



11-13  
SEPT.  
2024

LILLE  
GRAND PALAIS

# CONGRÈS FRANÇAIS d'HÉMOSTASE



## Masterclass #8

# Omics et Hémostase

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Marjorie Poggi - Marseille, Centre de Recherche en CardioVasculaire et Nutrition



Team 2

Thrombosis, Platelets and  
Vascular Disorders

12 septembre 2024



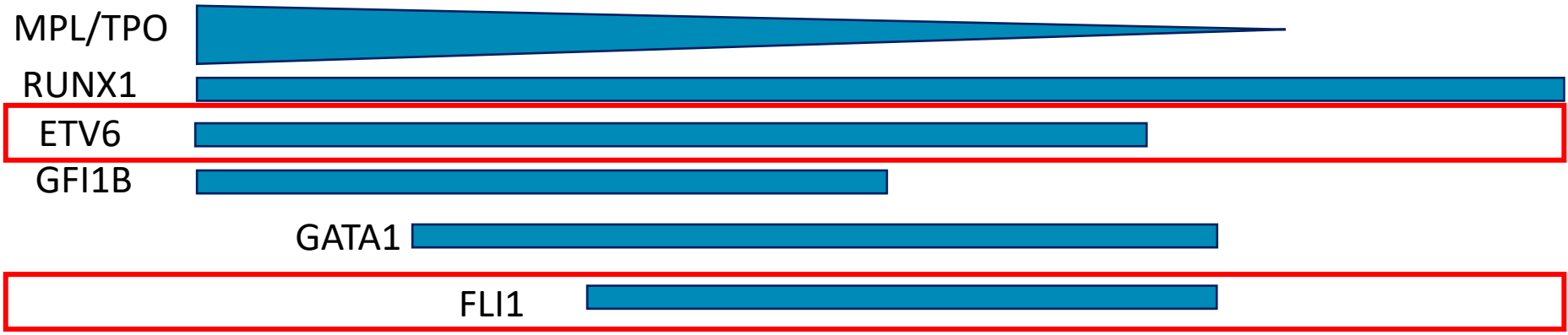
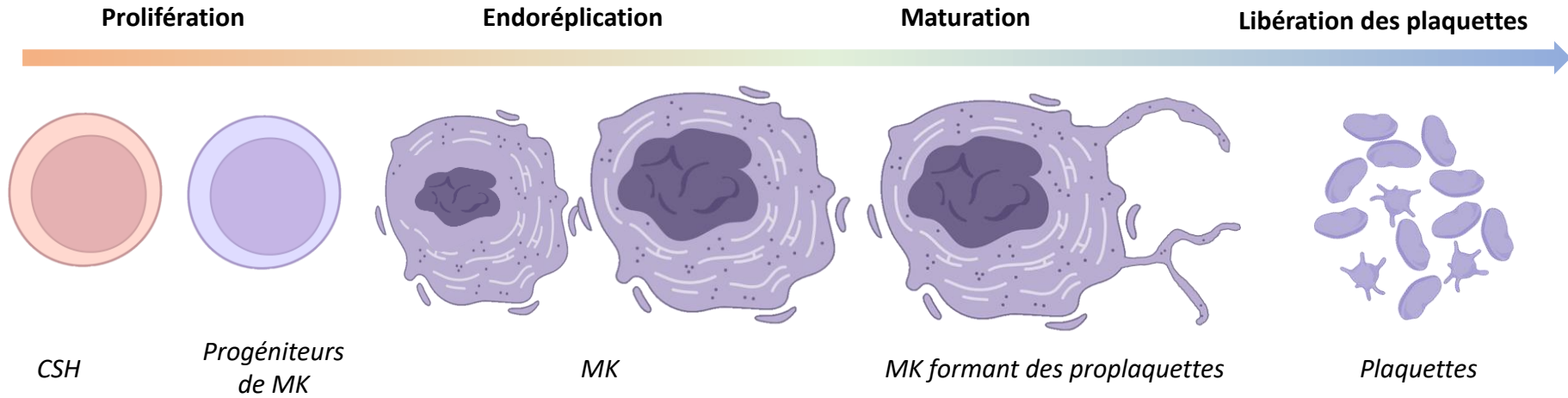
# Masterclass #8

## Omics et Hémostase

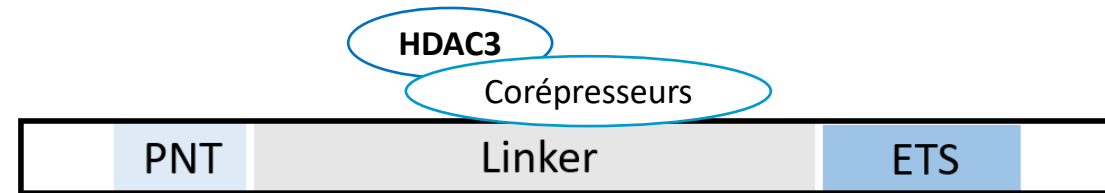
# Exploration fonctionnelle des thrombopénies constitutionnelles: apport du *single cell RNAseq*

Marjorie Poggi - Marseille, Centre de Recherche en CardioVasculaire et Nutrition

# La mégacaryopoïèse

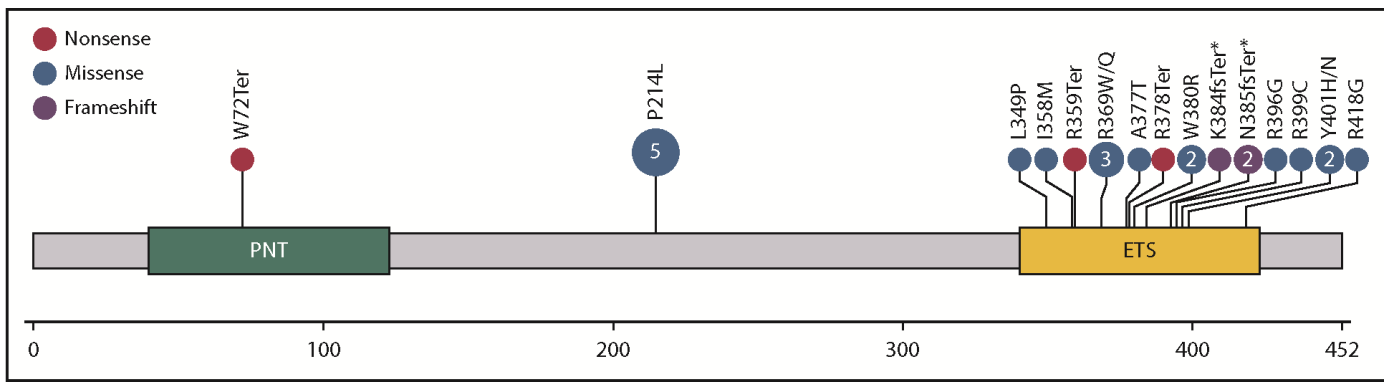


# Le facteur de transcription ETV6



- Angiogenèse *Whang et al., Genes Dev. 1998*
- Survie des cellules souches hématopoïétiques et maturation des mégacaryocytes *Hock et al., Genes Dev. 1997*
- Cible de réarrangements chromosomiques et de mutations somatiques → hémopathies malignes *Bejar et al., N.Eng.J.Med. 2011*

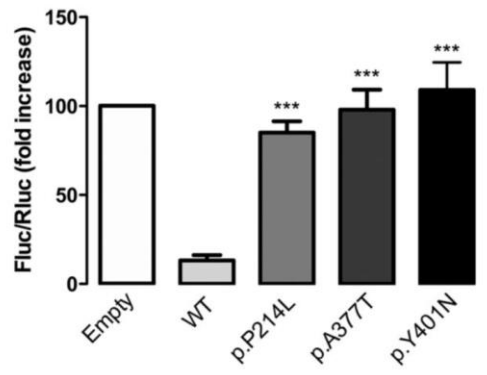
# Variants constitutionnels ETV6



- Thrombopénie légère à modérée
- Predisposition aux leucémies
- Défauts localisation nucléaire et activité transcriptionnelle
- Défaut de formation des pro-plaquettes
- Défaut de l'expression des gènes impliqués dans l'organisation du cytosquelette au cours de la formation des proplaquettes

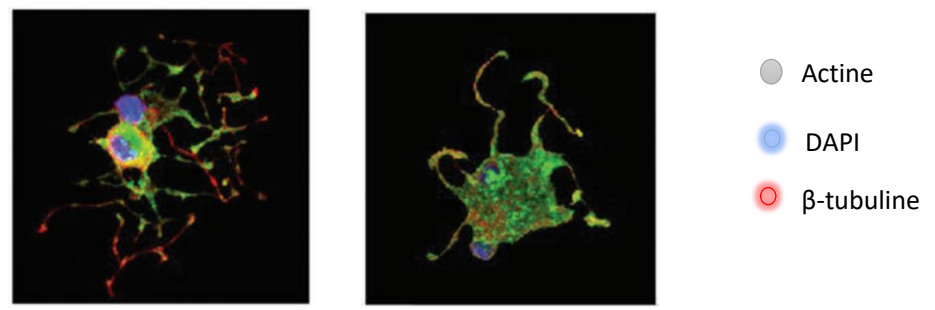
Di Paola *et al.*, Blood 2019

## Activité transcriptionnelle



cellules HEK 293 MSR

## Formation des proplaquettes



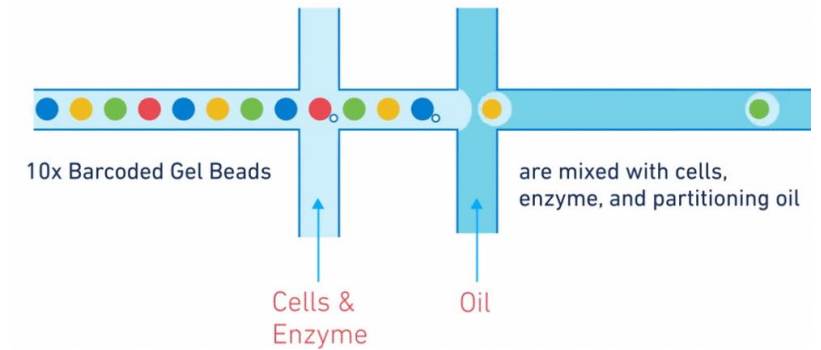
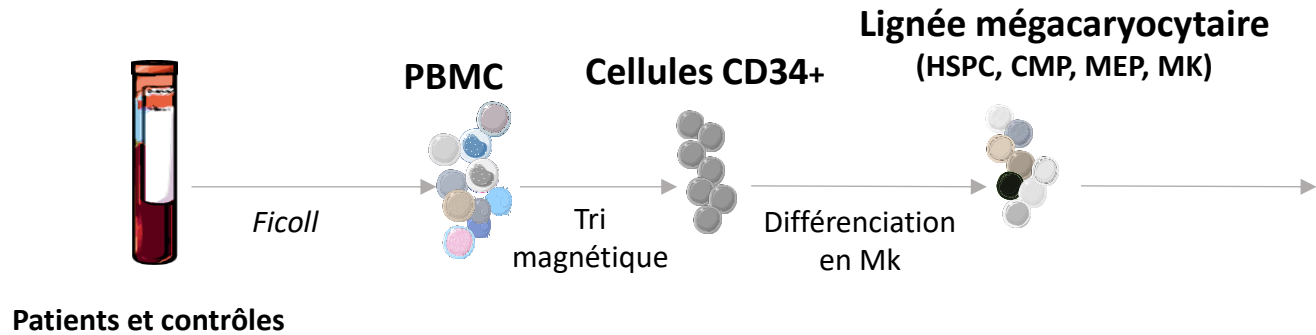
Sujet contrôle

Patient muté pour ETV6

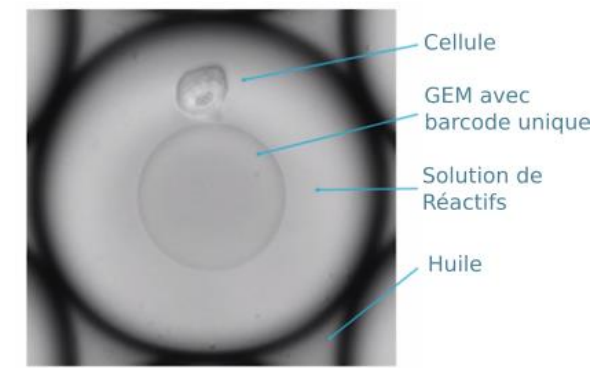
Poggi *et al.*, Haematologica 2017

**Mécanismes transcriptionnels ?**

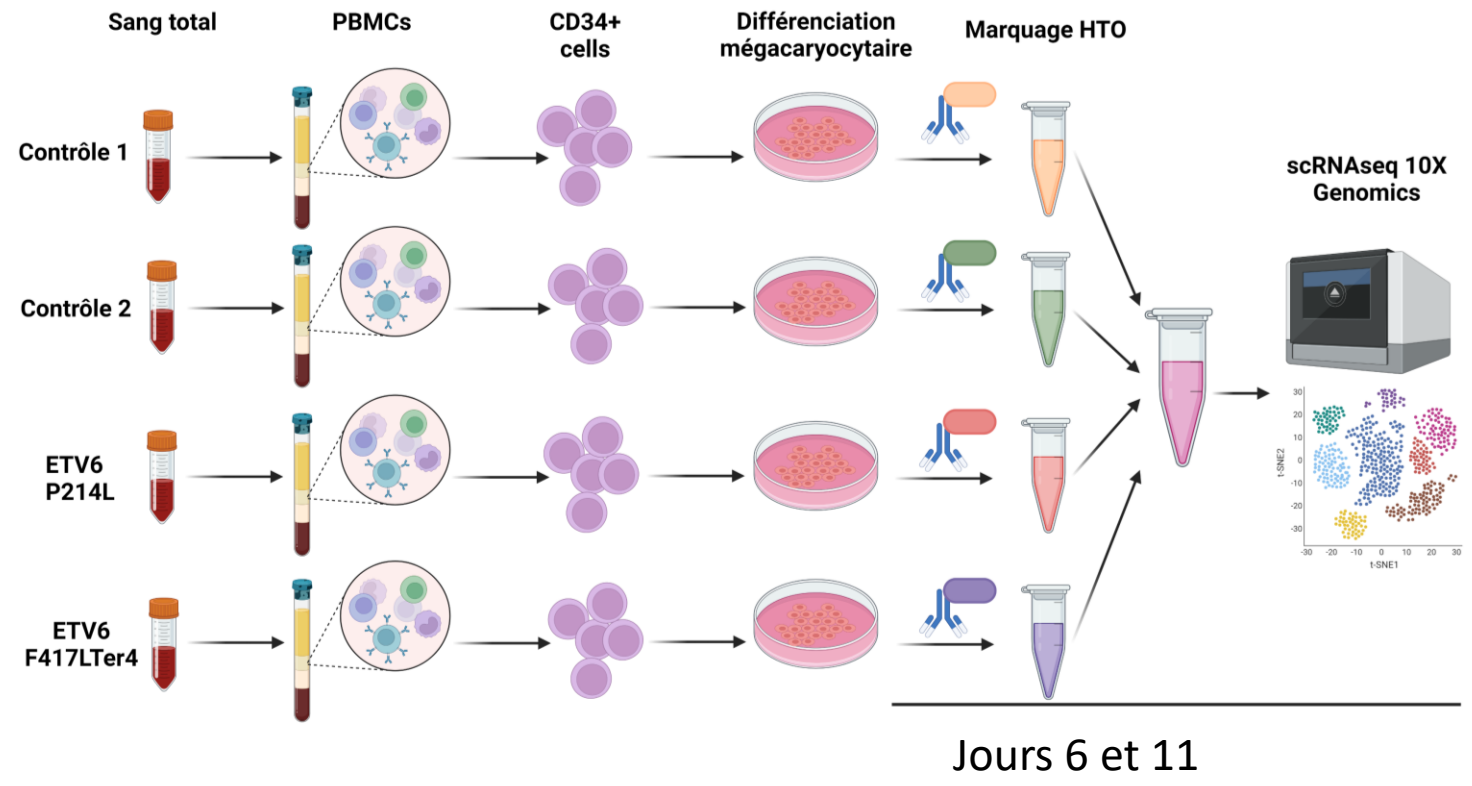
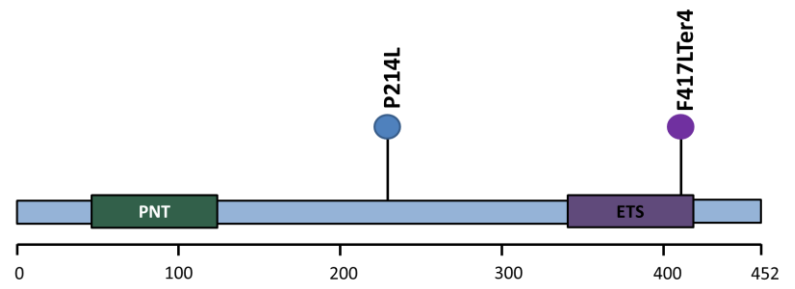
# Evaluer les conséquences transcriptionnelles des variations d'ETV6 au cours de la différenciation mégacaryocytaire



**scRNAseq**  
Jour 6 et jour 11

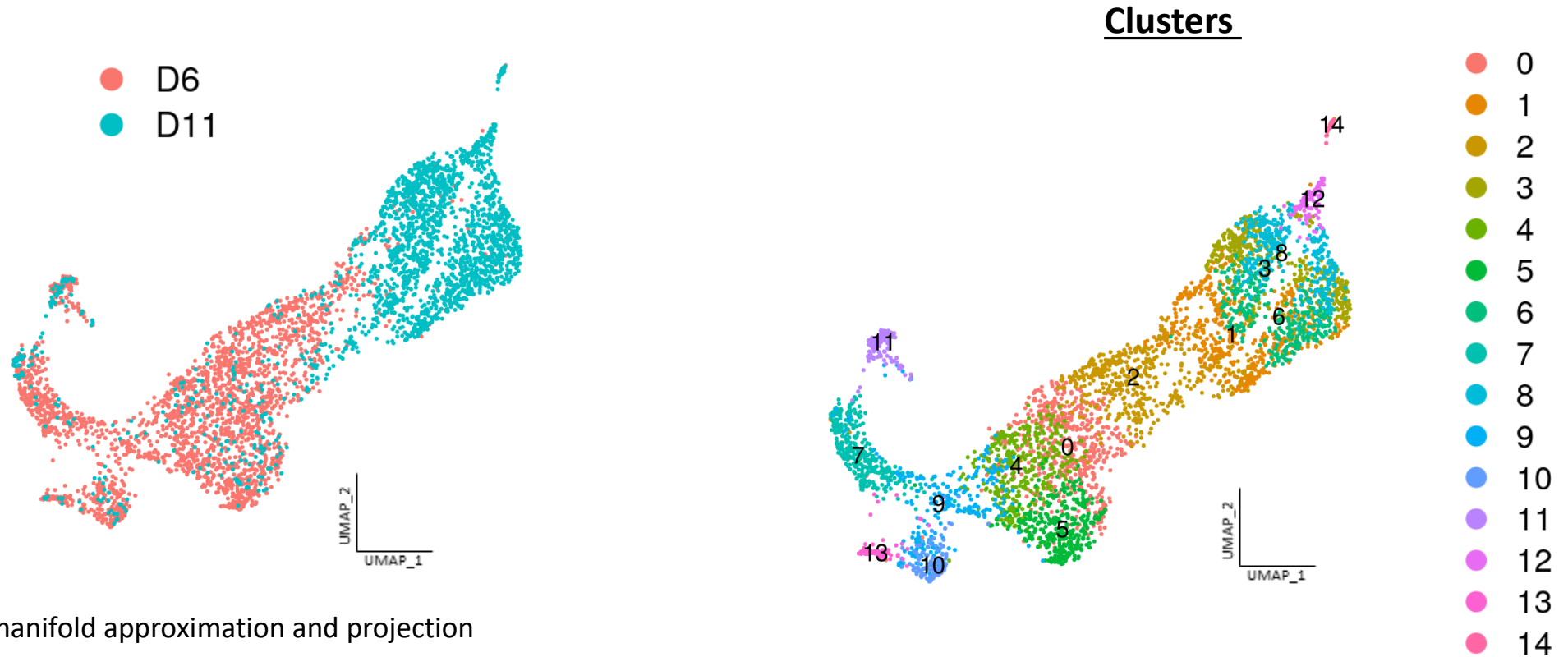


# HTO – Hash Tag Oligonucleotide



T Bigot, 2023

# Caractérisation de la culture « contrôle »



UMAP= Uniform manifold approximation and projection

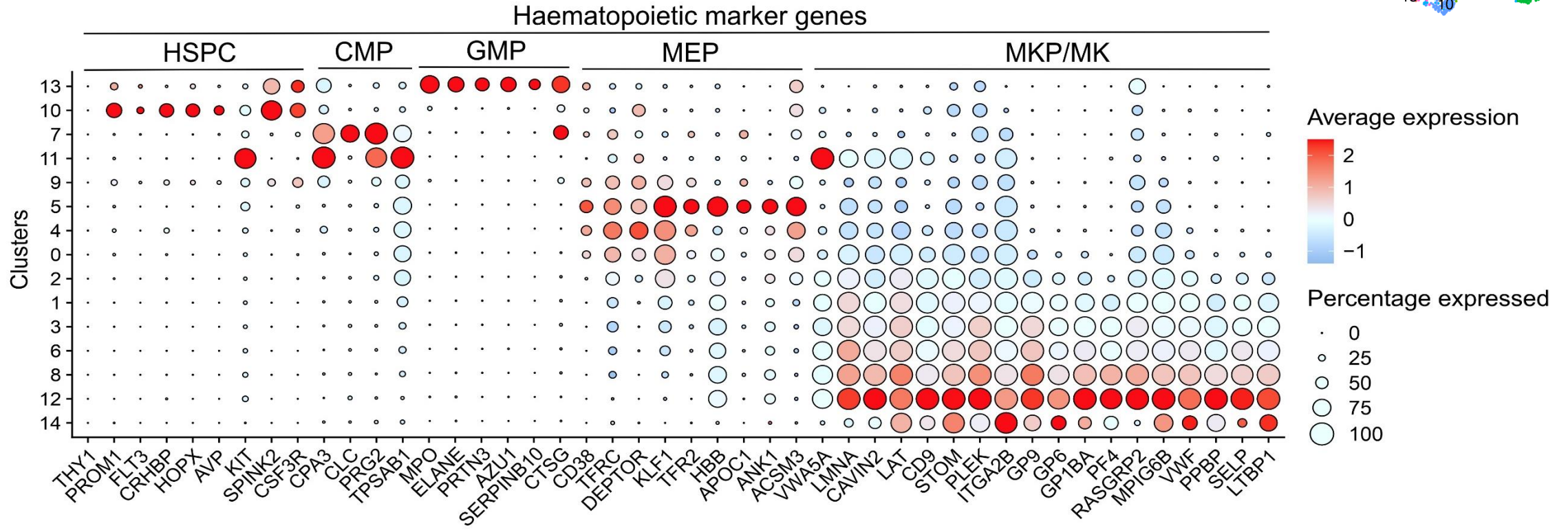
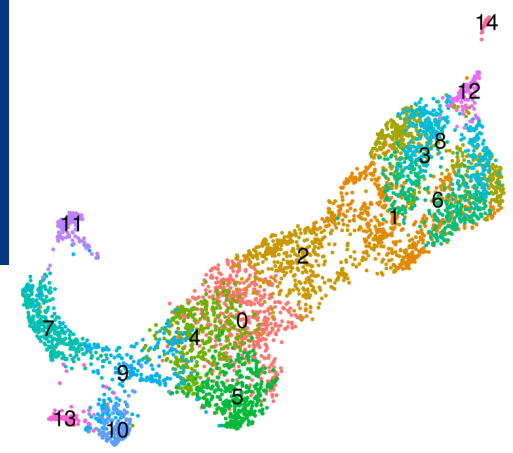
➔ Regroupement des cellules en fonction de leur proximité transcriptomique

*Bigot et al, JTH, 2023*



# Identification des types cellulaires

## Analyse « supervisée »



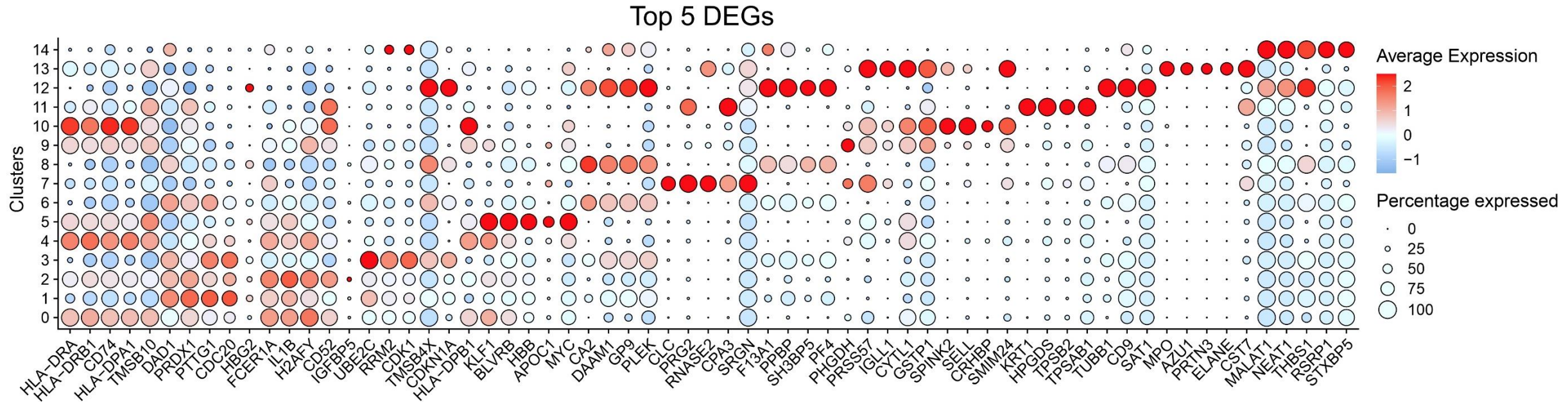
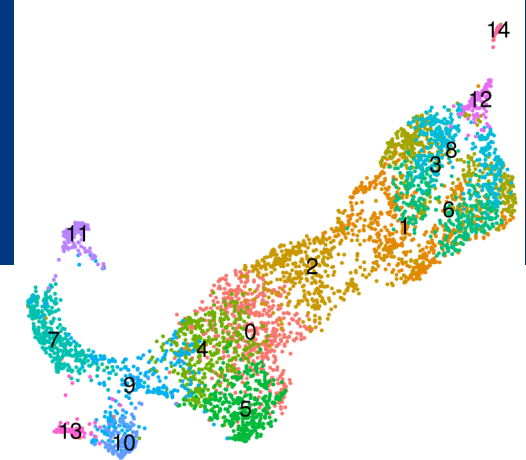
HSPC = Hematopoietic Stem/Progenitors cells  
 CMP = Common myeloid progenitors  
 GMP = Granulocyte-monocyte progenitors

MEP = Mega-Erythroid progenitors  
 Mkp/MK = Megakaryocyte progenitors/MK

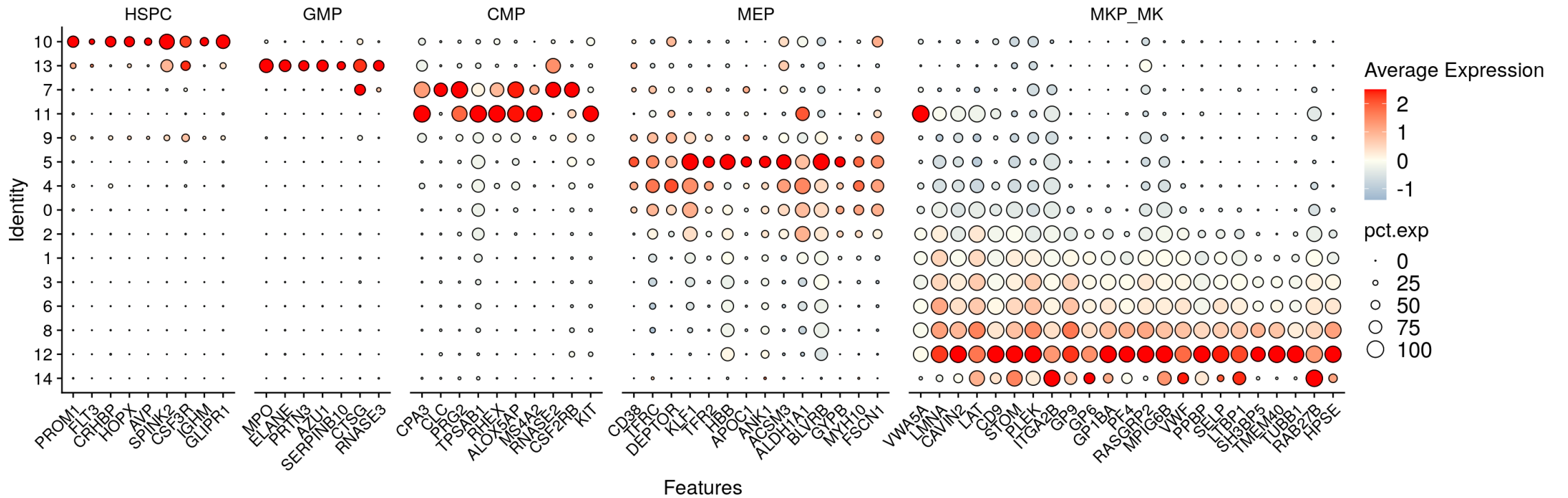
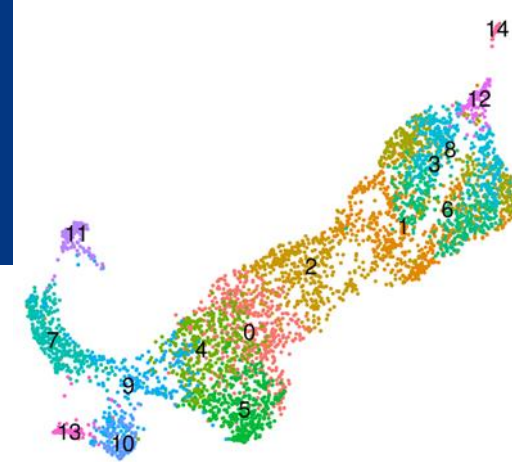
*Bigot et al, JTH, 2023*

# Identification des types cellulaires

## Analyse « non supervisée »



# Identification des types cellulaires

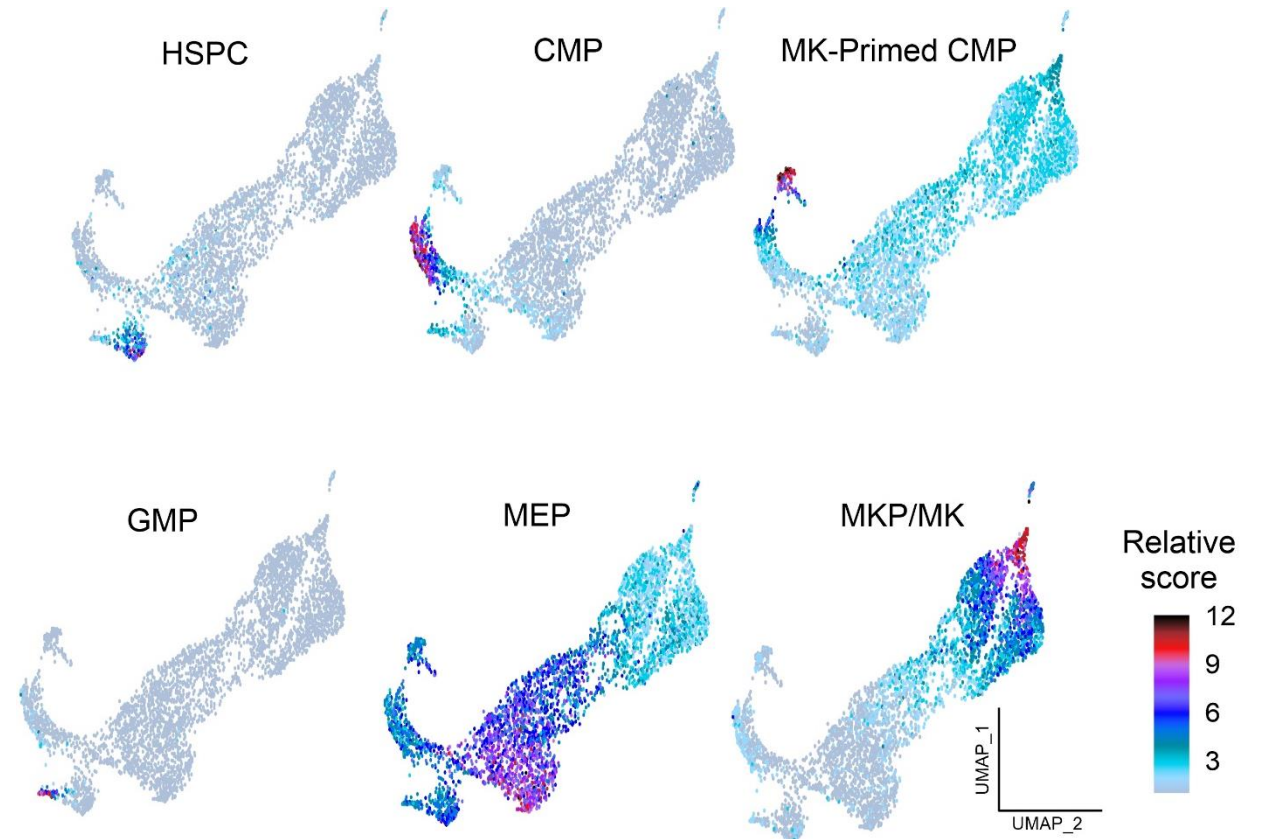
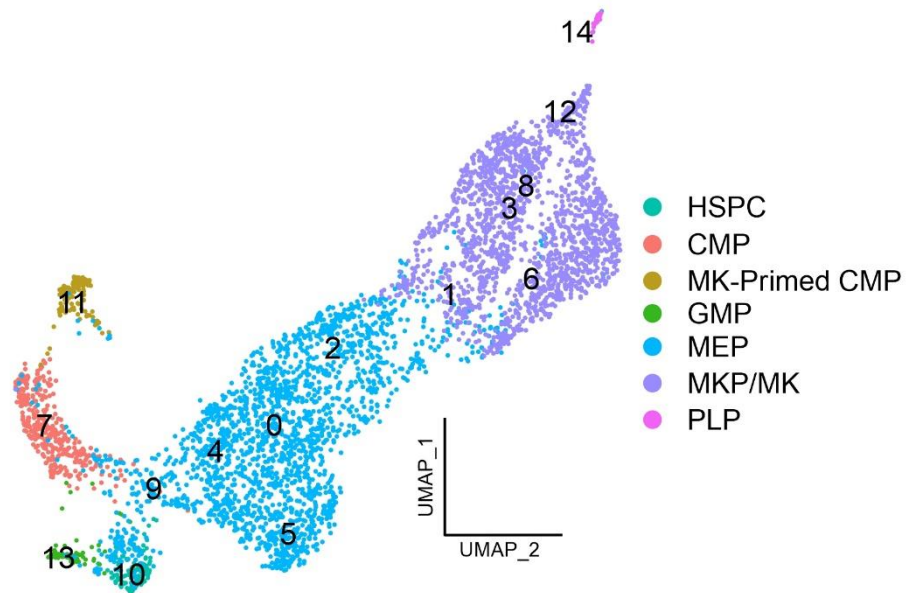


HSPC = Hematopoietic Stem/Progenitors cells  
 CMP = Common myeloid progenitors  
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# Identification des types cellulaires

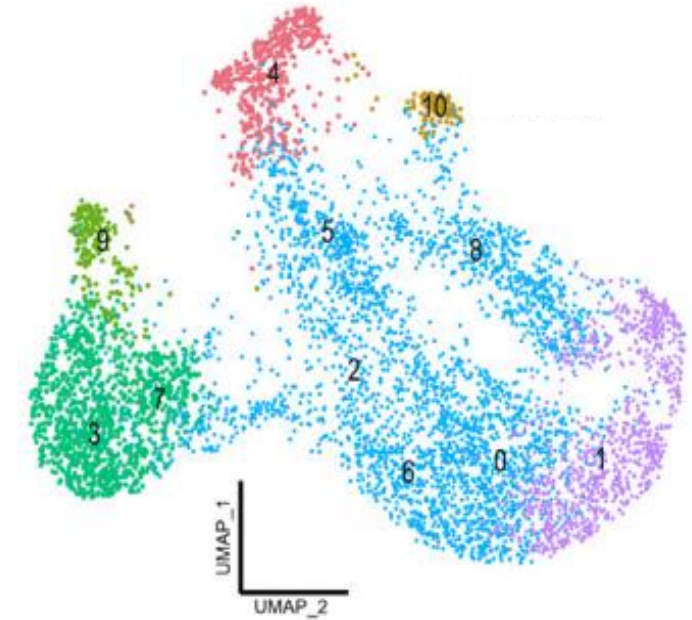
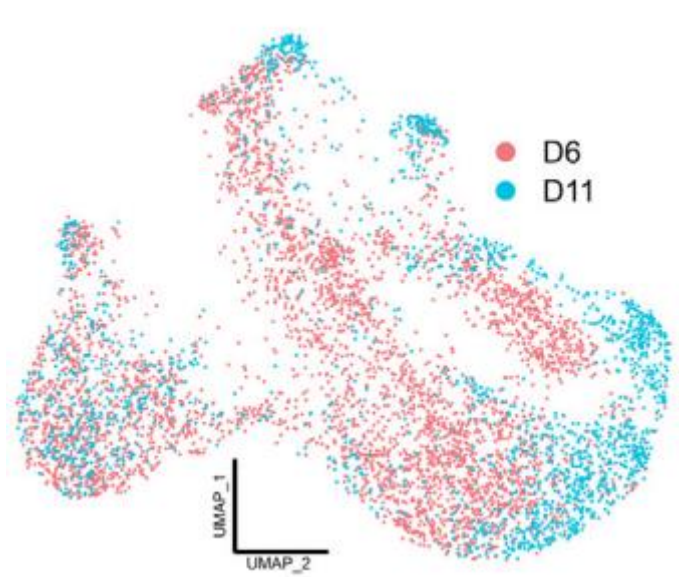


HSPC = Hematopoietic Stem/Progenitors cells  
 CMP = Common myeloid progenitors  
 GMP= Granulocyte-monocyte progenitors

MEP = Mega-Erythroid progenitors  
 Mkp/MK = Megakaryocyte progenitors/MK  
 PLP= platelet-like particles

*Bigot et al, JTH, 2023*

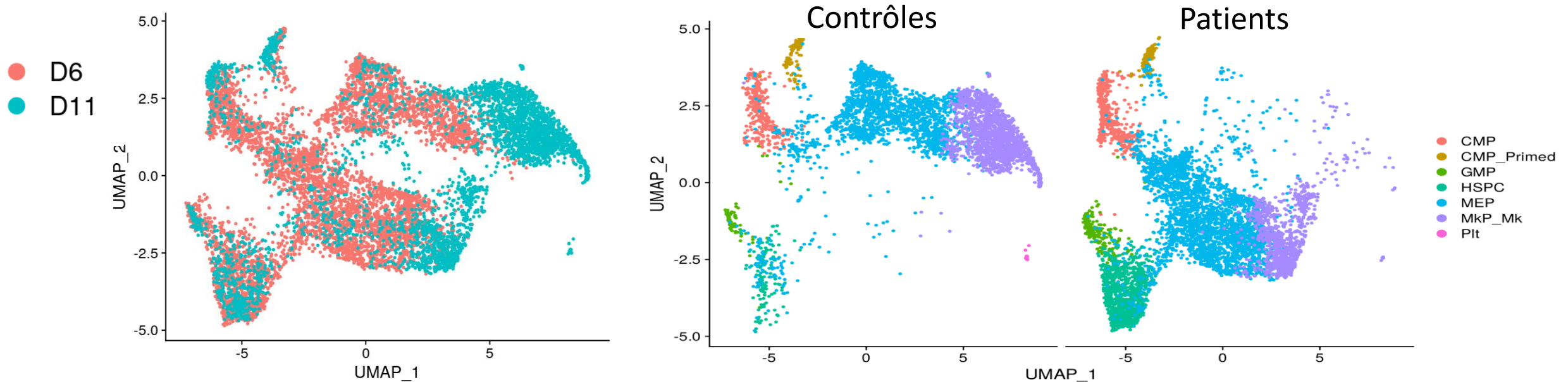
# Identification des types cellulaires déficiente en ETV6



- HSPC
- CMP
- MK-Primed CMP
- GMP
- MEP
- MKP/MK
- PLP

Bigot et al, JTH, 2023

# Identification de populations cellulaires aberrantes chez les patients porteurs de variants ETV6

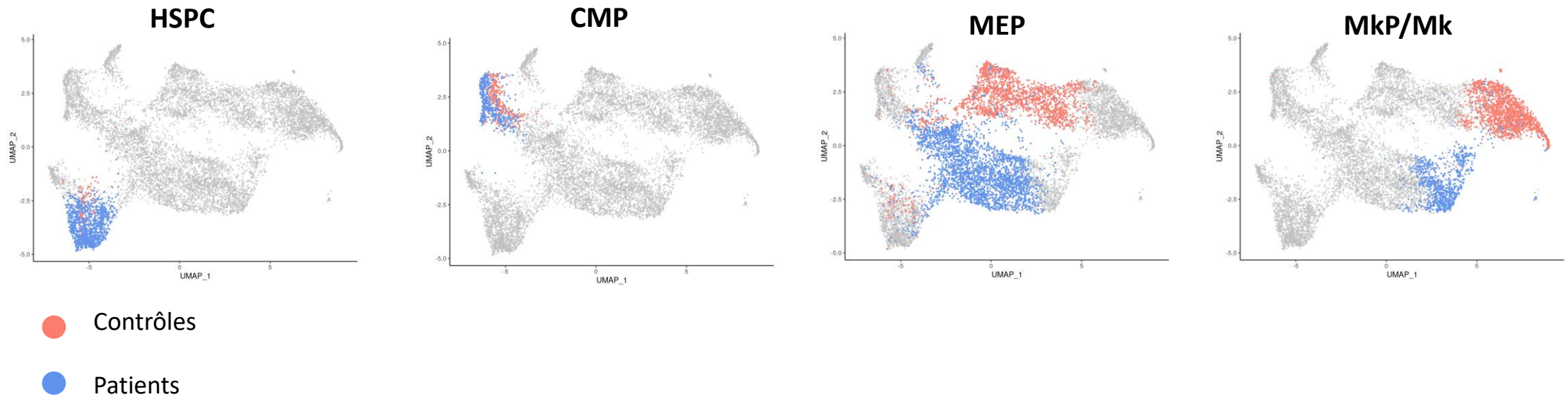


➔ Profils des HSPC, CMP et GMP similaires entre témoins et patients ETV6

➔ MEP et Mkp/MK mutés pour ETV6 présentent des profils très différents de ceux des cellules contrôles

*Bigot et al, JTH, 2023*

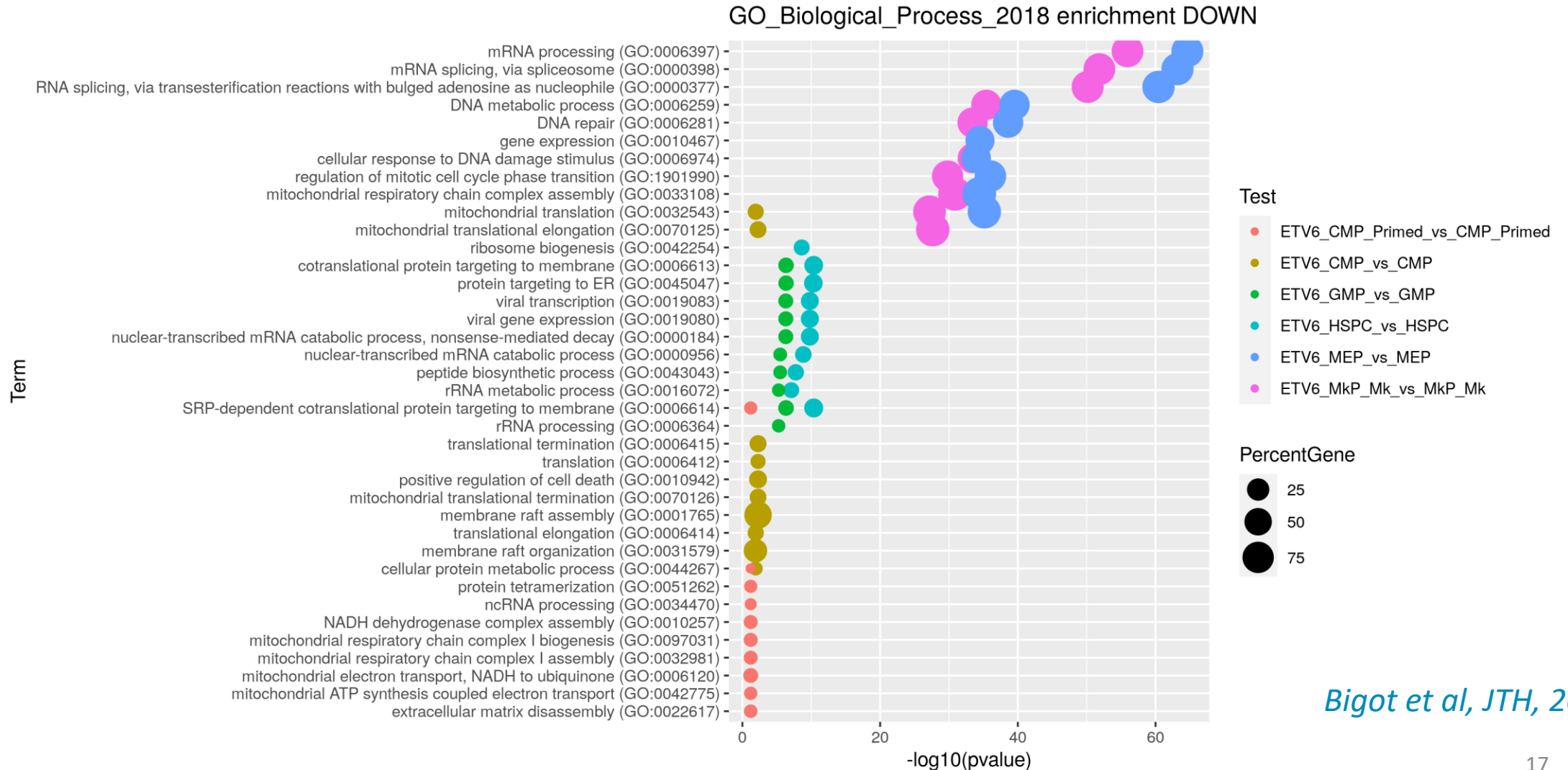
# Identification de populations cellulaires aberrantes chez les patients porteurs de variants ETV6



— Populations aberrantes de MEP et MkP/MK chez les patients porteurs de variants ETV6



# Voies dérégulées chez les patients ETV6



Bigot et al, JTH, 2023



# Voies dérégulées chez les patients ETV6

	Down	Up
MEP	<ul style="list-style-type: none"> <li>•mRNA processing - splicing- transport</li> <li>•DNA metabolic process, DNA repair</li> <li>•Mitochondrial metabolism</li> <li>•Mitochondrial translation</li> <li>•Localization to nucleus (mRNA export-protein import)</li> </ul>	<ul style="list-style-type: none"> <li>•Translation</li> <li>•Endothelial pathway (development, migration, regulation)</li> <li>•Interferon-gamma- and type 1 mediated signaling</li> <li>•Antigen processing and presentation</li> </ul>
MkP/MK	<ul style="list-style-type: none"> <li>•Mitochondrial translation</li> <li>•DNA metabolic process, DNA repair</li> <li>•Mitochondrial metabolism</li> <li>•RNA processing, splicing</li> <li>•Cell cycle</li> <li>•Localization to nucleus (mRNA export-protein import)</li> <li>•Platelet degranulation, aggregation, Mk differentiation</li> <li>•Regulation of actin polymerization or depolymerization</li> </ul>	<ul style="list-style-type: none"> <li>•Translation</li> <li>•Antigen processing and presentation</li> <li>•Interferon-gamma- and type 1 mediated signaling</li> <li>•Histone modifications (regulation, acetylation, demethylation, methylation, phosphorylation, ubiquitinylation)</li> </ul>

## C2VN – Groupe « plaquette / mega »



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Gabinaud Elisa  
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Medical  
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