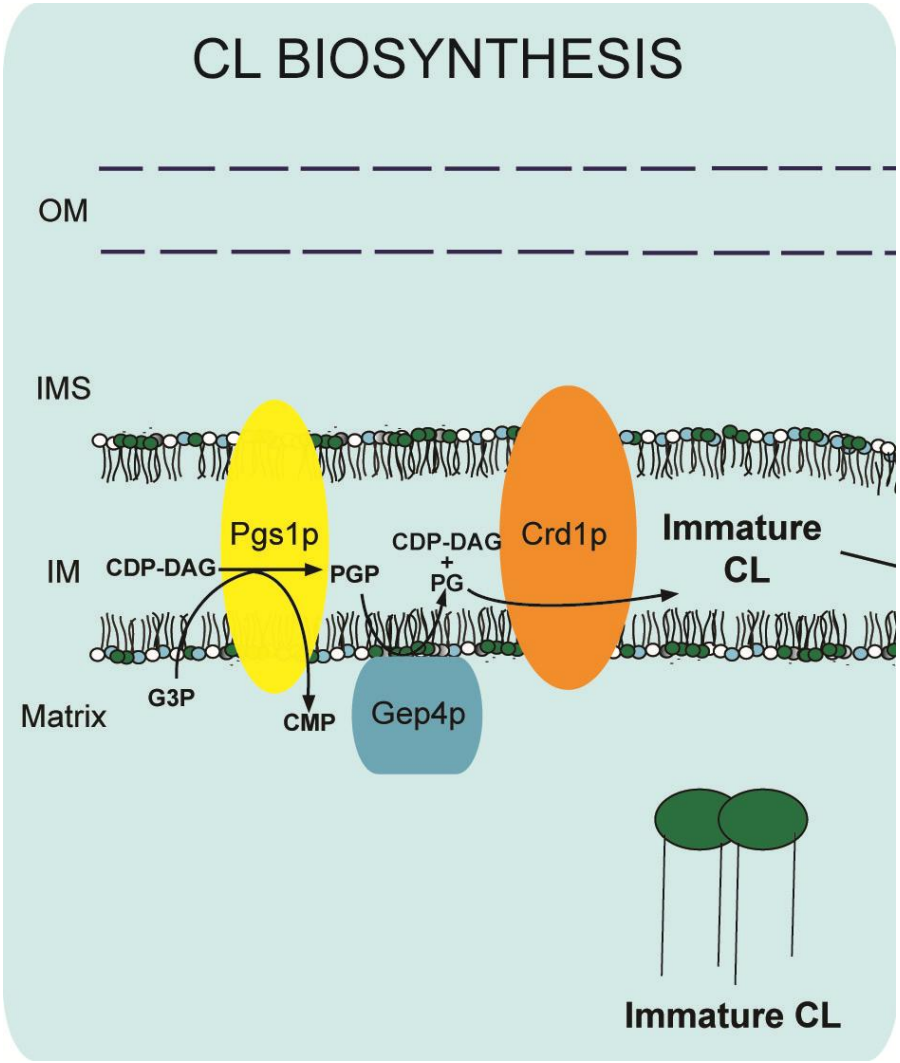
The topology of cardiolipin remodeling in yeast

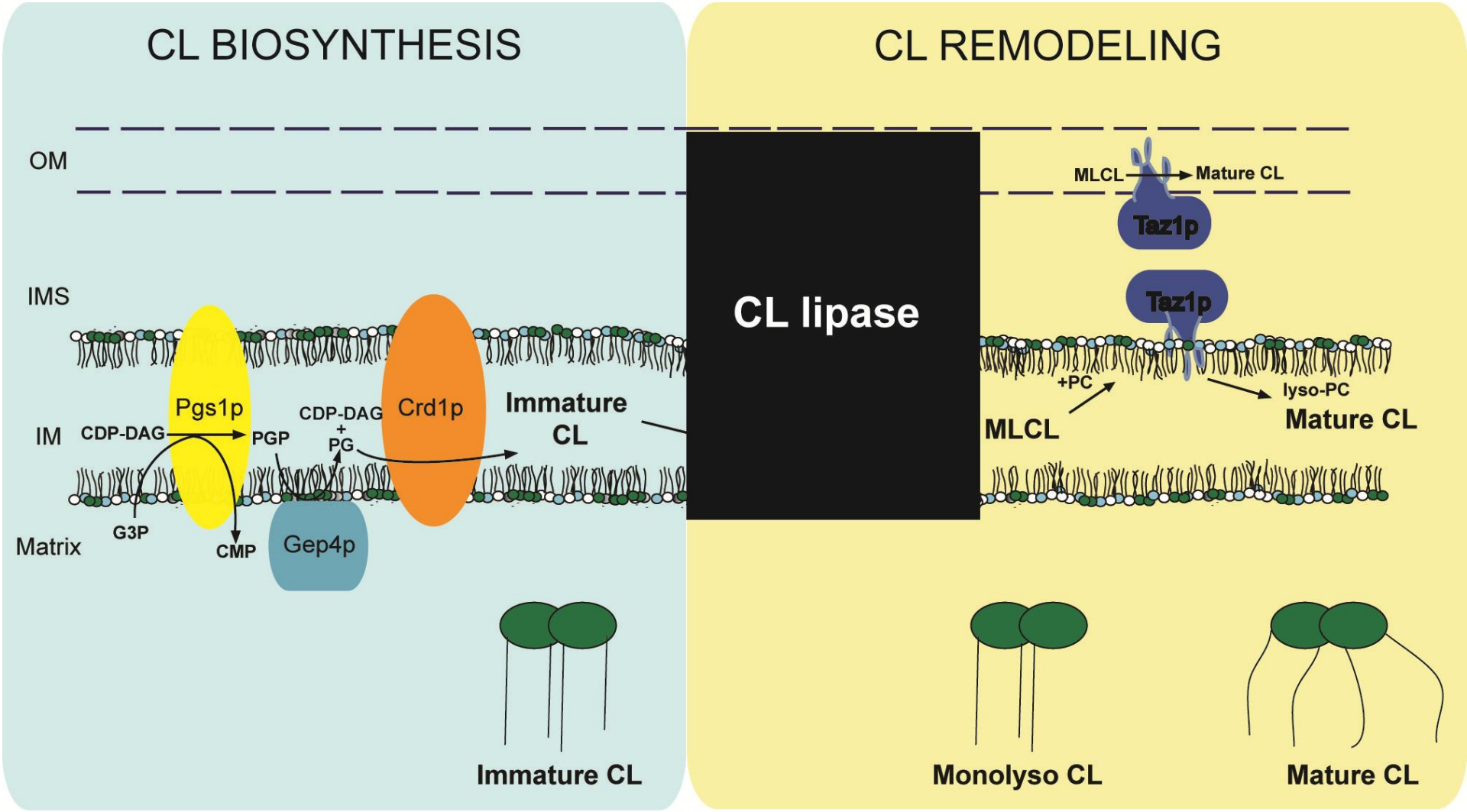
2012 Barth Syndrome Foundation Conference

June 28, 2012

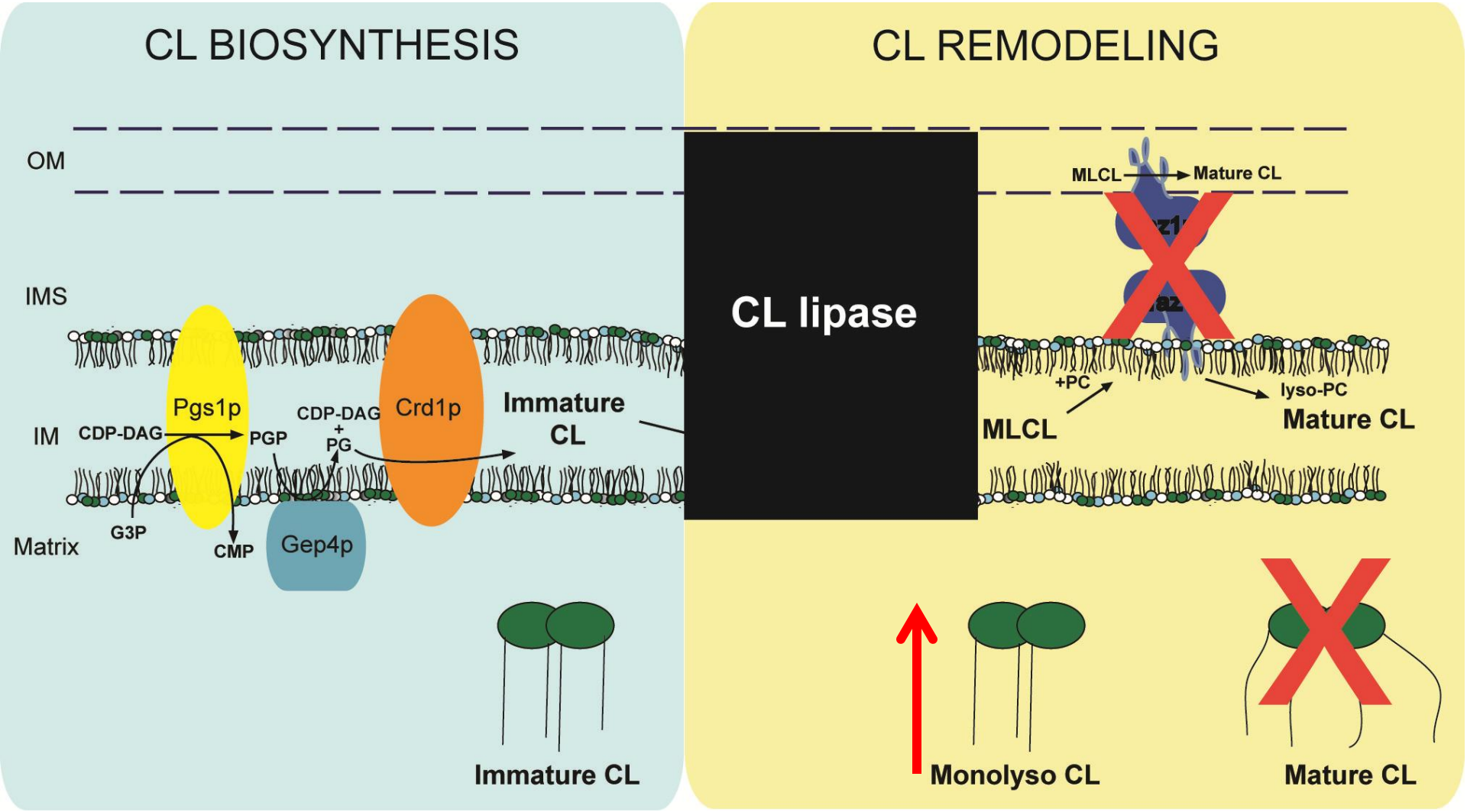
Cardiolipin Biosynthesis



Cardiolipin Biosynthesis and Remodeling



Cardiolipin Biosynthesis and Remodeling



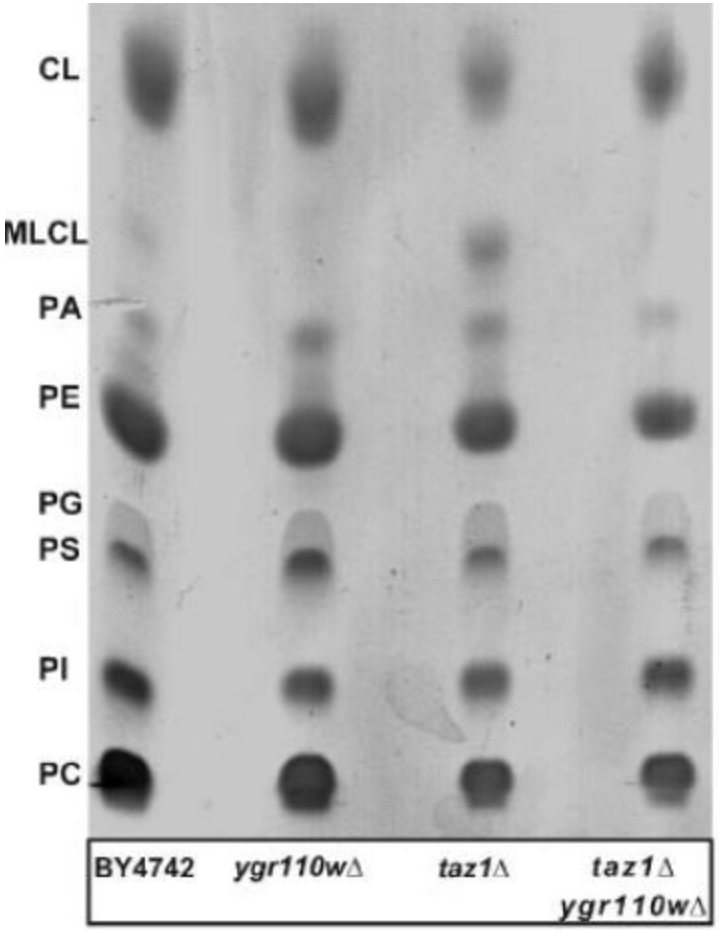
Cardiolipin-Specific Deacylase 1

- Identified in yeast
- Co-localizes with mitochondria by fluorescence (GFP-Cld1p)
- Co-fractionates with mitochondria (GST-Cld1p)
- Δ*cld1* = increased $C_{16:0}$ acyl chains in CL

  decreased $C_{18:1}$ and $C_{16:1}$
- Cld1p able to deacylate CL and PC *in vitro*

From: Beranek, A, *et. al. J Biol Chem* **284** (2009) 11572-11578

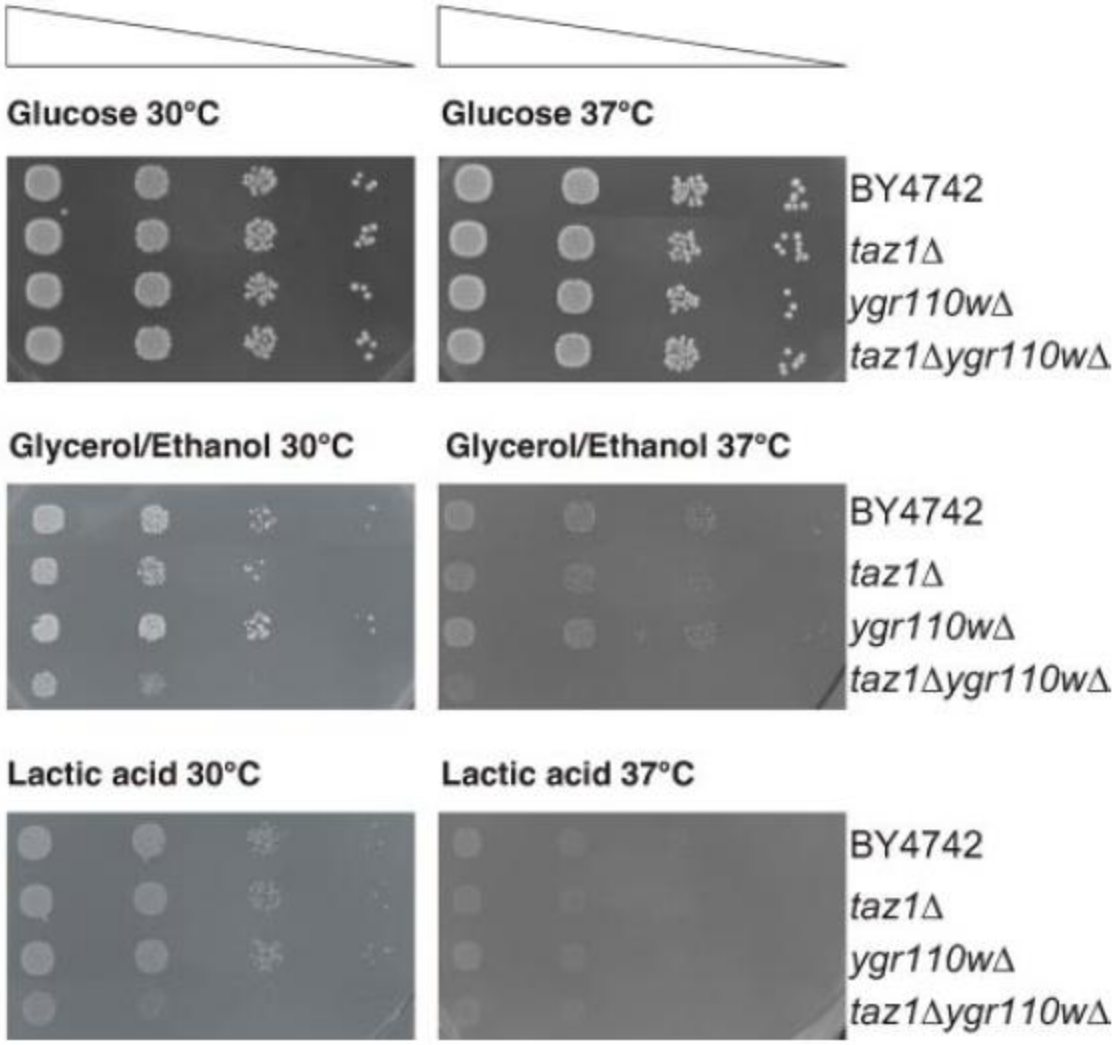
Cardiolipin Remodeling Epistasis Analysis



= Cld1p and Taz1p Function in Linear Pathway

From: Beranek, A, *et. al. J Biol Chem* **284** (2009) 11572-11578

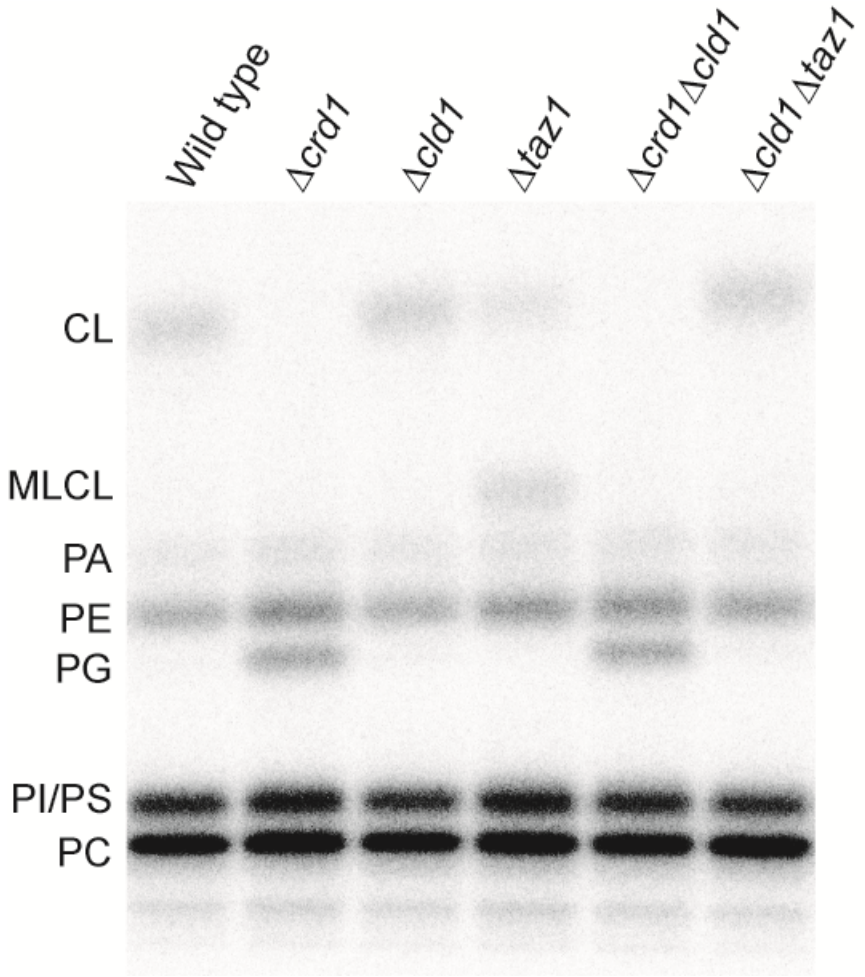
Cardiolipin Remodeling Epistasis Analyses



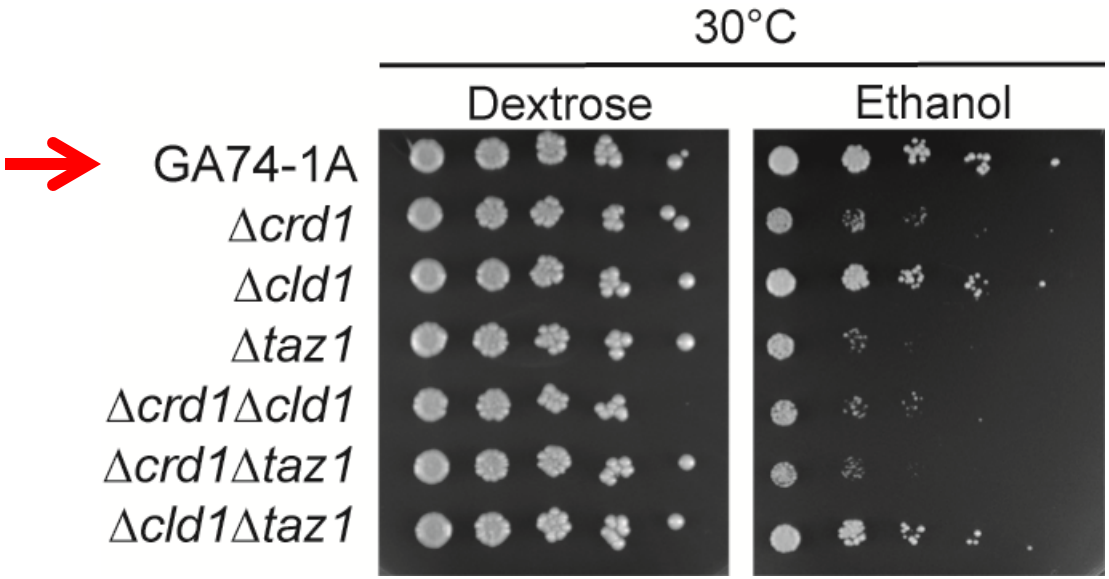
= Cld1p and Taz1p Function in Distinct Pathways

From: Beranek, A, *et. al. J Biol Chem* **284** (2009) 11572-11578

Cardiolipin Remodeling Epistasis Analysis



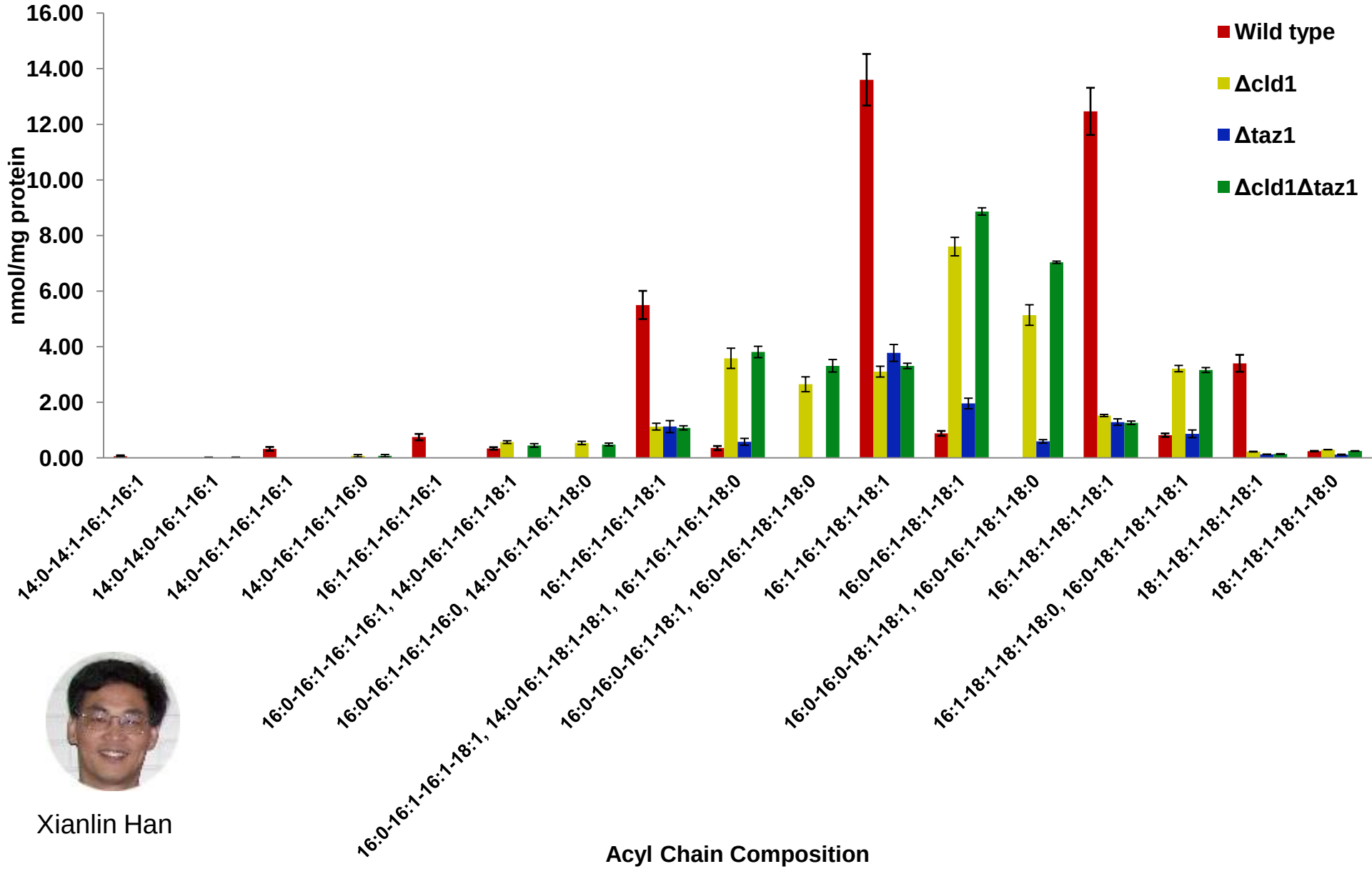
Cardiolipin Remodeling Epistasis Analyses



= Cld1p acts upstream of Taz1p and downstream of Crd1p

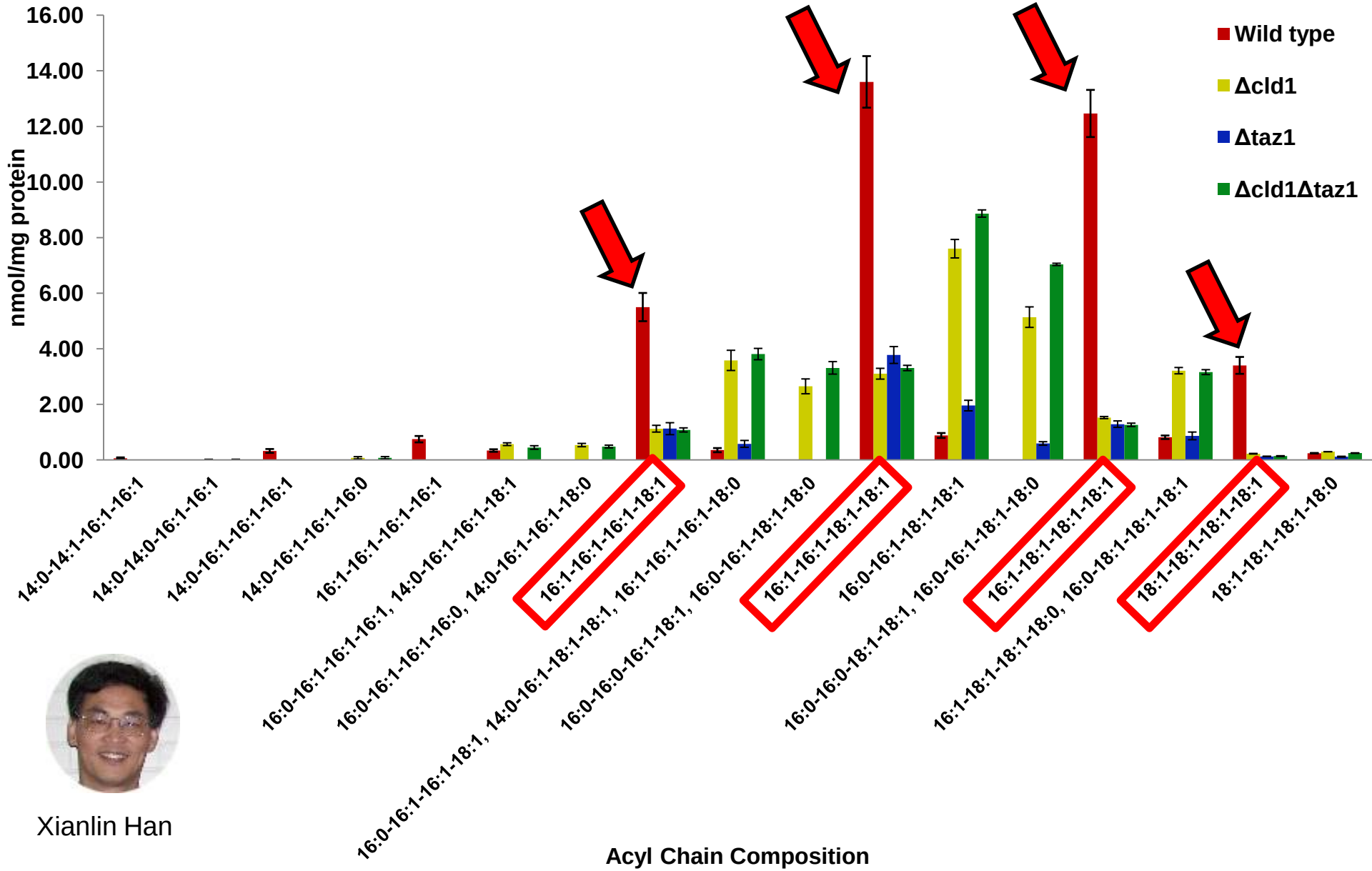
Matt Baile

Immature CL accumulates in Δ*cld1*



Xianlin Han

Immature CL accumulates in Δ*cld1*



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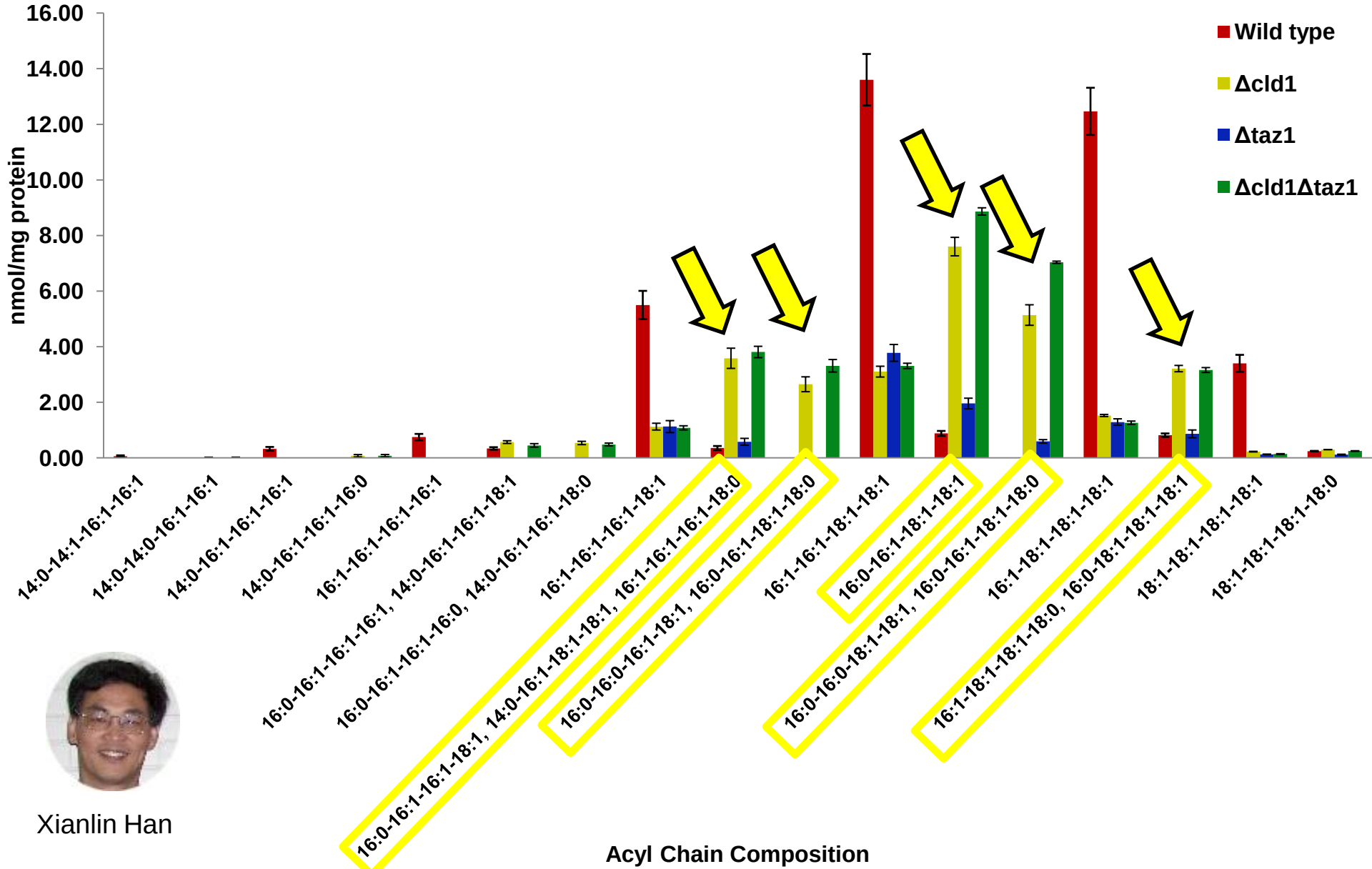

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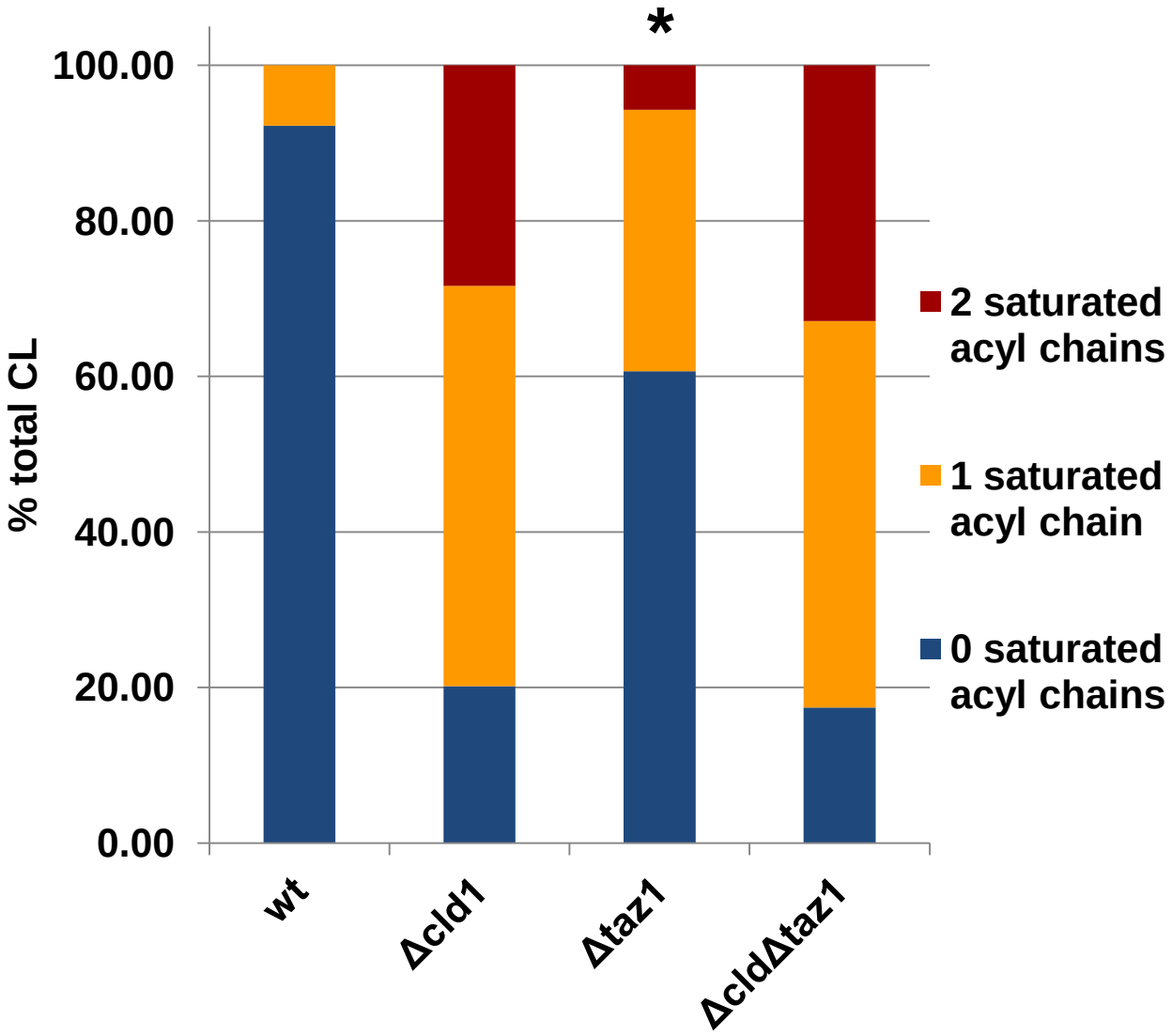

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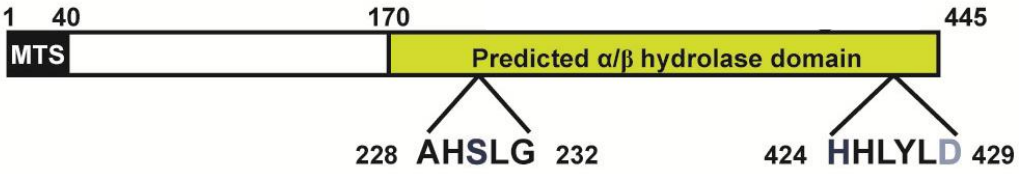
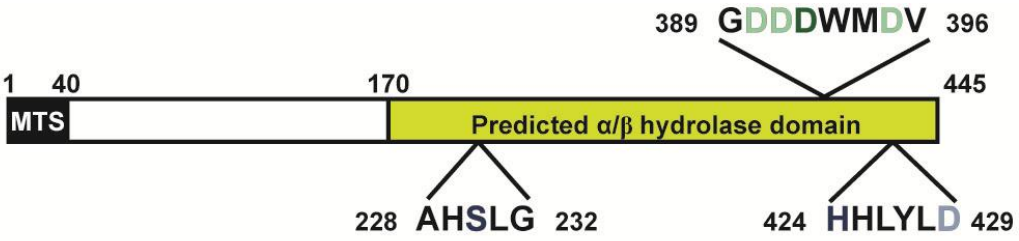
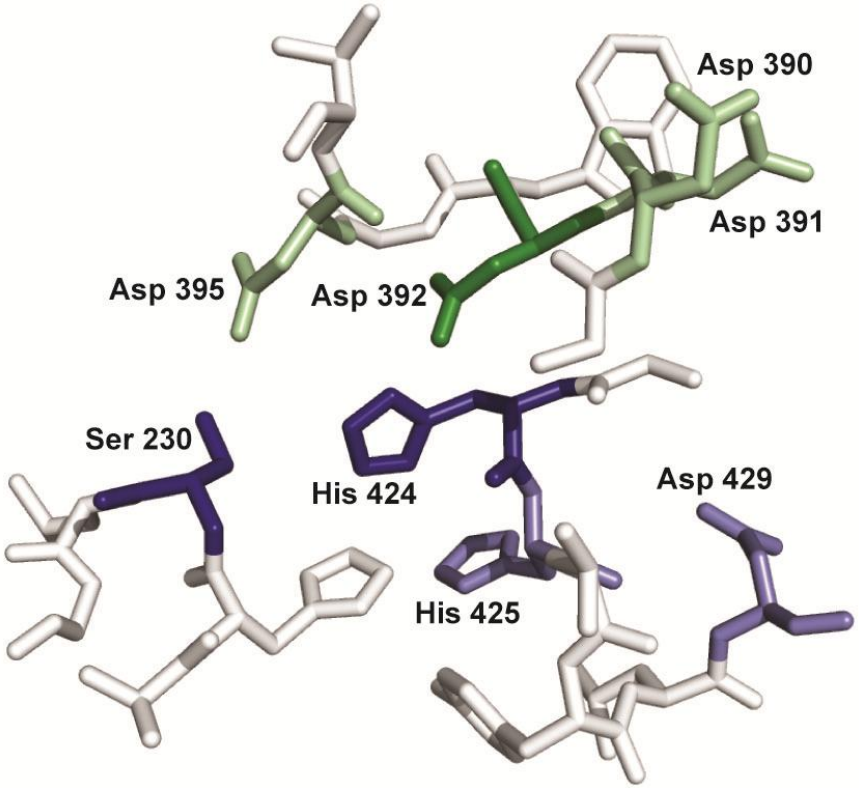
Predicted catalytic residues of Cld1p



Predicted catalytic residues of Cld1p



Homology Model used *Pseudomonas fluorescens* hydrolase, CumD as template



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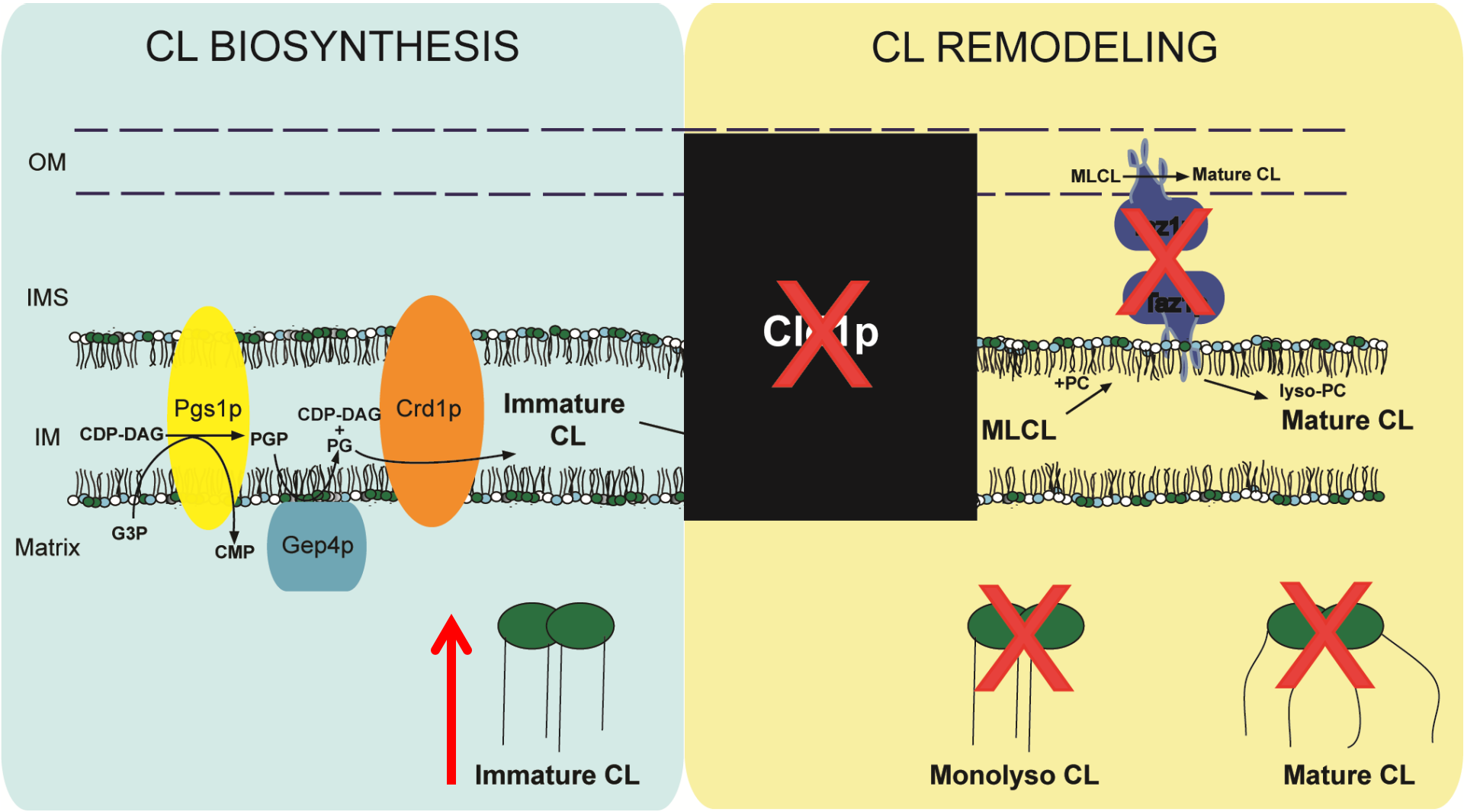
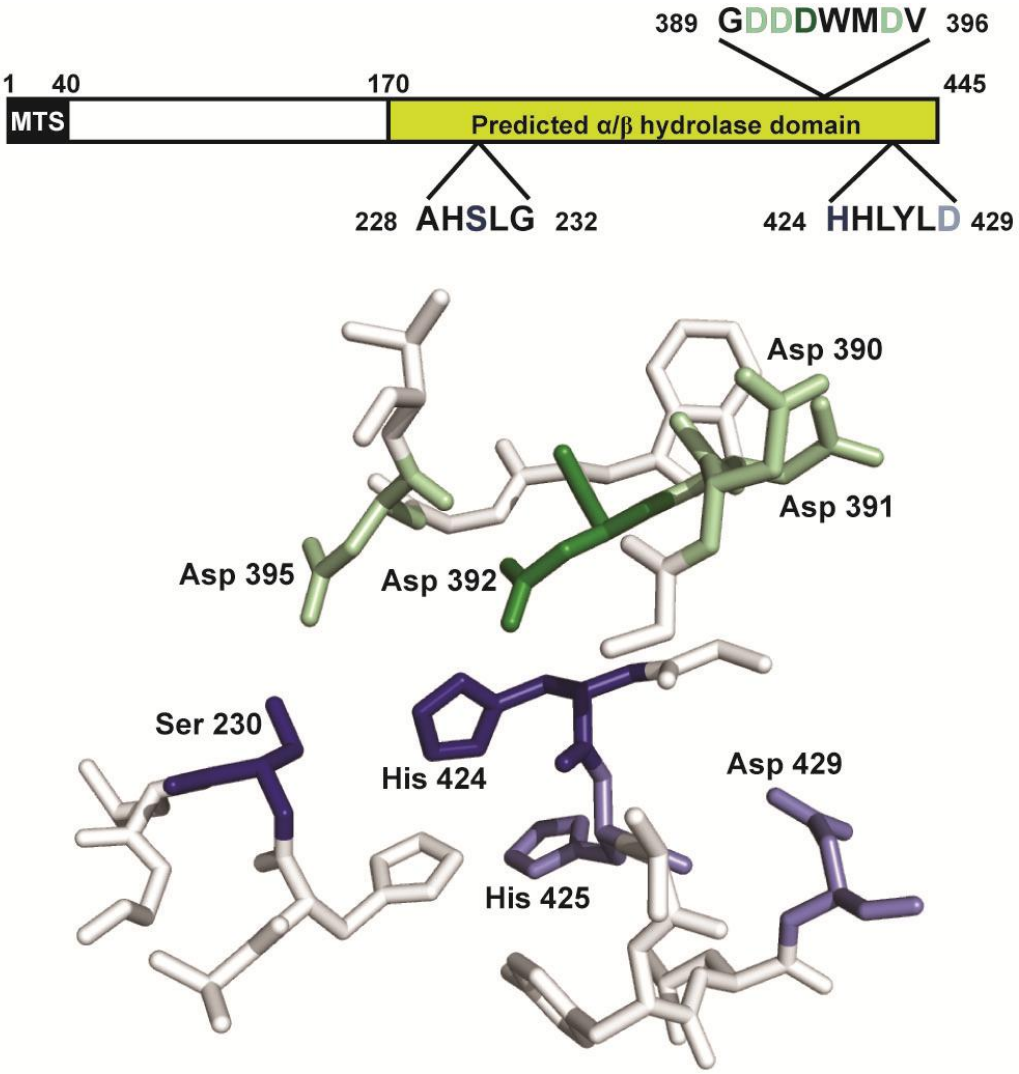
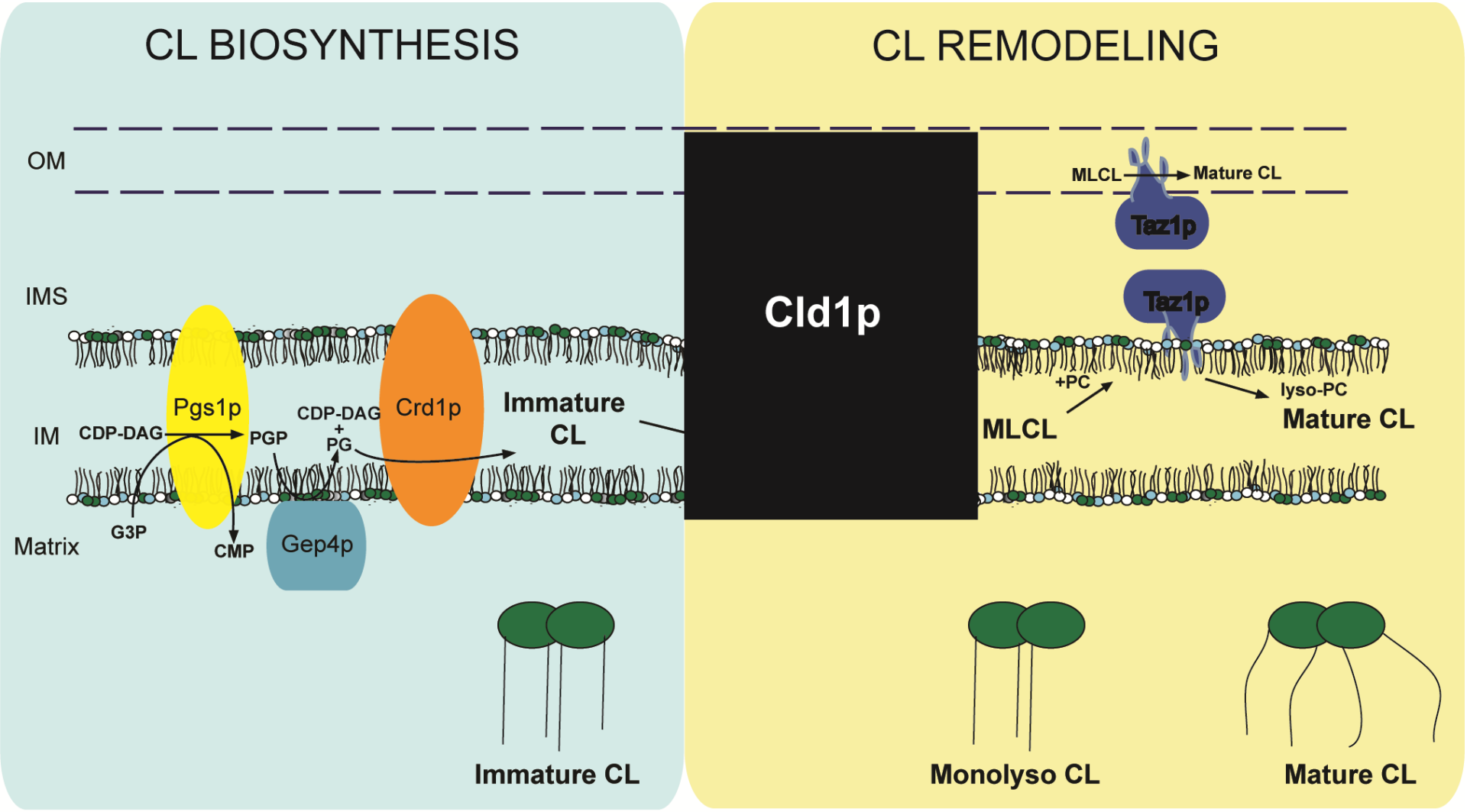
Defining the Catalytic Triad of Cld1p

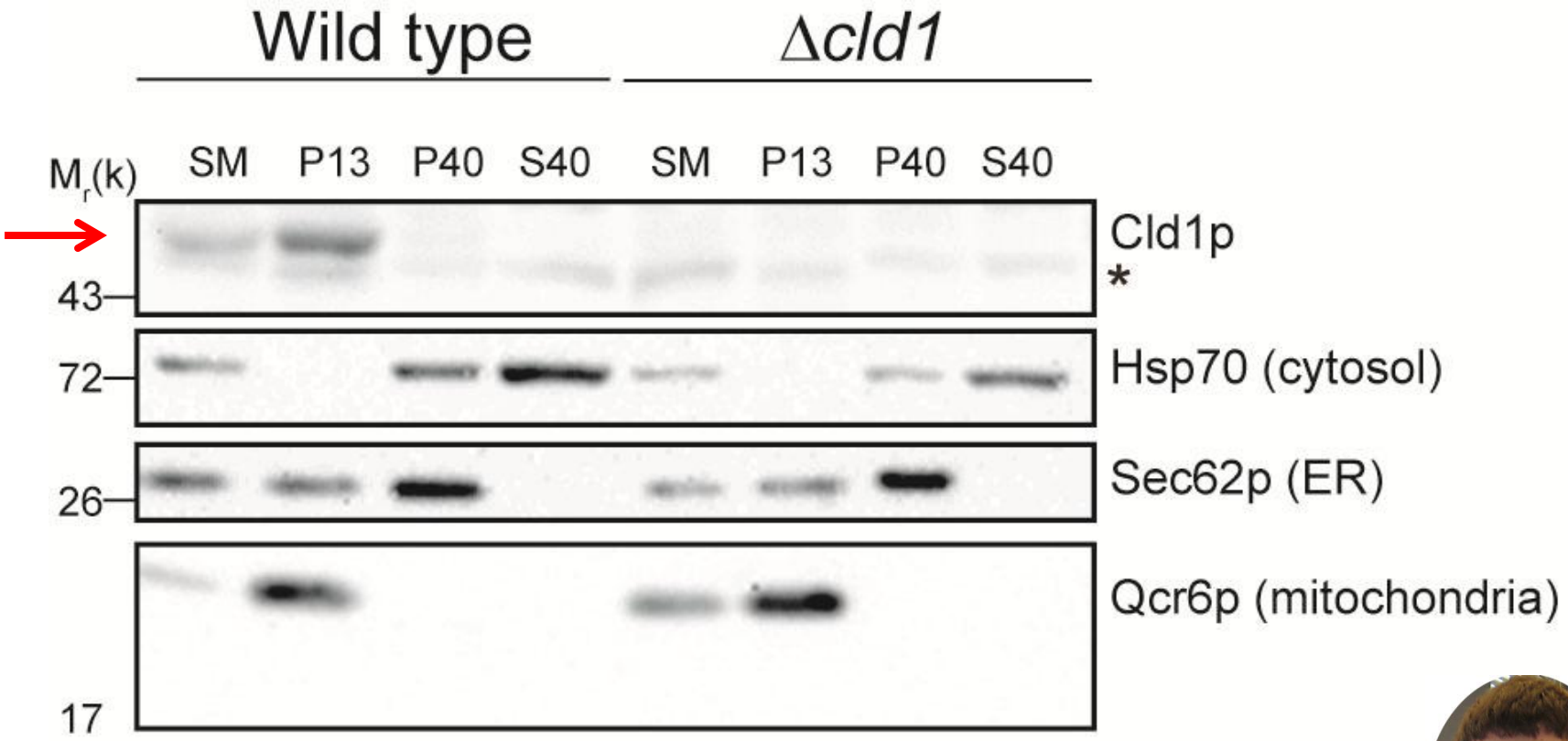


Ser230, His424 and Asp392 form Cld1p's Catalytic Triad




CL BIOSYNTHESIS
CL REMODELING
OM
IMS
IM
Matrix
Pgs1p
CDP-DAG
PGP
G3P
CMP
CDP-DAG
+
PG
Crd1p
Gep4p
Immature
CL
Cld1p
MLCL
Mature CL
Taz1p
Taz1p
+PC
lyso-PC
MLCL
Mature CL
Immature CL
Monolyso CL
Mature CL

Cld1p co-fractionates with mitochondria



SM = starting material
P13 = pellet at 13,000 x *g*
P40 = pellet at 40,000 x *g*
S40 = supernatant at 40,000 x *g*

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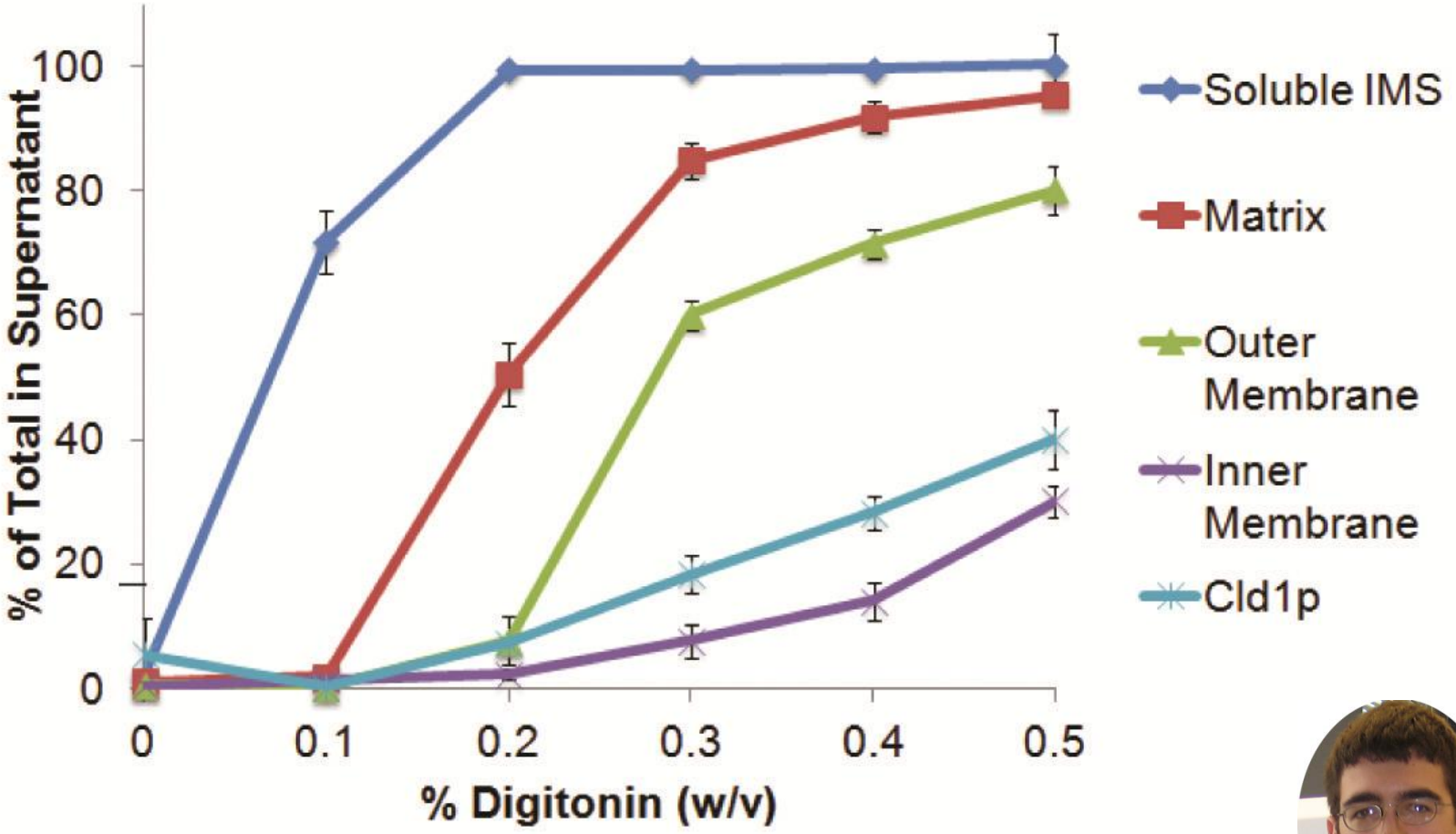
Cld1p is located on the IM



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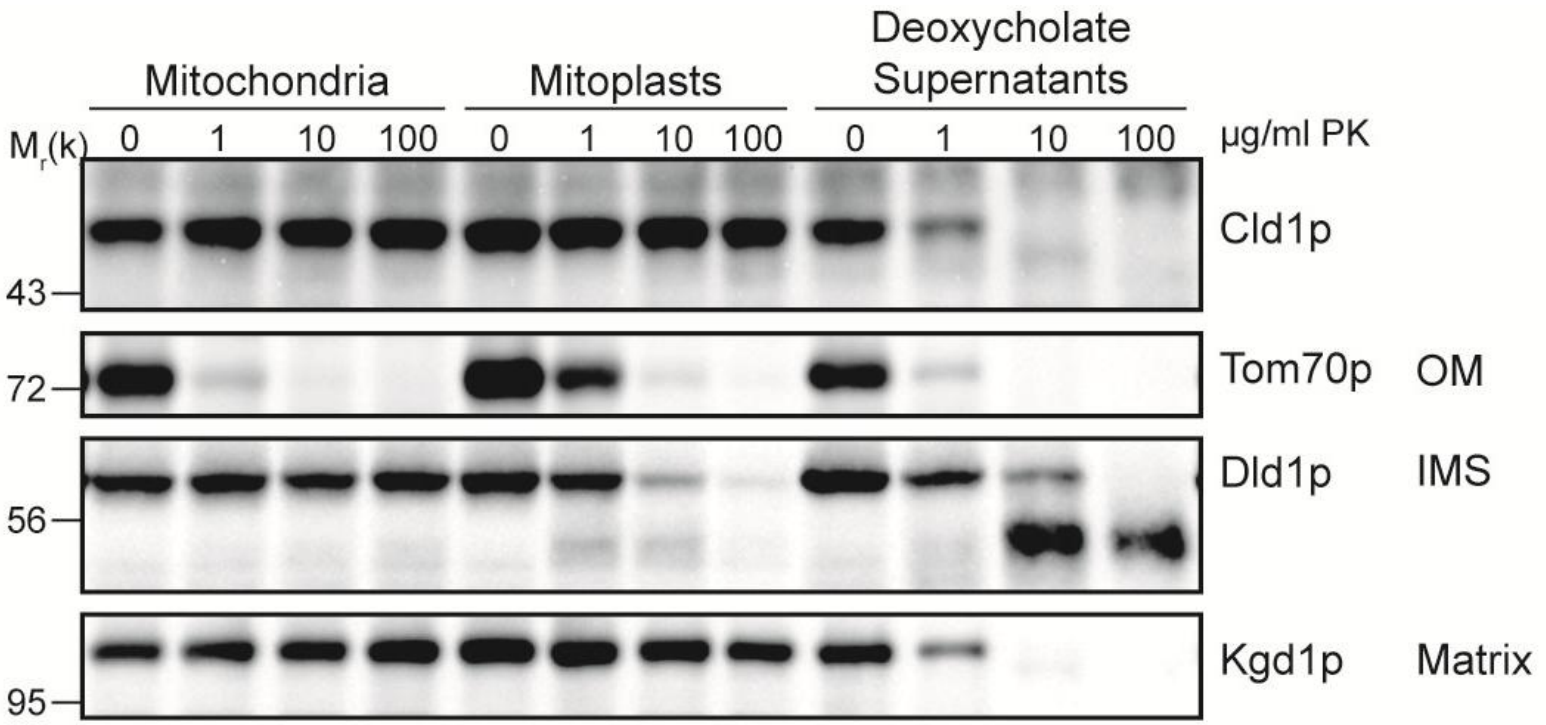
Cld1p faces the matrix



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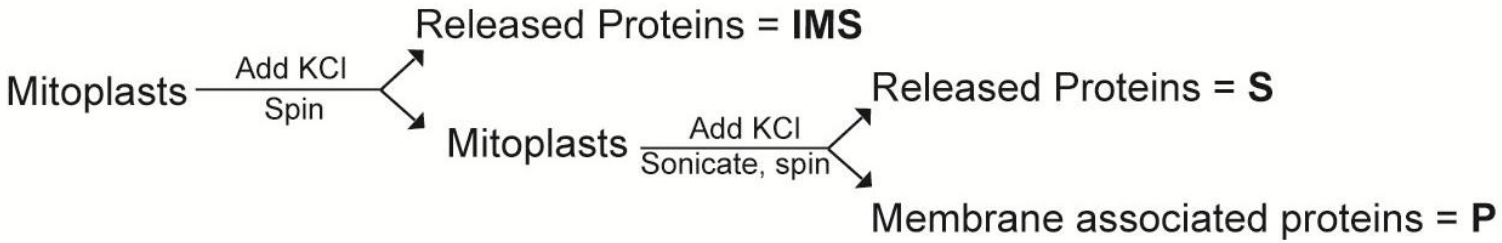
Cld1p is electrostatically associated with the IM



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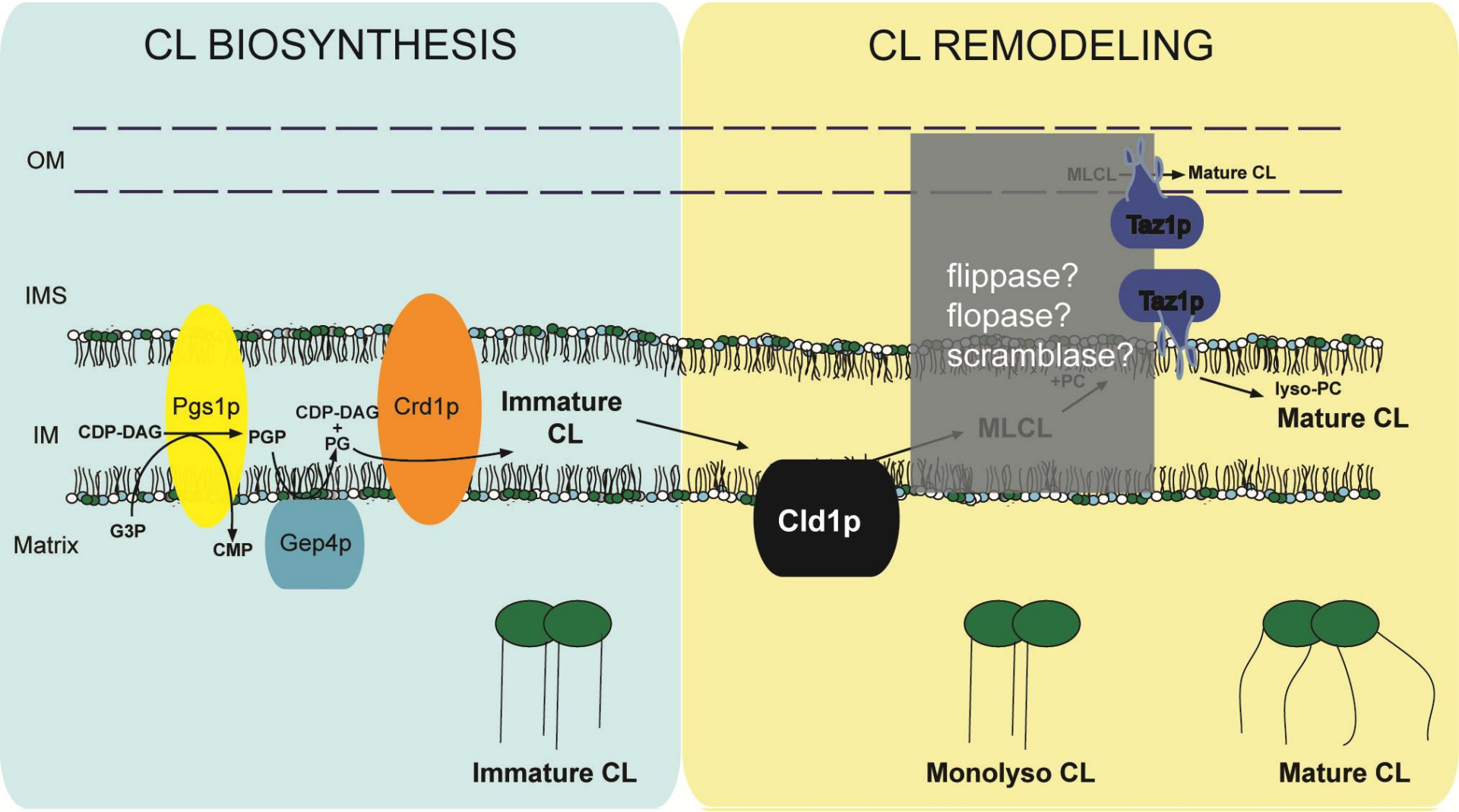
The Topology of Cardiolipin Biosynthesis and Remodeling



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