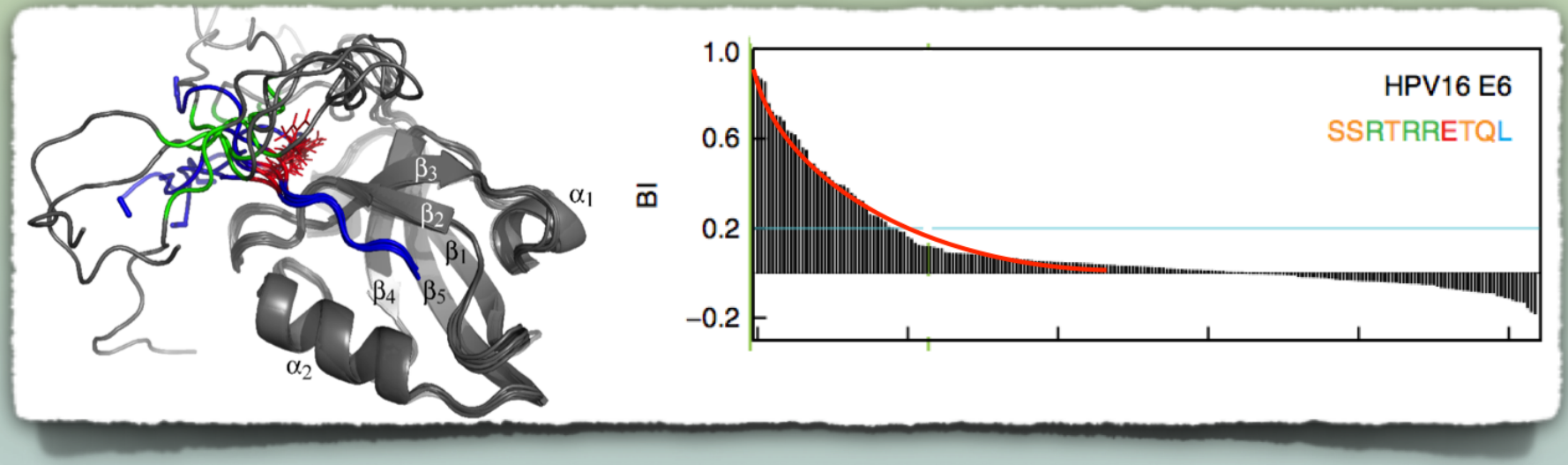
Perspectives biologique méthodologique de **InQuant :** du **ciblage** par des protéines virales à **ProFeatMap** pour la visualisation de listes



Yves Nominé, McF HC HDR

Equipe 'Oncoprotéines virales et réseaux domaine/motif' (Dr. G. Travé)

CBI – IGBMC

igbmc institut de génétique et de biologie moléculaire et cellulaire

CANCÉROPÔLE Est Régions Bourgogne-Franche-Comté / Grand Est

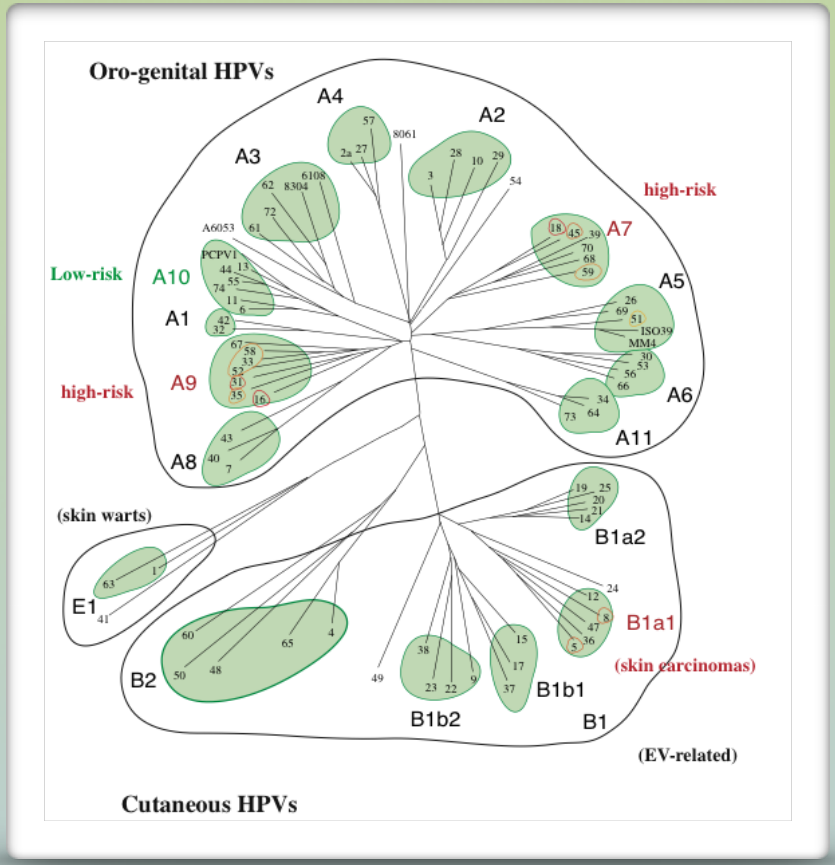
I/ Papilloma Virus & cancers

HPV

>200 strains
epithelia (mucosal, cutaneous)

90% → **low-risk**
warts
lesions

10% → **high-risk**
CANCER:
cervical
skin
anal
head & neck

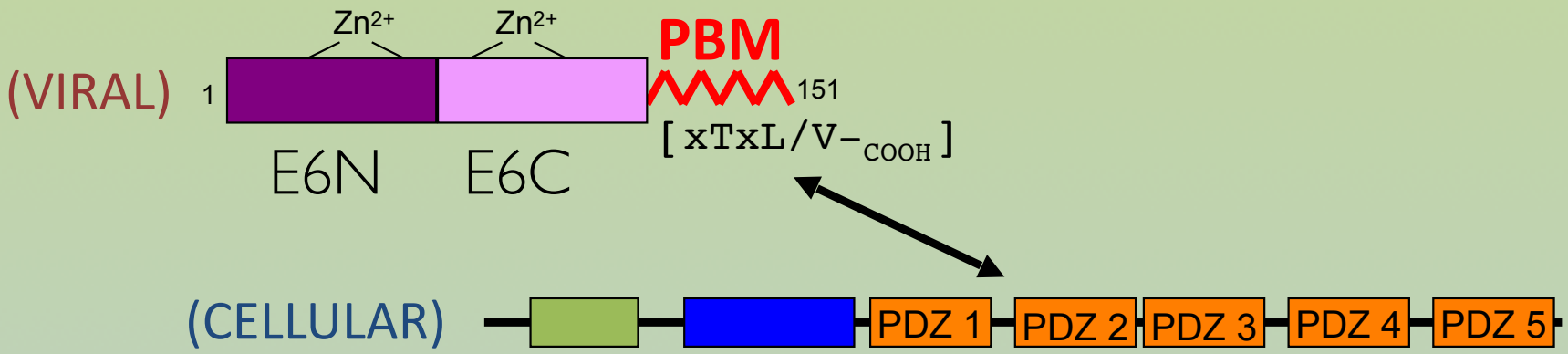


Phylogenetic tree of HPVs

Synergy of 2 proteins: **E6** & **E7**

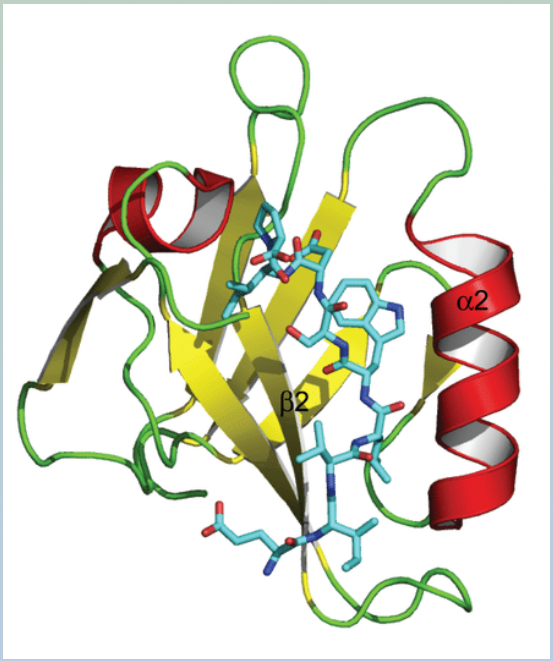
- the 2 major oncoproteins of high-risk HPVs
- induced cell proliferation
- required for viral replication

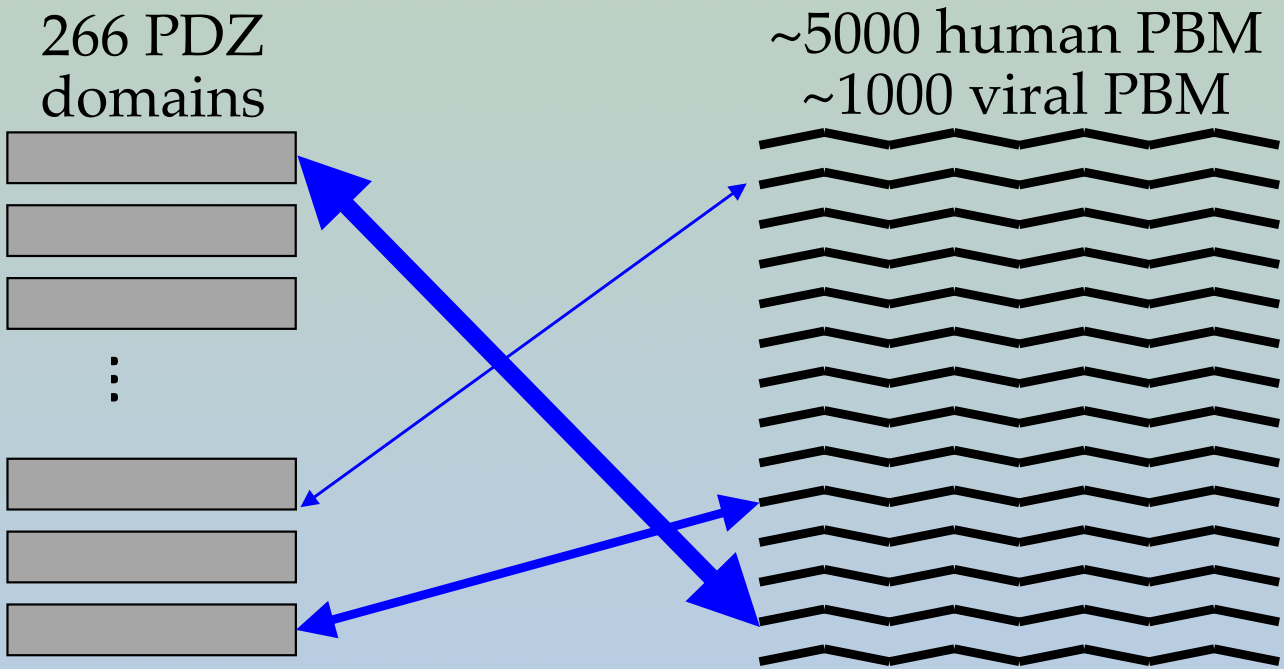
E6 *h.r.* agit sur le réseau PDZ/PBM humain



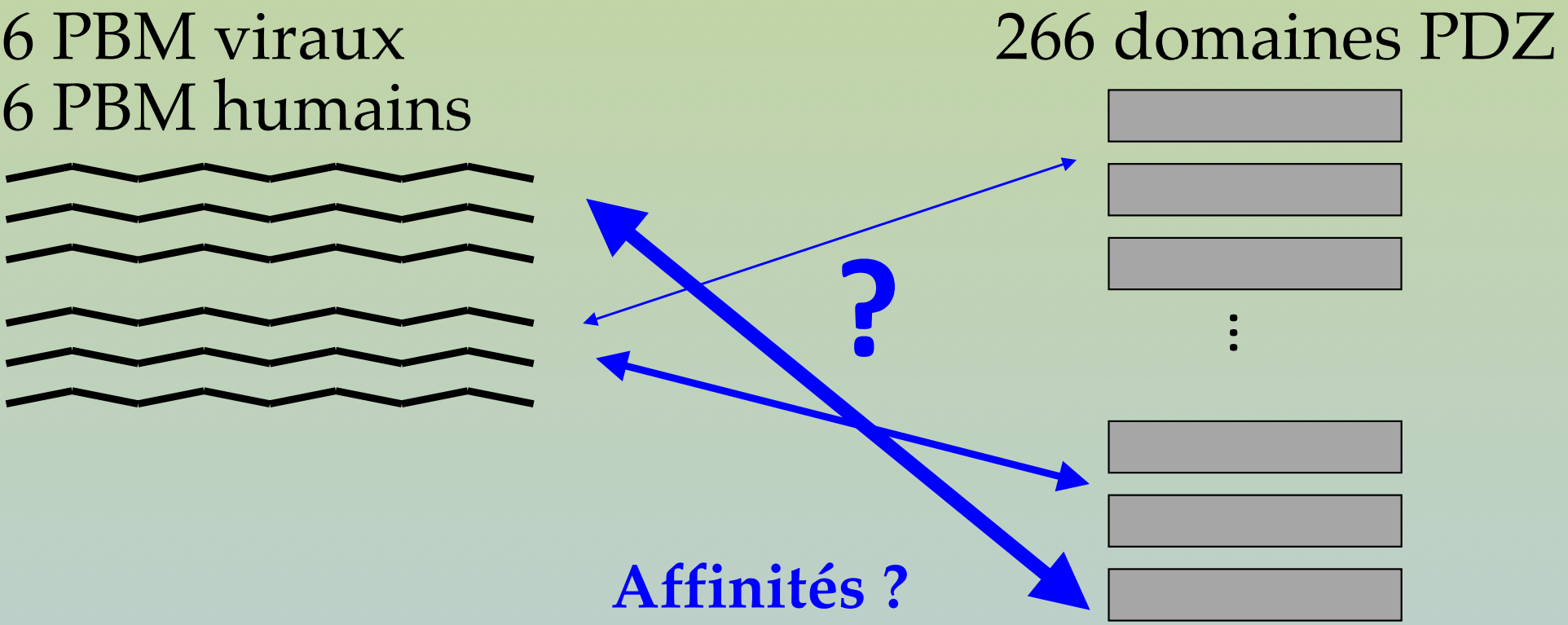
Tous les E6 h.r. possèdent un motif de liaison aux PDZ (PBM).

PDZ : signalisation cellulaire, adhesion, …





I/ Le projet InQuant (Cancéropôle)

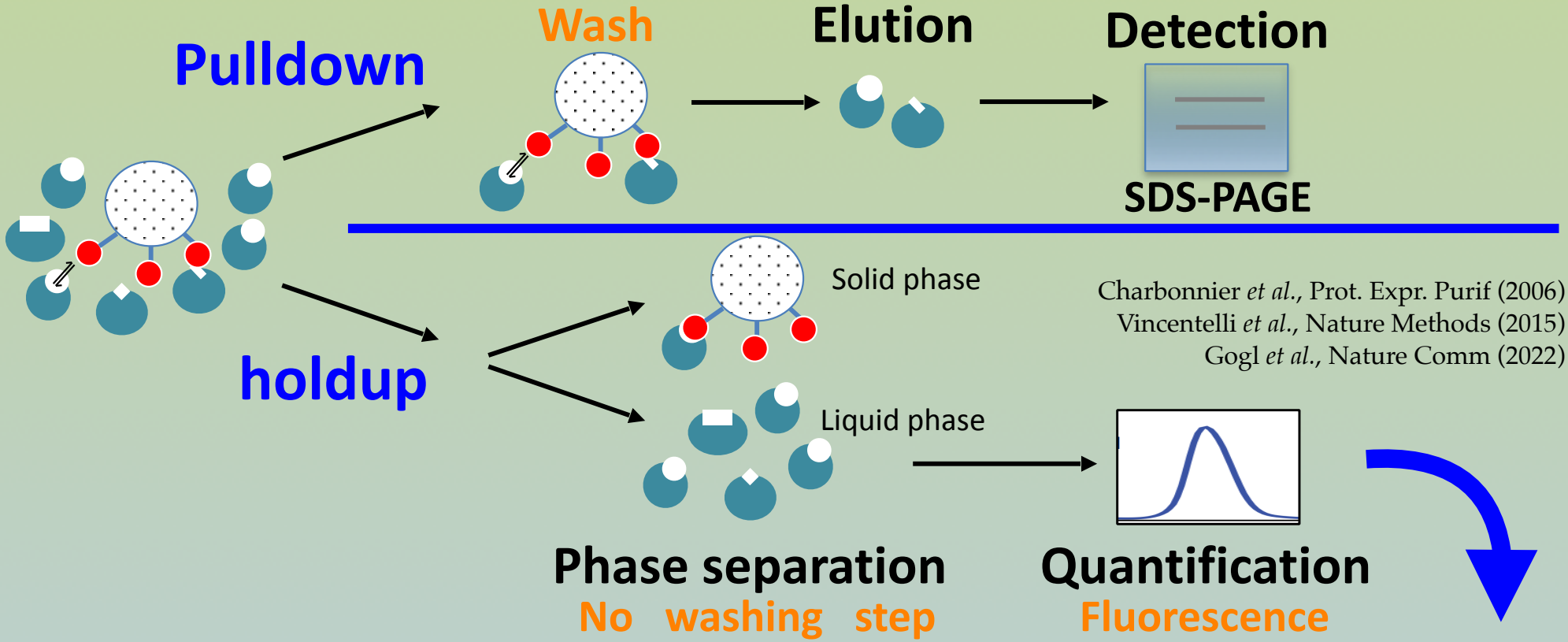


Gain de spécificité des PBM viraux ?

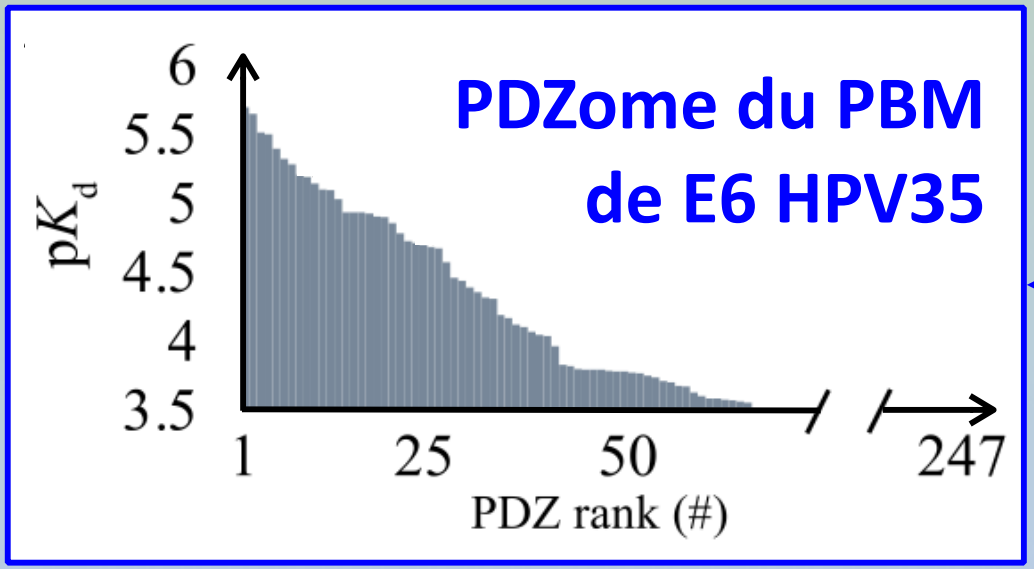
Compétition entre PBM viraux et PBM humains ?

PBM viraux : E6 de HPV16, 18, 35 (sauvage ou phosphorylé)
PBM humains : NET1, PTEN (sauvage, acetylé, acétylo-mimétique)

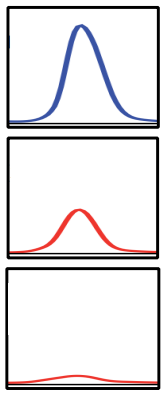
II/ La méthode holdup



Charbonnier *et al.*, Prot. Expr. Purif (2006)
Vincentelli *et al.*, Nature Methods (2015)
Gogl *et al.*, Nature Comm (2022)



Quantification pour chaque PDZ/PBM



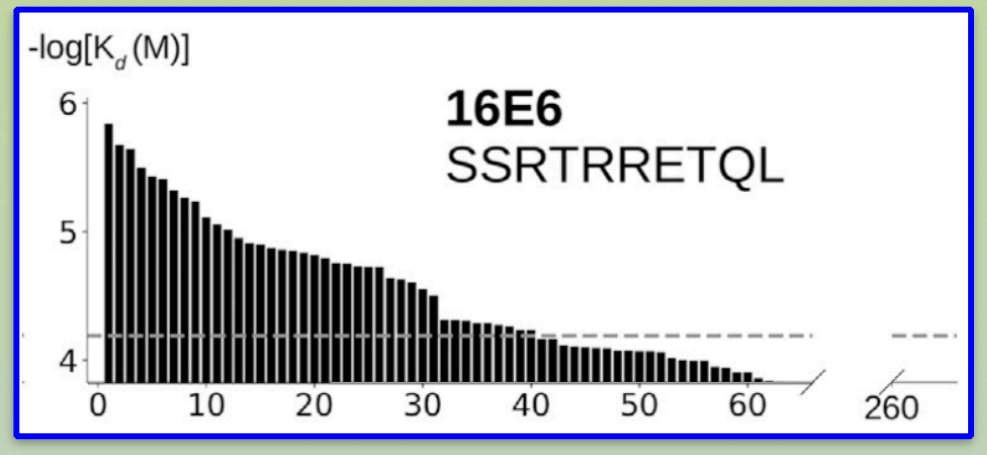
Pas d'interaction

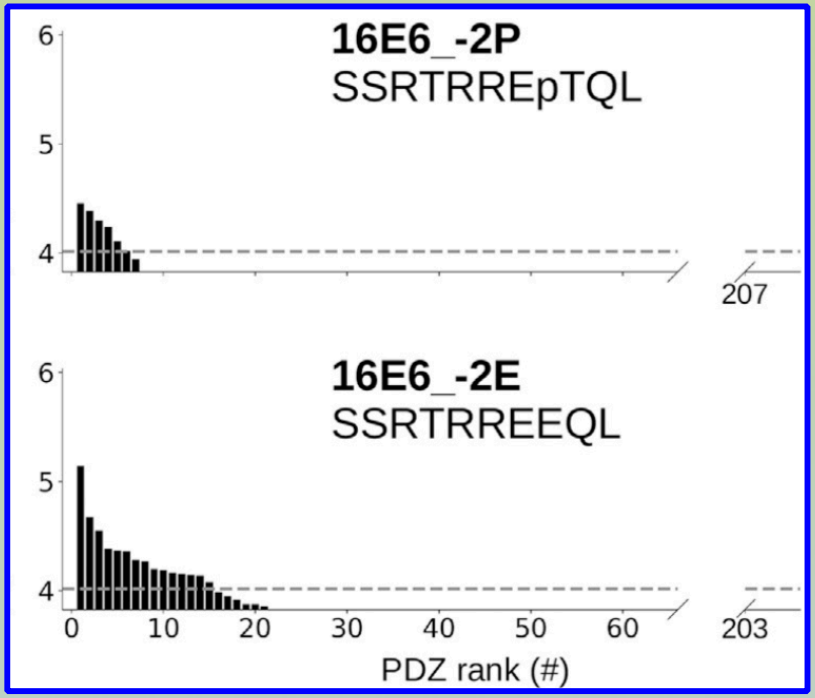
Interaction modérée

Interaction forte

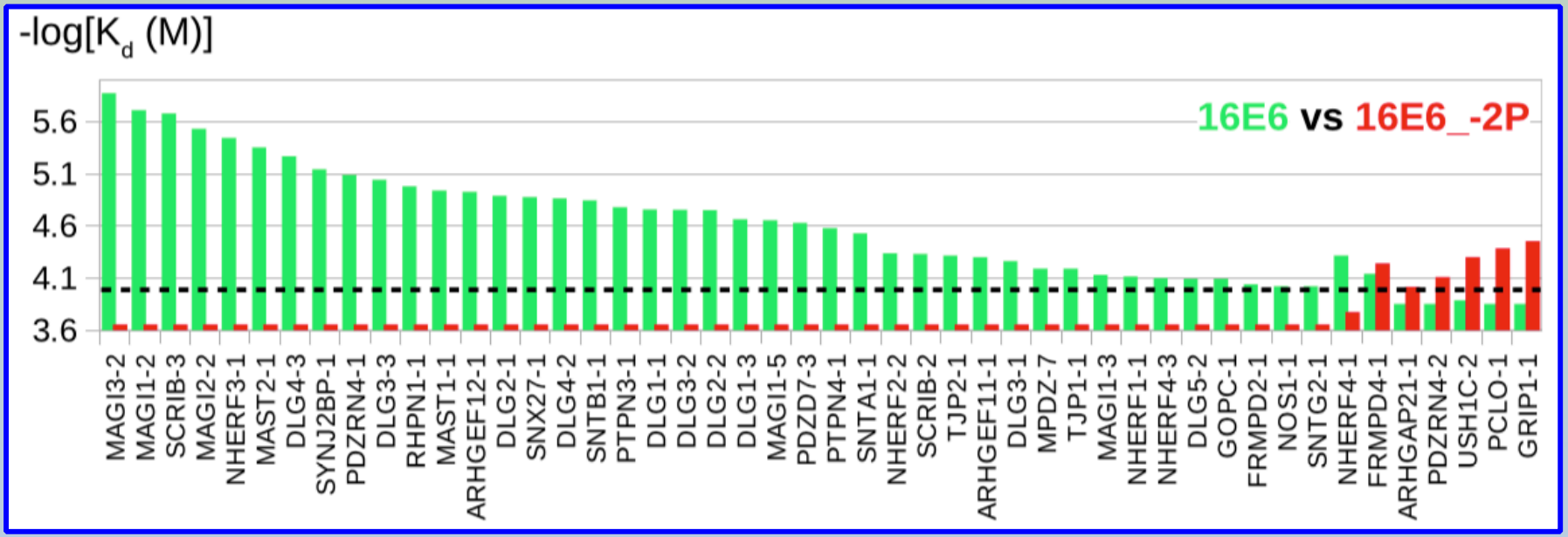
Info sur le K_D

PBM de E6 et mutations



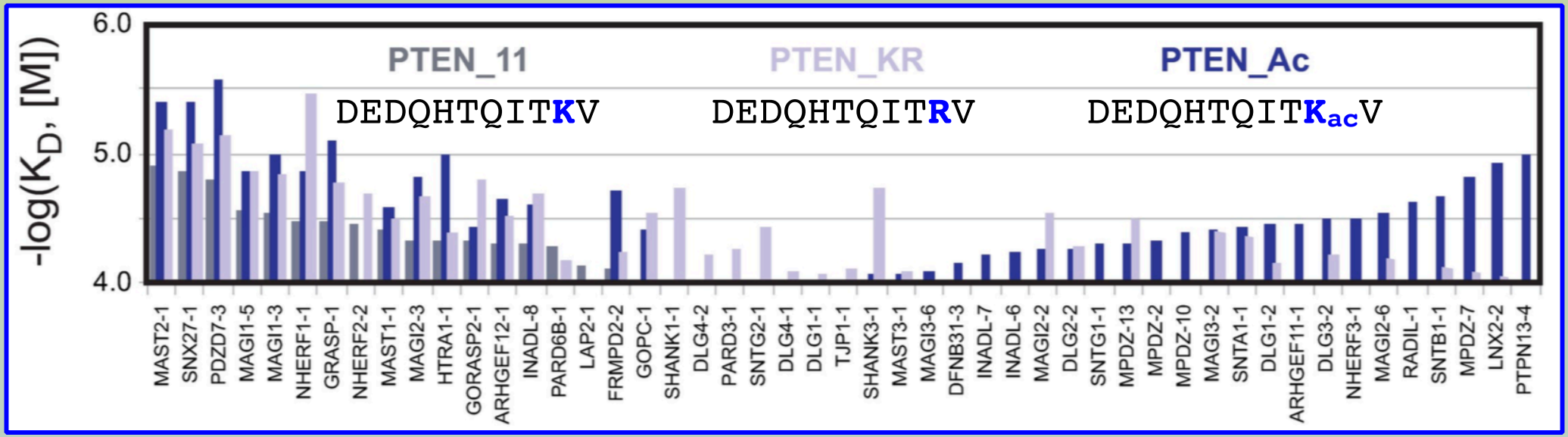


Phosphorylation & phosphomimetic affect the binding profiles



G. Gogl, Structure, 2020

PTEN

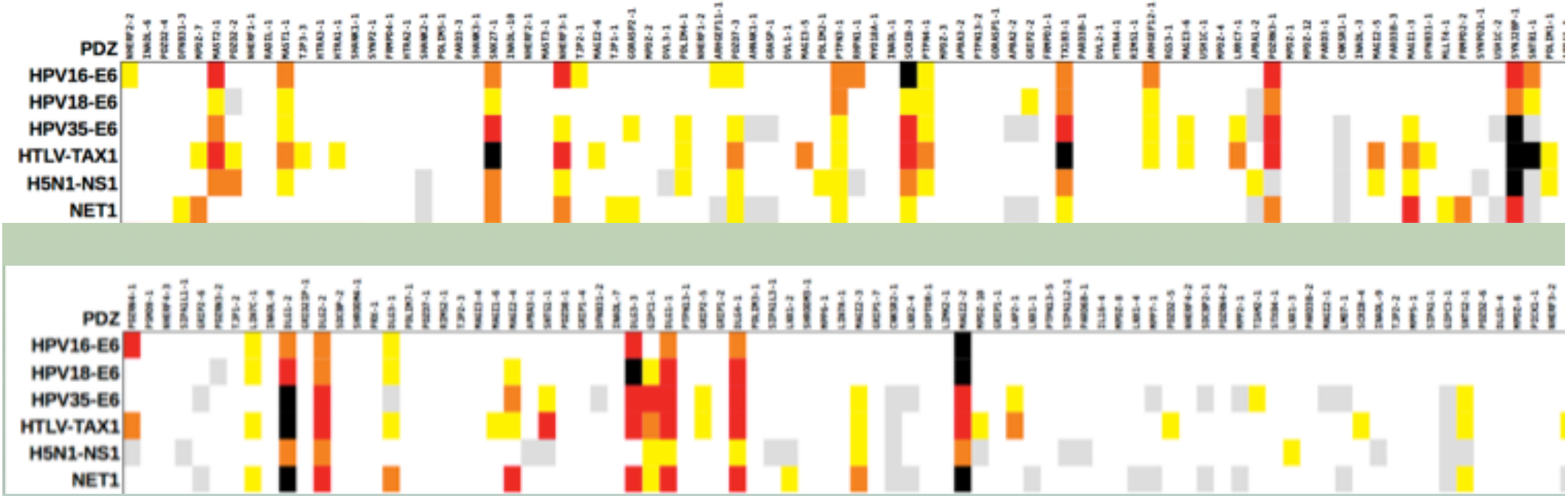


P. Jané, Plos One, 2021

Differential targets depending on the acetylated state

Switch ON/OFF

Comparing viral and human PBM



G. Bich

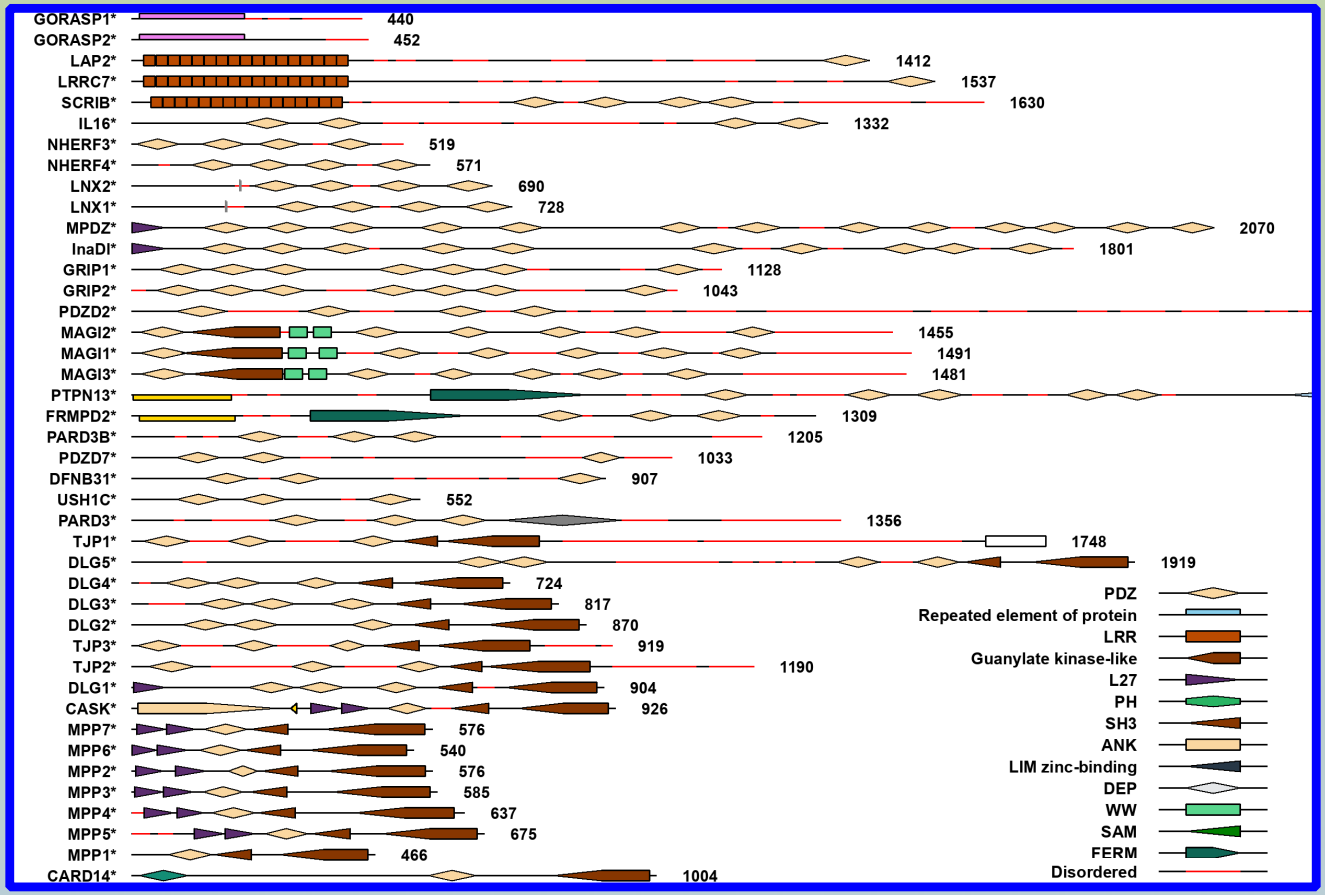
Targeted PDZ highly similar

Reshuffling of the PDZome

ProFeatMap

Protein Feature Map

- QR-code :



URL : https://profeatmap.pythonanywhere.com/

GitHub : https://github.com/profeatmap/ProFeatMap

G. Bich *et al.*, Bioinf. Adv. (2023)

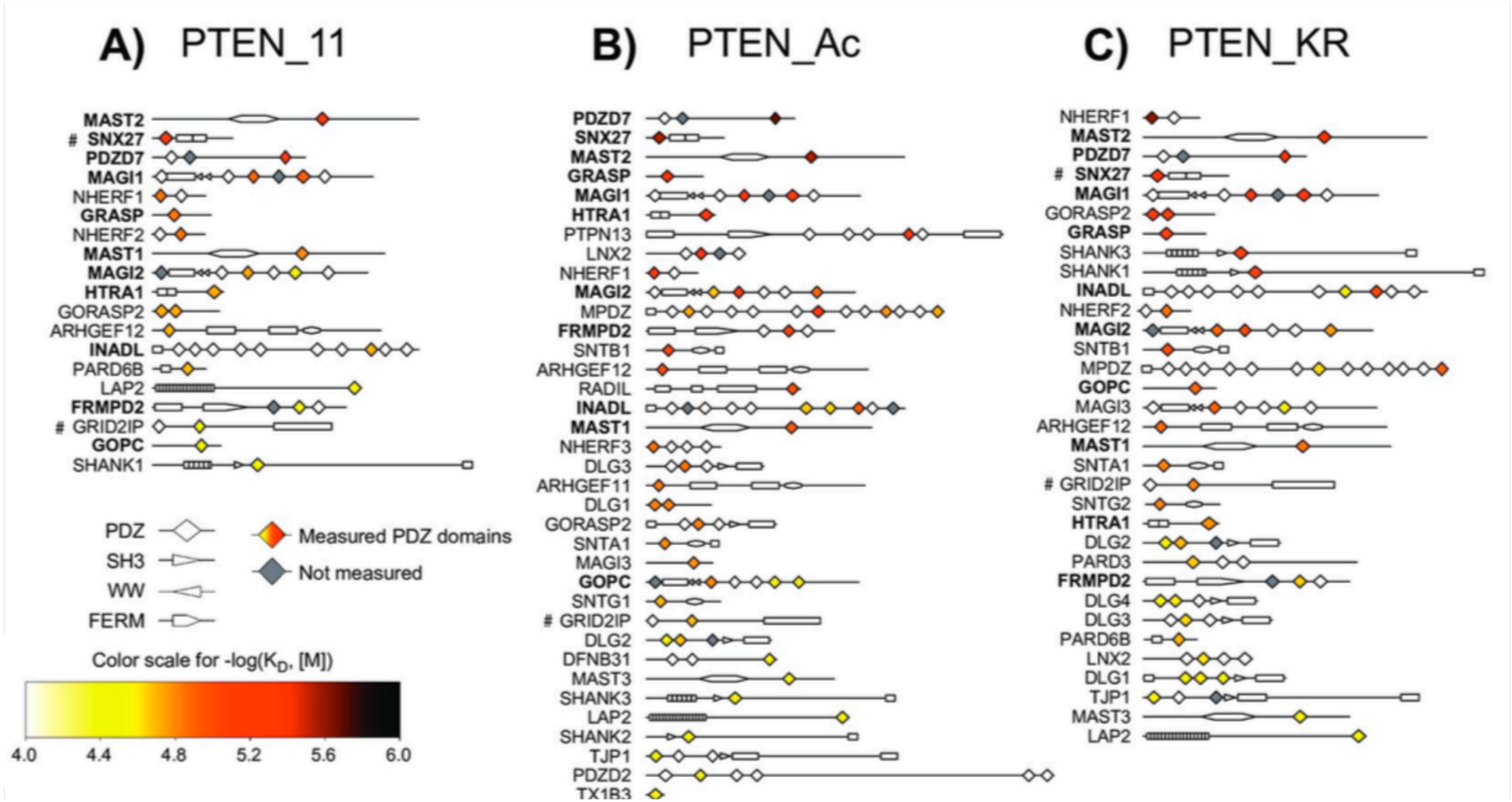
Avantages de ProFeatMap

	Uniprot	Interpro	Pfam	SMART	Prosite	CF-Visual	iTOL	ProFeatMap
Simple 2D view			✓	✓	✓	✓	✓	✓
Multiple proteins				✓		✓	✓	✓
Customisation					✓	✓	✓	✓
Savable images		✓	✓	✓	✓	✓	✓	✓
Showing values					~		~	✓
Editing in UI					✓	✓	~	✓
Web Interface	✓	✓	✓	✓	✓		✓	✓

- Domains > x
  Repeats > y
- Multiple proteomes
- Around 300 families per proteome

- Map
- Legend
- Sorted protein list
- Sequence of the family (.fa)
- Extracted data
- Shapes and colors file

ProFeatMap sur PTEN



P. Jané, Plos One, 2020

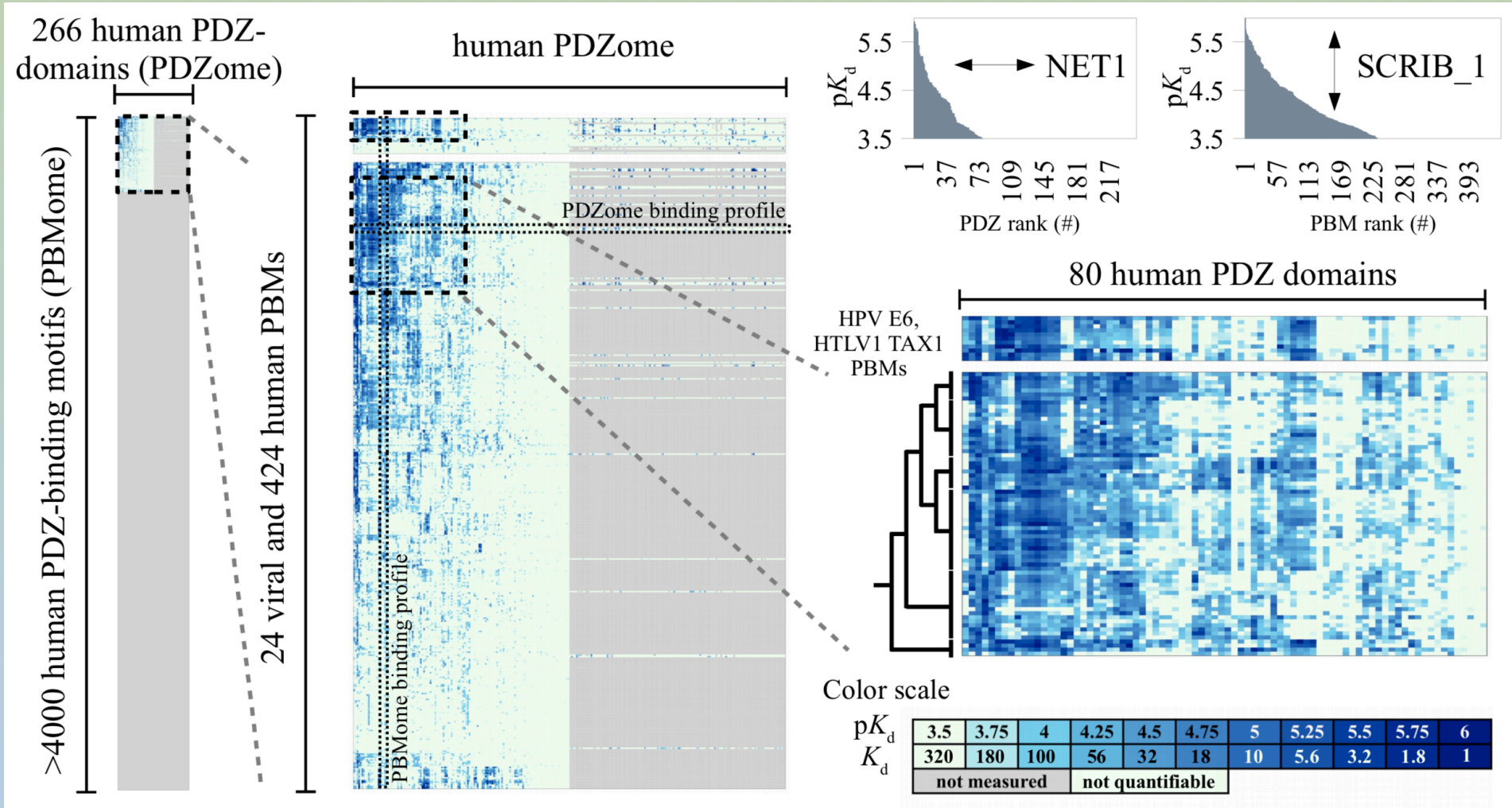
III/ Effet de levier de InQuant

Goran Bich
Ph.D. 2019-2023

Elodie Monsellier
Chercheur CNRS permanente (2020)

Le projet ProfAff

G. Gogl *et al.* Nat. Comm. (2022)



Acknowledgments

- Dr. Gilles Travé
- Members of the lab: G. Bich, P. Jané, A. Bonhoure & G. Gogl