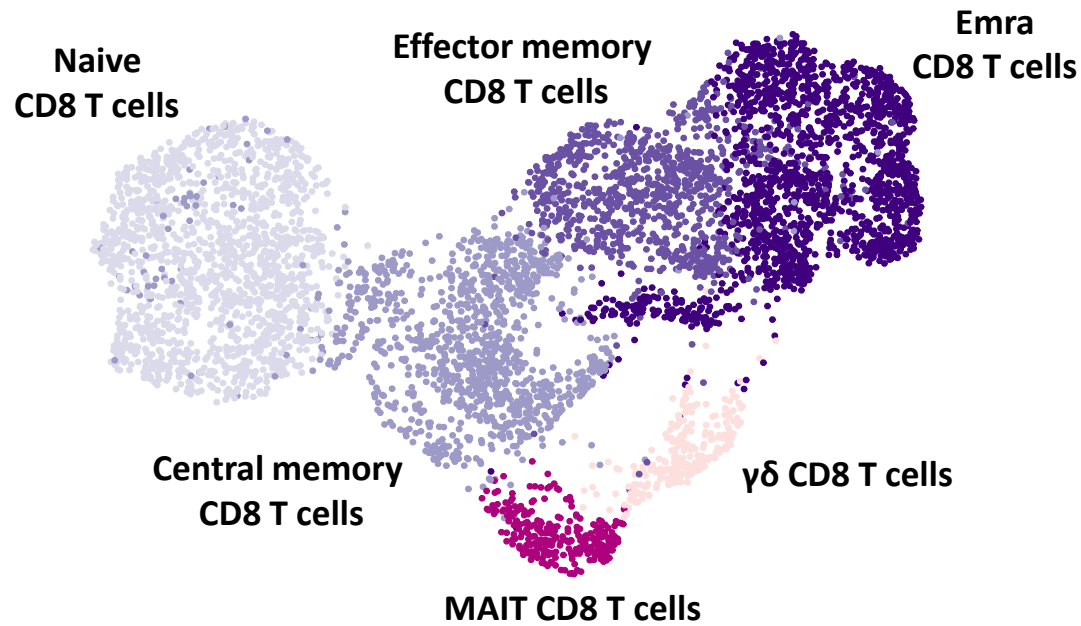
Differential expression analysis



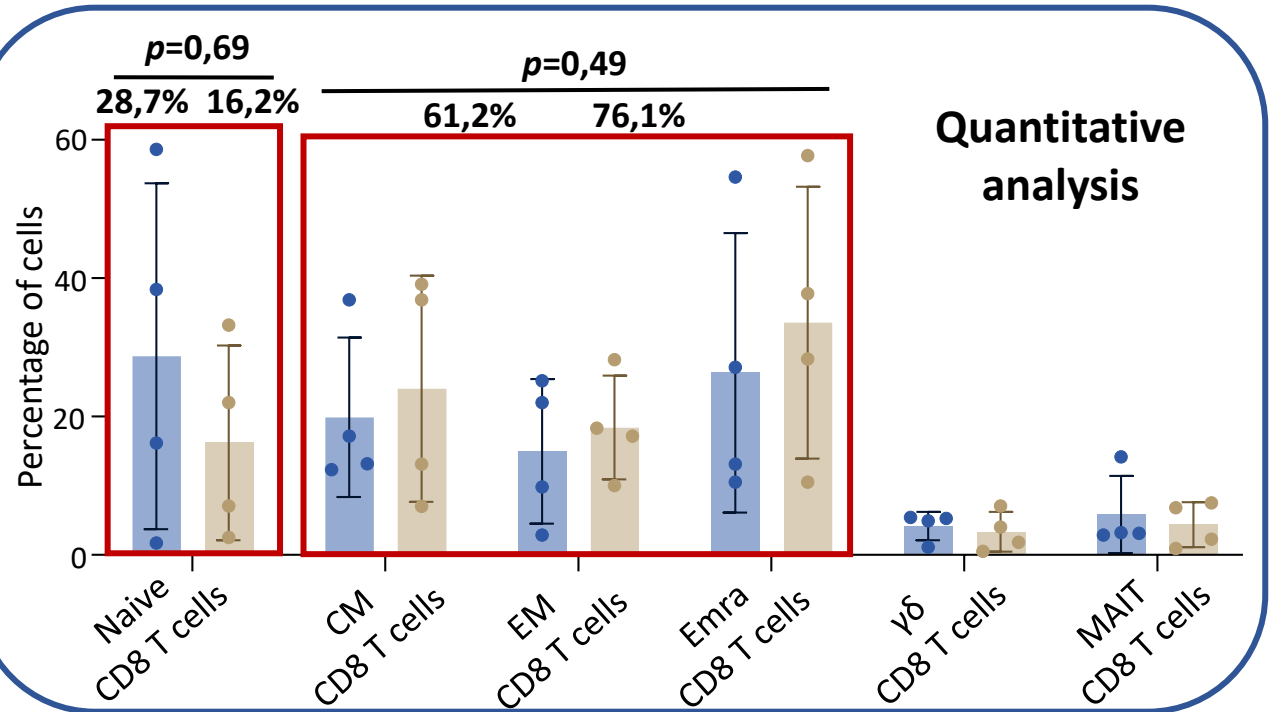
Pathway analysis



scRNA-seq CD8 T cell analysis

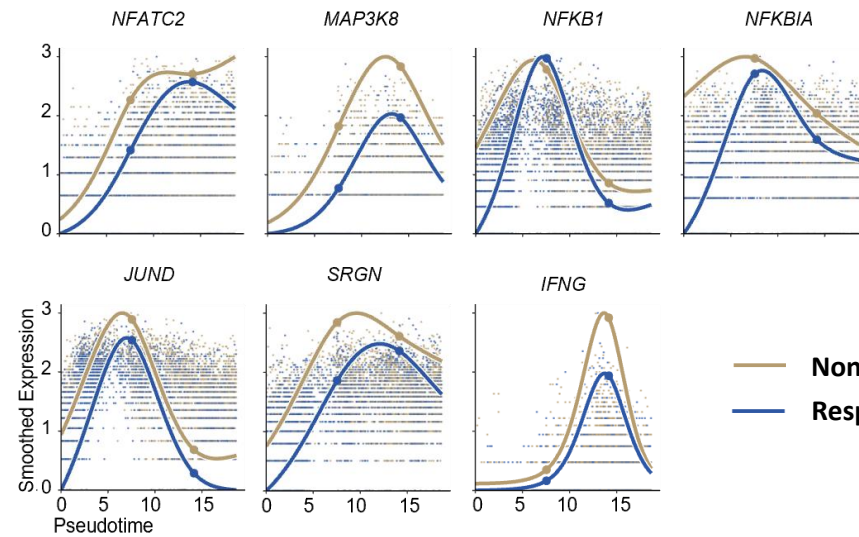
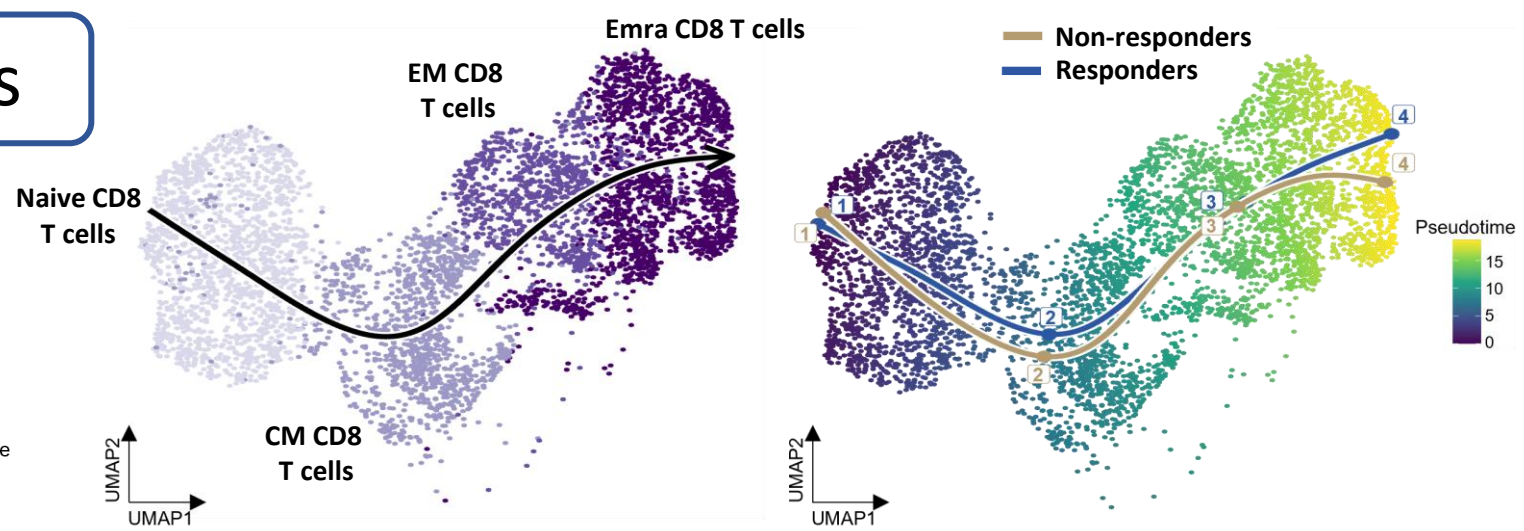
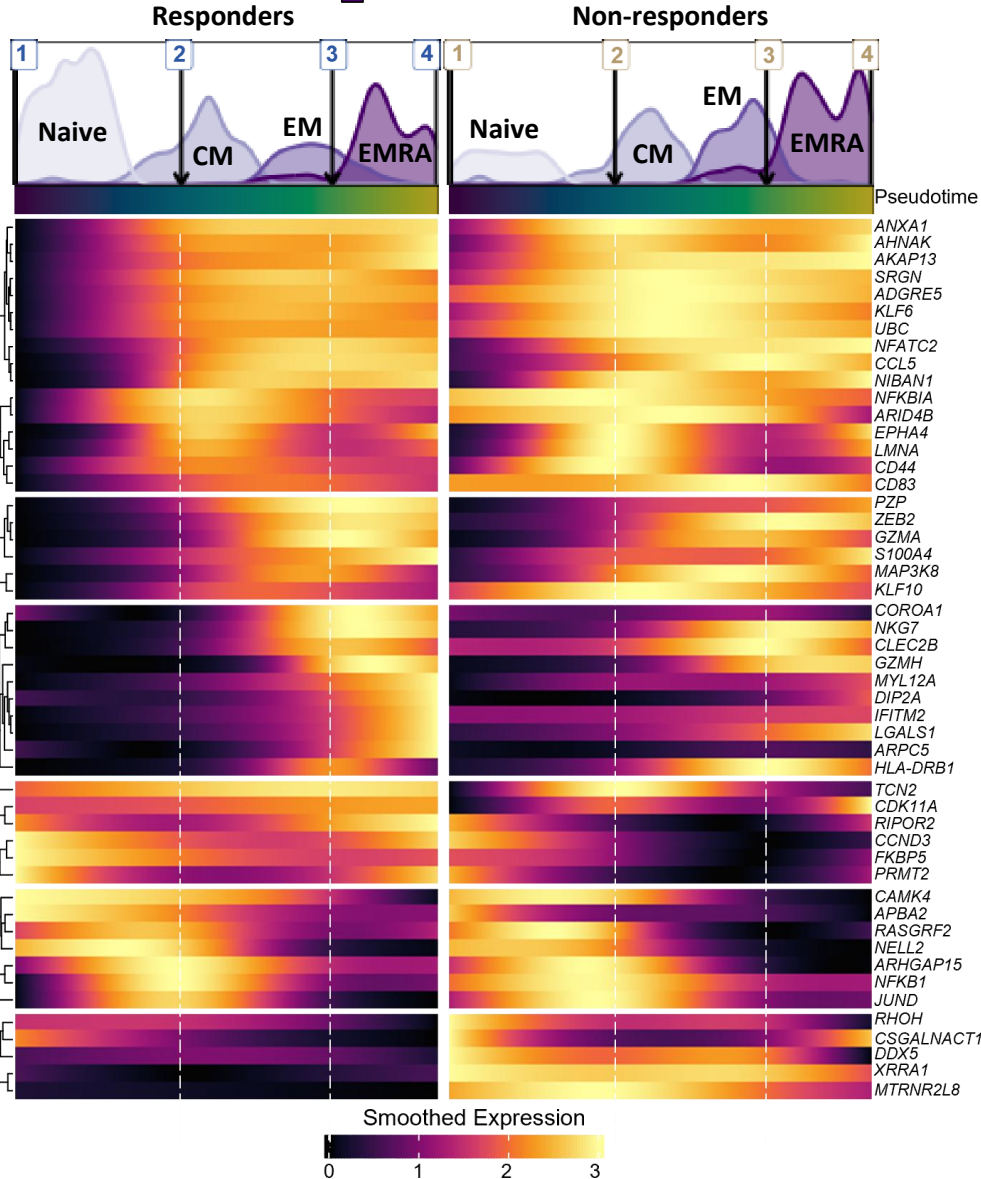


CD8 T cells in non-responders appear to be more differentiated



scRNA-seq CD8 T cell analysis

■ naïve CD8+ T
■ central mem CD8+ T
■ eff mem CD8+ T
■ CD8+ TEMRA

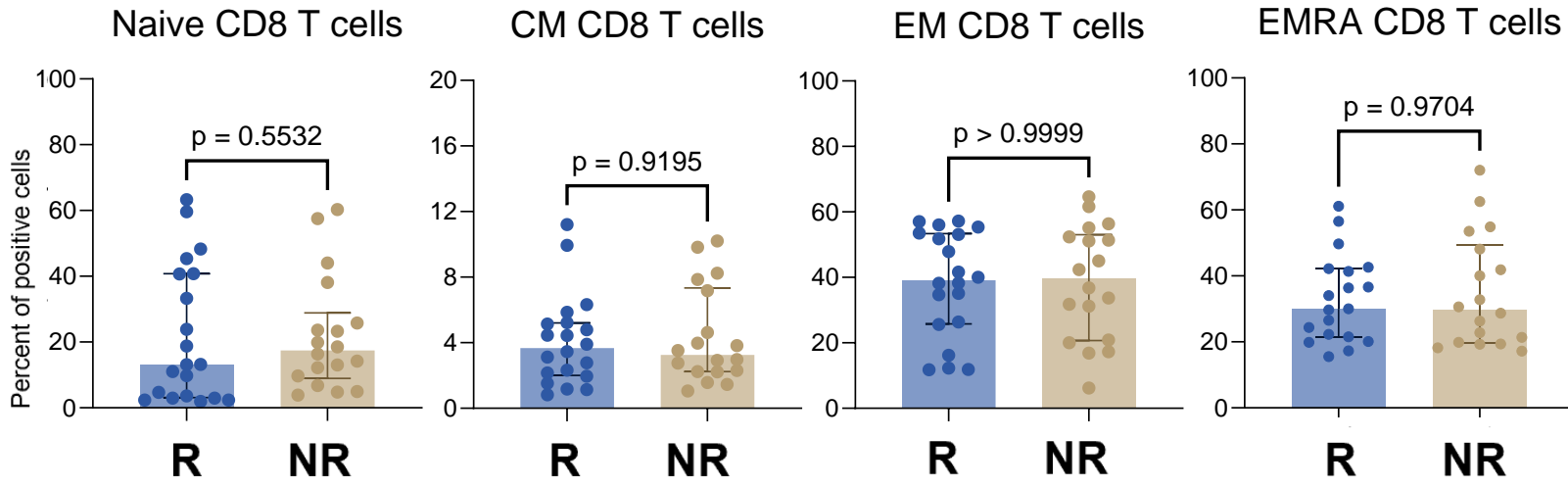
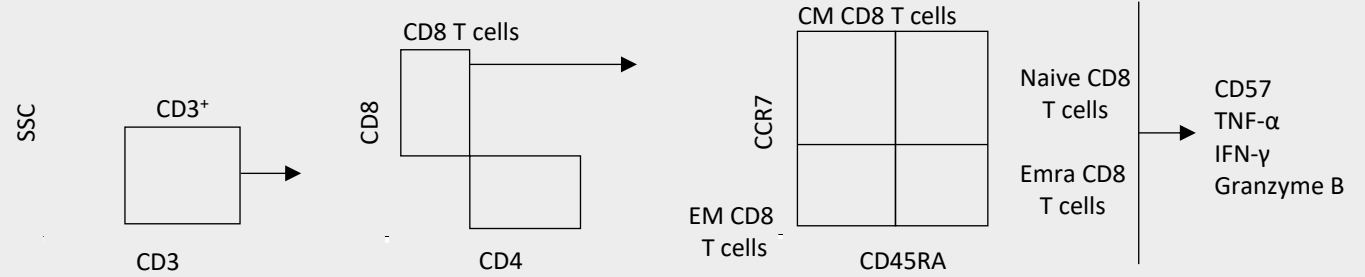


Differentiation trajectory analysis

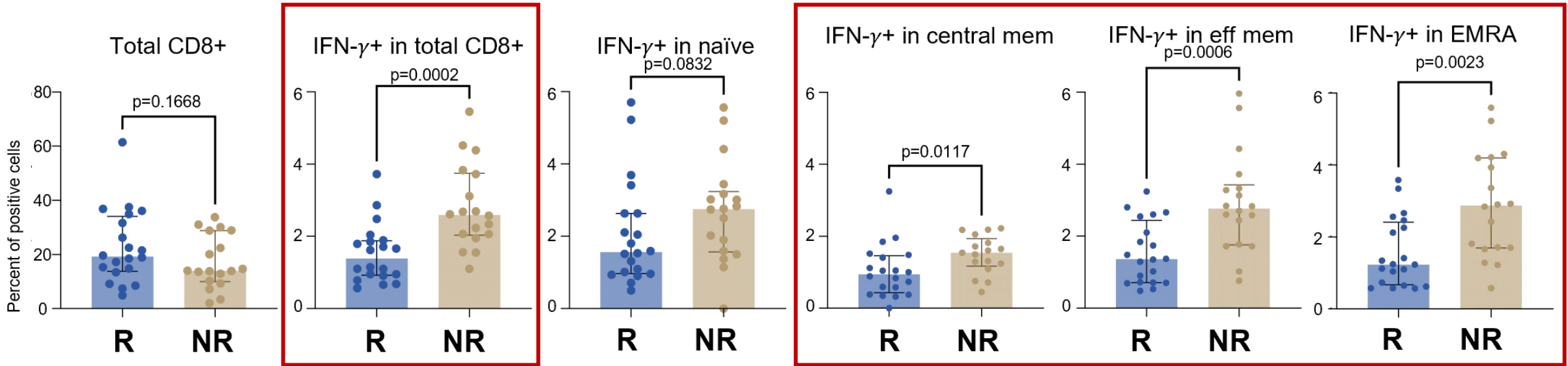
CD8 T cells in non-responders appear to:

- Exhibit increased activation
- Produce higher levels of IFN- γ

Cytometry CD8 T cell analysis



CD8 T cells in non-responders :
 - Are more activated
 - Produce higher levels of IFN- γ at baseline



Conclusion



These findings highlight a baseline state of heightened CD8 T-cell activation in patients who subsequently fail rituximab.



Suggesting that CD8 T cell-mediated immunity may play a more important role than B cell-driven mechanisms in these individuals.



Validation in independent cohorts could support the development of stratified therapeutic strategies and refine clinical decision-making in ITP.



Ritux Plus 2 Trial

Thank you for your attention



Sylvain Audia, MD, PhD



Baptiste Lamarthée, PhD



Alexis Varin, PhD, bioinfo ingeneer

Noémie Herrman, lab tech

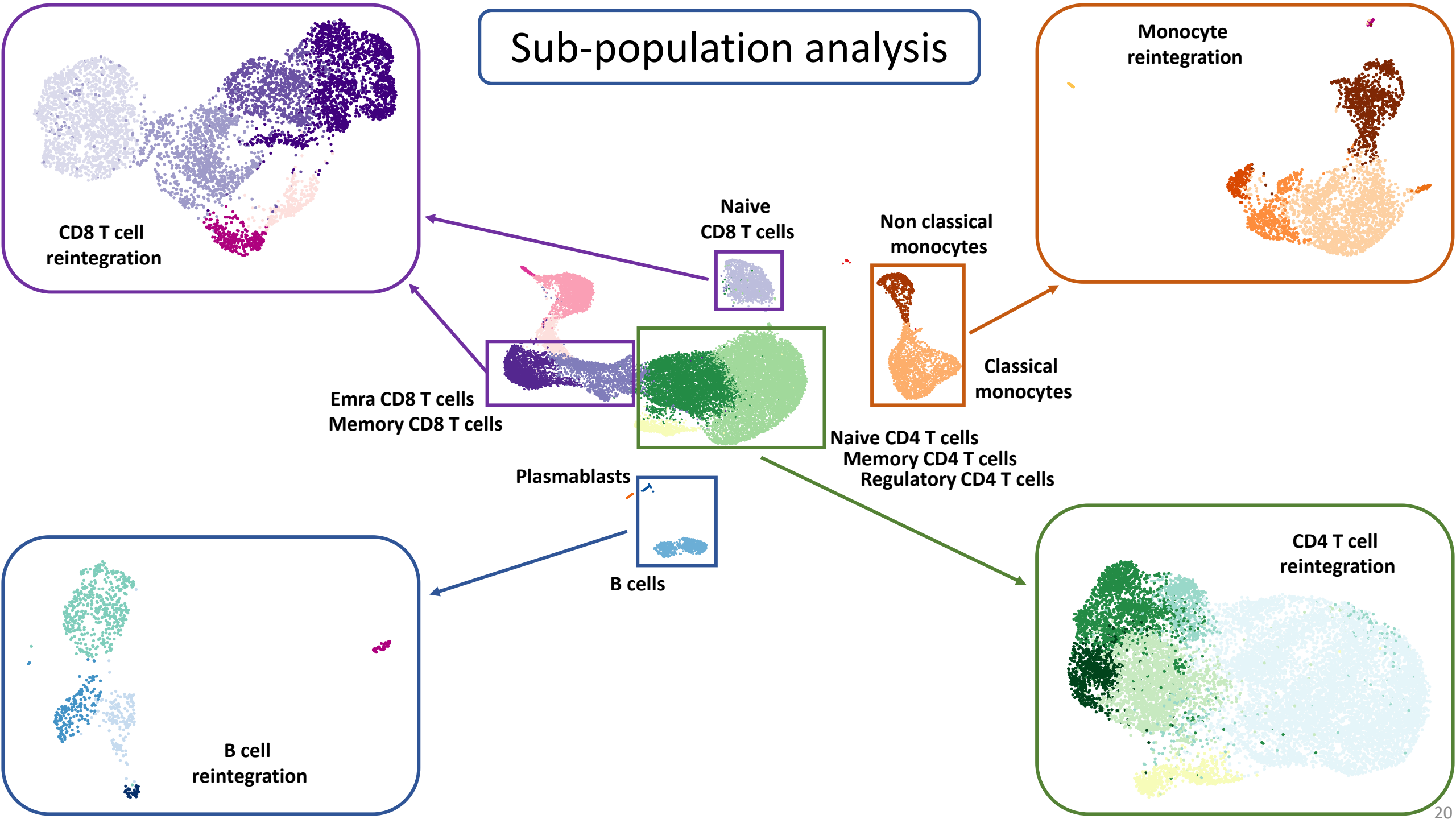
Claudie Cladière, lab tech

Bernard Bonnotte, MD, PhD



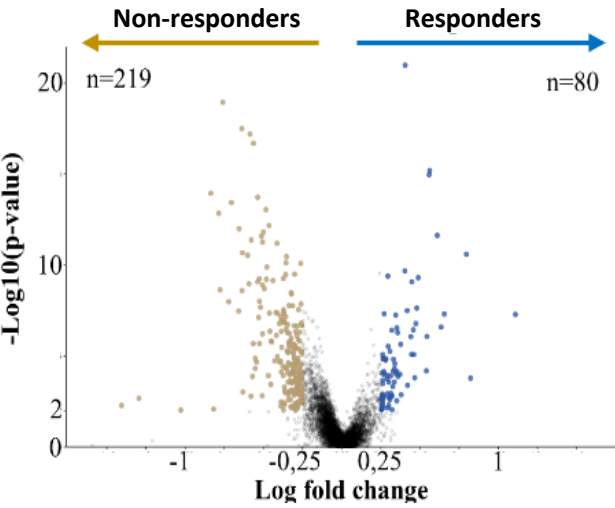
Contact information: roman.pralieux@chu-dijon.fr
sylvain.audia@ube.fr

Sub-population analysis

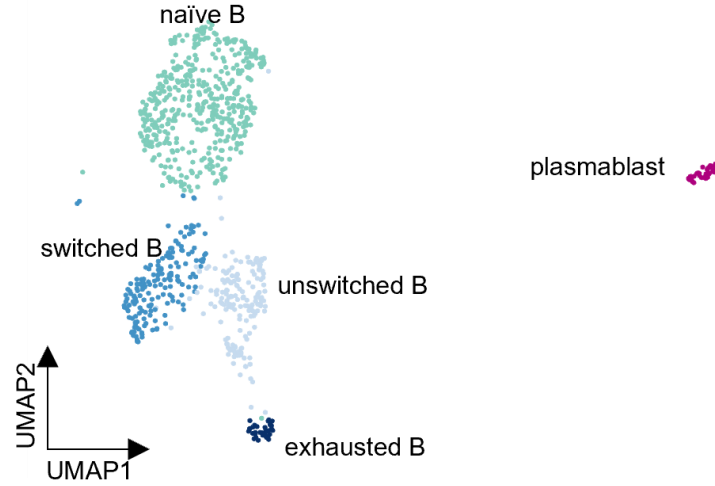


B cell analysis

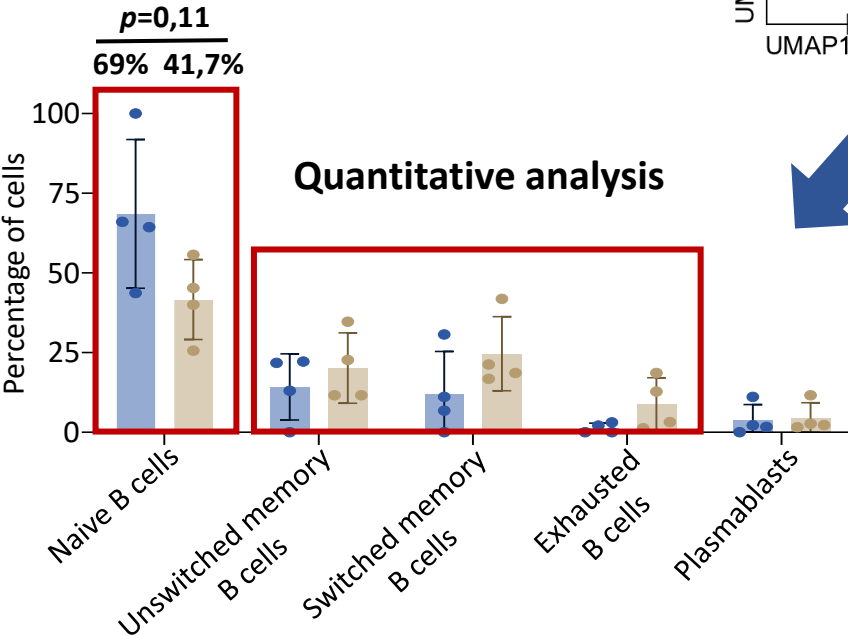
Differential expression analysis



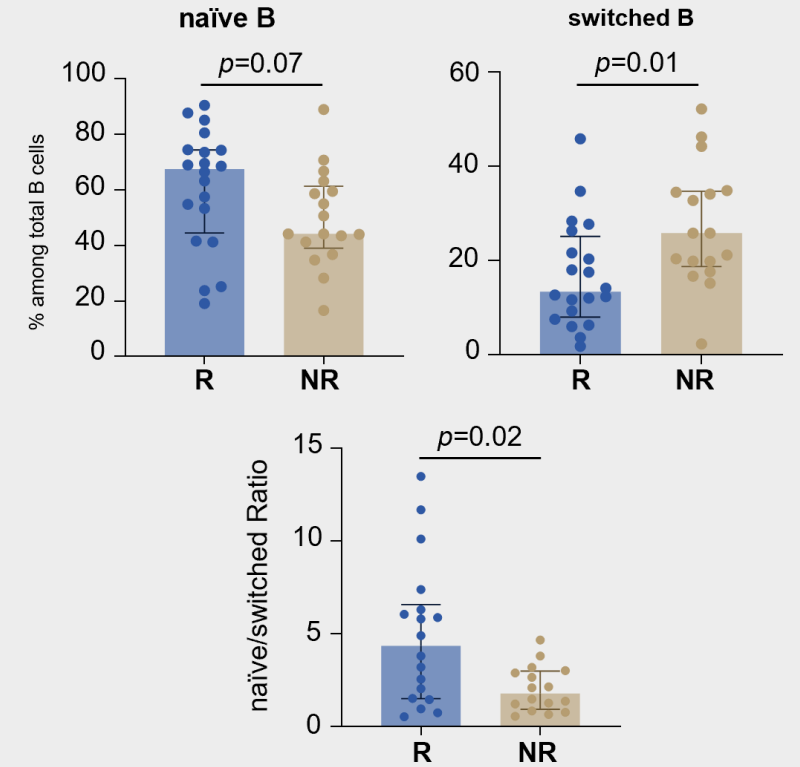
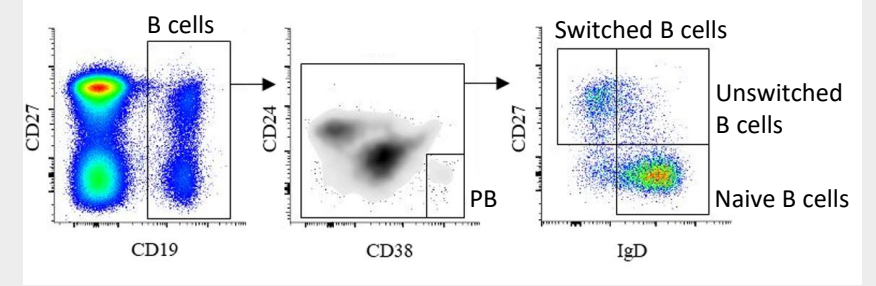
scRNA-seq B cell analysis



Quantitative analysis



Cytometry B cell analysis



B cells in non-responders are more differentiated

Patient characteristics for cytometry analysis

	Responders n=20		Non-responders n=18		p-value
Age (years)	58	[45-69]	64	[45-75]	0.61*
Gender					
Men	11	55%	9	50%	0.99**
Women	9	45%	9	50%	
Platelets at sampling (x10 ⁹ /L)	21	[10-35]	14	[5-27]	0.28*
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Persistent (3-12 months)	5	25%	3	16.7%	0.7**
Chronic (>12 months)	11	55%	11	61.1%	0.75**
Type of ITP					
Primary	13	65%	15	83.3%	0.28**
Secondary [†]	7	35%	3	16.7%	
Previous treatments received					
Steroids	19	95%	16	88.9%	0.59**
IVIg	8	40%	8	44.4%	0.99**
TPO receptor agonists	5	25%	3	16.7%	0.7**
Dapsone	10	50%	7	38.9%	0.53**
Rituximab	3	15%	0	0%	0.23**
Splenectomy	5	25%	0	0%	0.05**
Others	4	20%	1	5.6%	0.2**
Treatments received <4 weeks prior to sampling					
Steroids	6	30%	7	38.9%	0.73**
IVIg	0	0%	1	5.6%	0.5**
TPO receptor agonists	2	10%	3	16.7%	0.65**
Dapsone	5	25%	3	16.7%	0.7**
Others	1	5%	2	11.1%	0.59**
Number of rituximab cycles (1g D1-D15) received during the follow-up					
1 cycle	15	75%	18	100%	-
2 cycles [‡]	2	10%	0	0%	-
3 cycles [‡]	3	15%	0	0%	-

[†]Secondary ITP: 6 Evans syndrome and 1 antiphospholipid syndrome for responders, 2 systemic lupus and 1 antiphospholipid syndrome for non-responders.

[‡]Multi-responders: some responder having experienced multiple relapses during the course of treatment, each followed by a response lasting more than one year after subsequent rituximab administration.

Data reported as median [1st quartile-3rd quartile] or number with %. *Mann-Whitney test, **Fisher's exact test.
ITP = Immune thrombocytopenia; IVIg = Intravenous immunoglobulin; TPO = Thrombopoietin.