

# About OMICS Group

OMICS Group is an amalgamation of [Open Access publications](#) and worldwide international science conferences and events. Established in the year 2007 with the sole aim of making the information on Sciences and technology 'Open Access', OMICS Group publishes 500 online open access [scholarly journals](#) in all aspects of Science, Engineering, Management and Technology journals.

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# About OMICS International Conferences

OMICS International is a pioneer and leading science event organizer, which publishes around 500 open access journals and conducts over 500 Medical, Clinical, Engineering, Life Sciences, Pharma scientific conferences all over the globe annually with the support of more than 1000 scientific associations and 30,000 editorial board members and 3.5 million followers to its credit.

OMICS Group has organized 500 conferences, workshops and national symposiums across the major cities including San Francisco, Las Vegas, San Antonio, Omaha, Orlando, Raleigh, Santa Clara, Chicago, Philadelphia, Baltimore, United Kingdom, Valencia, Dubai, Beijing, Hyderabad, Bengaluru and Mumbai.



# **The phospholipid enzyme Pcyt2 is a new target for oxidative stress and heart disease**

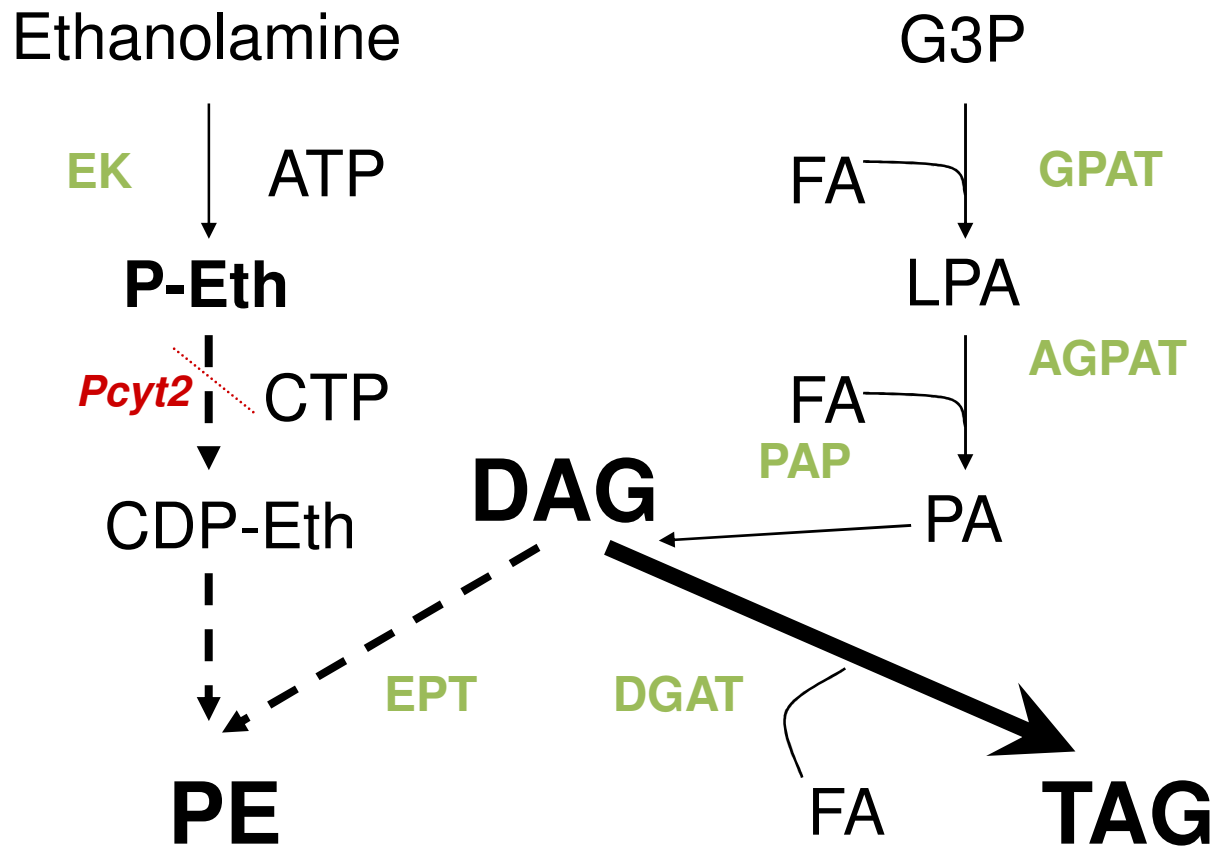
**Marica Bakovic**

*Department of Human Health and Nutritional Sciences, University of Guelph, Guelph, ON, Canada*

August 2015

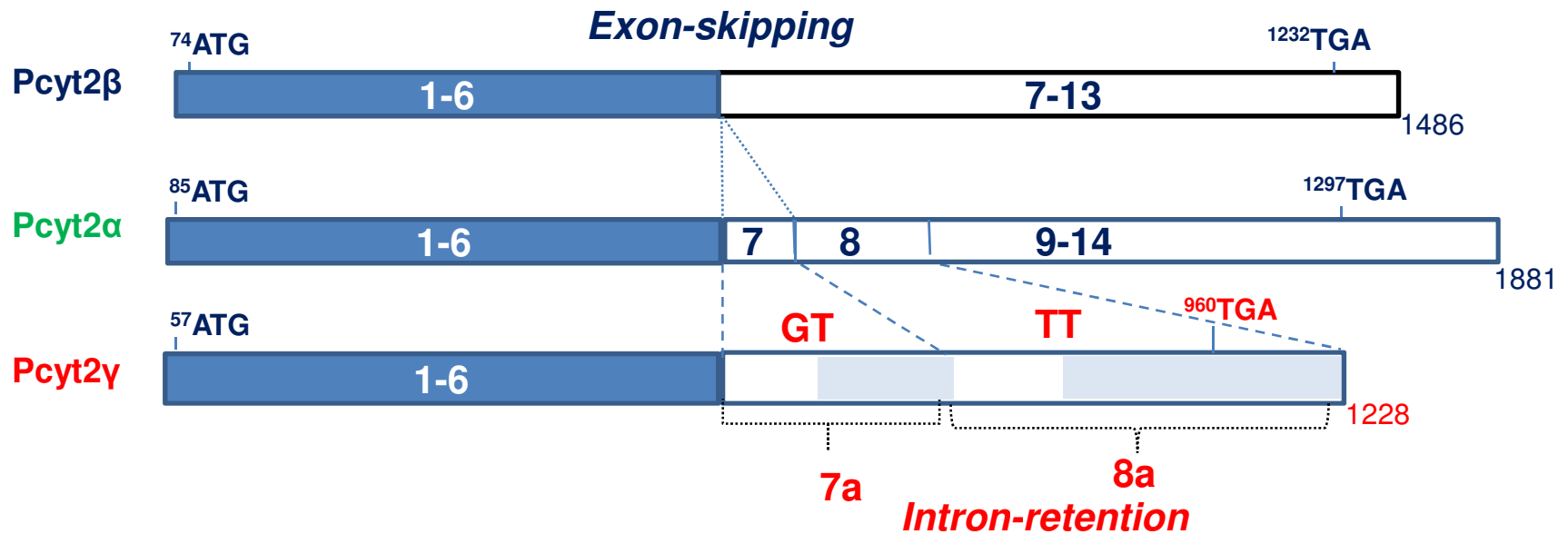
## Kennedy Pathway

## DAG/TAG Pathway

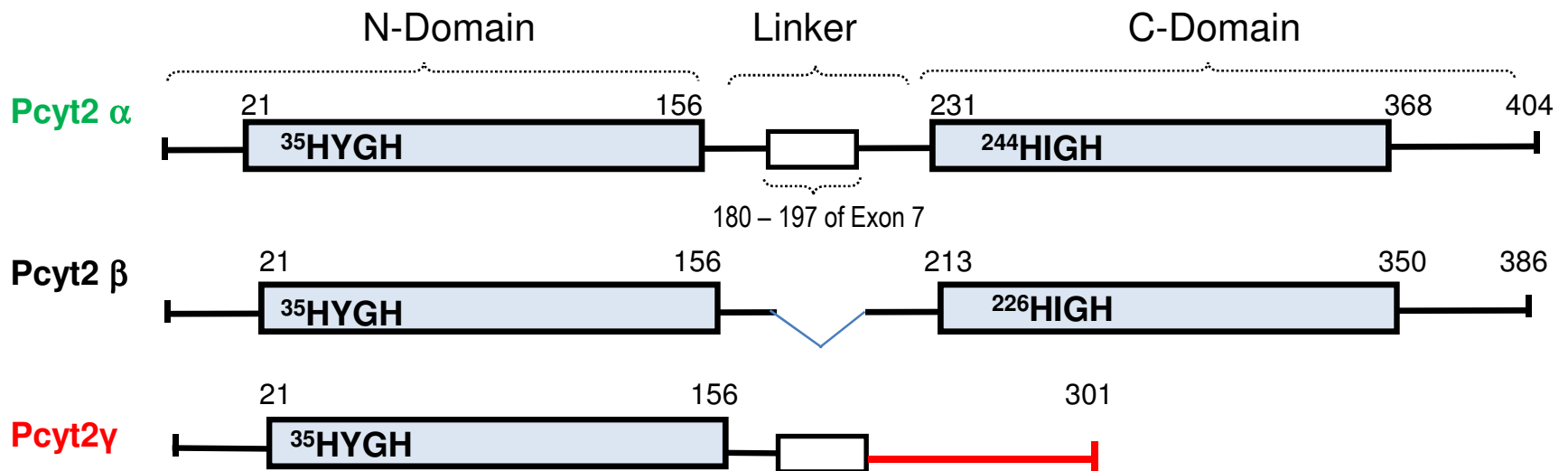


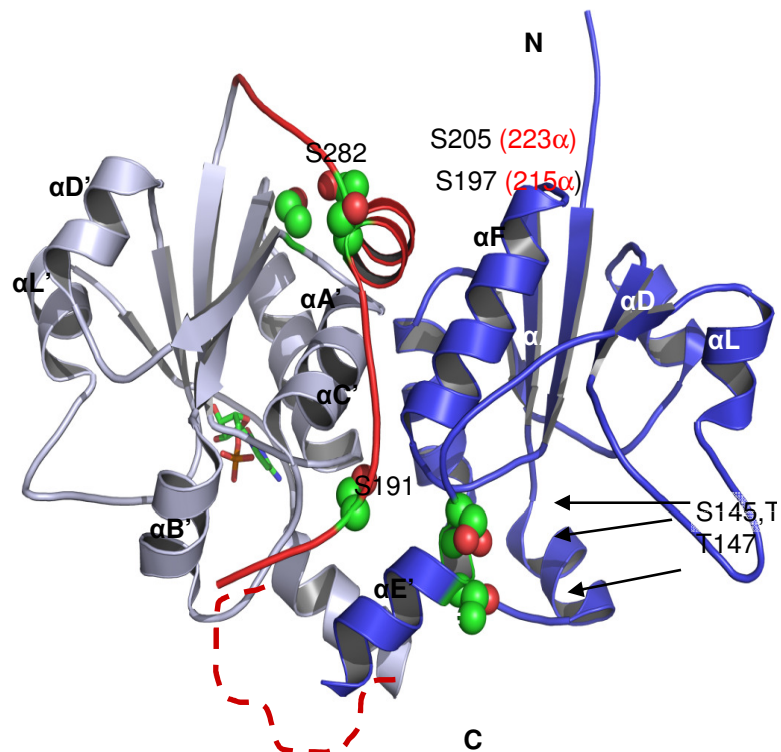
**Pcyt2 regulates DAG partitioning between PE and TAG**

# A. Pcyt2 Splicing



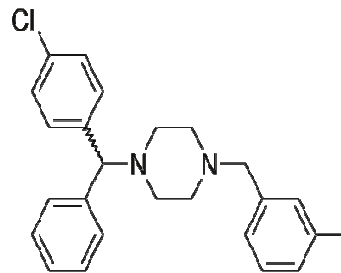
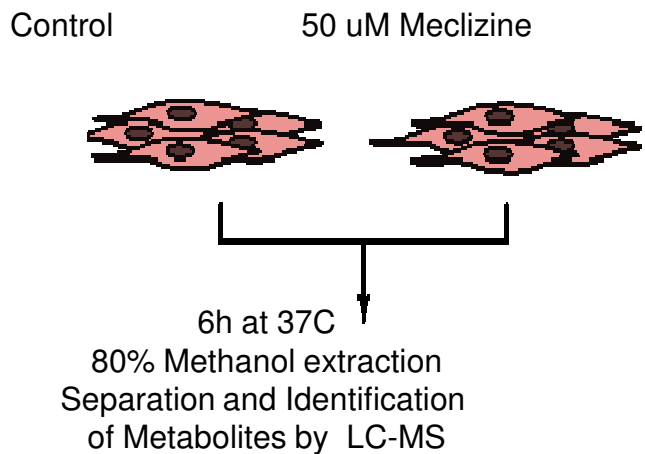
# B. Pcyt2 Proteins



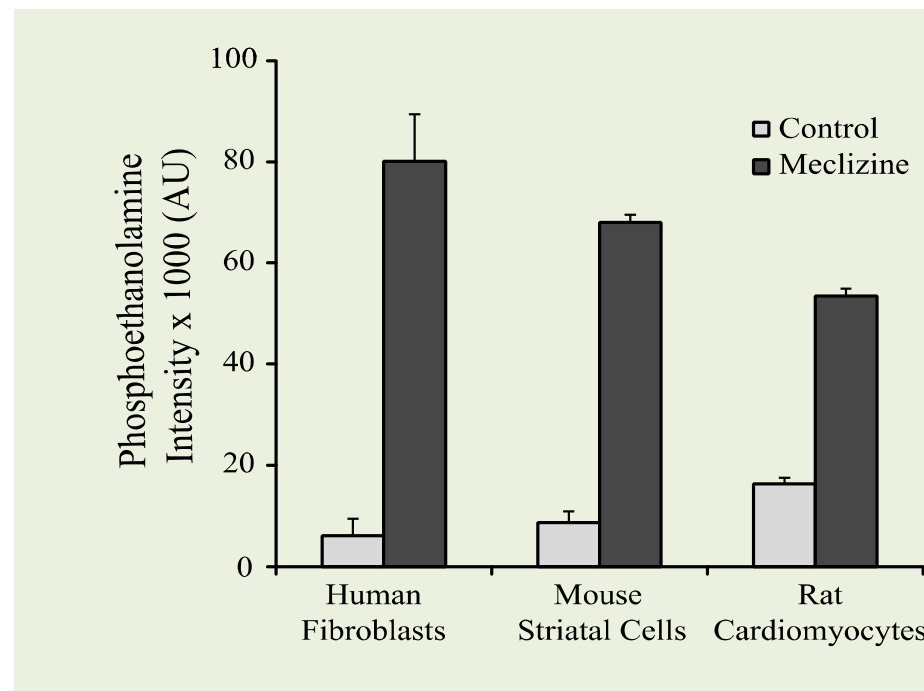
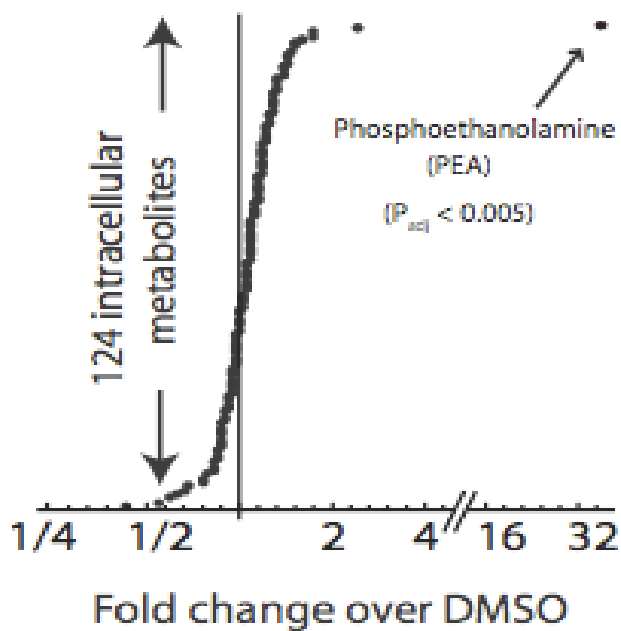


mPcyt2 $\alpha$	20	RRIVRVW	CDGICYDMVHYGHSNQLRQAR	AMGDYLIVGV	HTDEEIAKHK
hPcyt2 $\beta$	20	RRAVRVW	CDGICYDMVHYGHSNQLRQAR	AMGDYLIVGV	HTDEEIAKHK
3elb structure		ss	sss	hhhhhhhhhhh h	ssssss hhhhhh
			$\beta 1$	$\alpha A$	$\beta 2$ $\alpha B$
mPcyt2 $\alpha$	67	GPPVFTQEER	YKMVQAIKWDEVVPAAPYV	TTLETLDKHN	CDFCVHGNDI
hPcyt2 $\beta$	67	GPPVFTQEER	YKMVQAIKWDEVVPAAPYV	TTLETLDKYN	CDFCVHGNDI
3elb structure		hhh	hhhh	sssss	hhhhhh sss
			$\alpha C$	$\beta 3$	$\alpha D$ $\beta 4$
mPcyt2 $\alpha$	117	TLTVDGRDTY	EEVKQAGRYR	ECKRTQGVSTDLVGRMLL	VTKAHSSQEM
hPcyt2 $\beta$	117	TLTVDGRDTY	EEVKQAGRYR	ECKRTQGVSTDLVGRMLL	VTKAHSSQEM
3elb structure		hhhhh	sss	ss	hhhhhhh
			$\alpha L$	$\beta 5$	$\alpha E$
mPcyt2 $\alpha$	167	SSEYREYADS	FGKPPHPTPAGDTLSSEVSS	CPGGQSPWT	GV <del>S</del> QFLQTSQ
hPcyt2 $\beta$	187	SS <del>E</del> YREYADS	FGK.....	CPGGRNPWT	GV <del>S</del> QFLQTSQ
3elb structure		-----	-----	-----	-----
		unresolved			
mPcyt2 $\alpha$	217	KIIQFASGKEPQPG	ETVIYVAGAFDLFHIGHVDFLQEVHK	LAKRPYVIAG	
hPcyt2 $\beta$	199	KIIQFASGKEPQPG	ETVIYVAGAFDLFHIGHVDFLEKVRH	LAERPYYIAG	
3elb structure		hhhhh	sssssss	hhhhhhhhhhh	sssssss
		$\alpha F$	$\beta 1'$	$\alpha A'$	$\beta 2'$
mPcyt2 $\alpha$	267	LHFDQEVNRY	KGKNYPIMNLHERTSLVLC	RYVSEVVIGA	PYSVTAELLN
hPcyt2 $\beta$	249	LHFDQEVNRY	KGKNYPIMNLHERTSLVLC	RYVSEVVIGA	PYAVTAELLS
3elb structure		ss	hhhhhhh h	sssss	hhhhh
		$\alpha B'$	$\alpha C'$	$\beta 3'$	$\alpha D'$
mPcyt2 $\alpha$	317	HFKVDLVCHG	KTEIVPDRDG	SDPYQEPKRR	GIFYQIDSGS
hPcyt2 $\beta$	299	HFKVDLVCHG	KTEIIPDRDG	SDPYQEPKRR	GIFRQIDSGS
3elb structure		hh	sss	hhhhh	sssss
		$\beta 4'$	$\alpha L'$	$\beta 5'$	$\alpha E'$

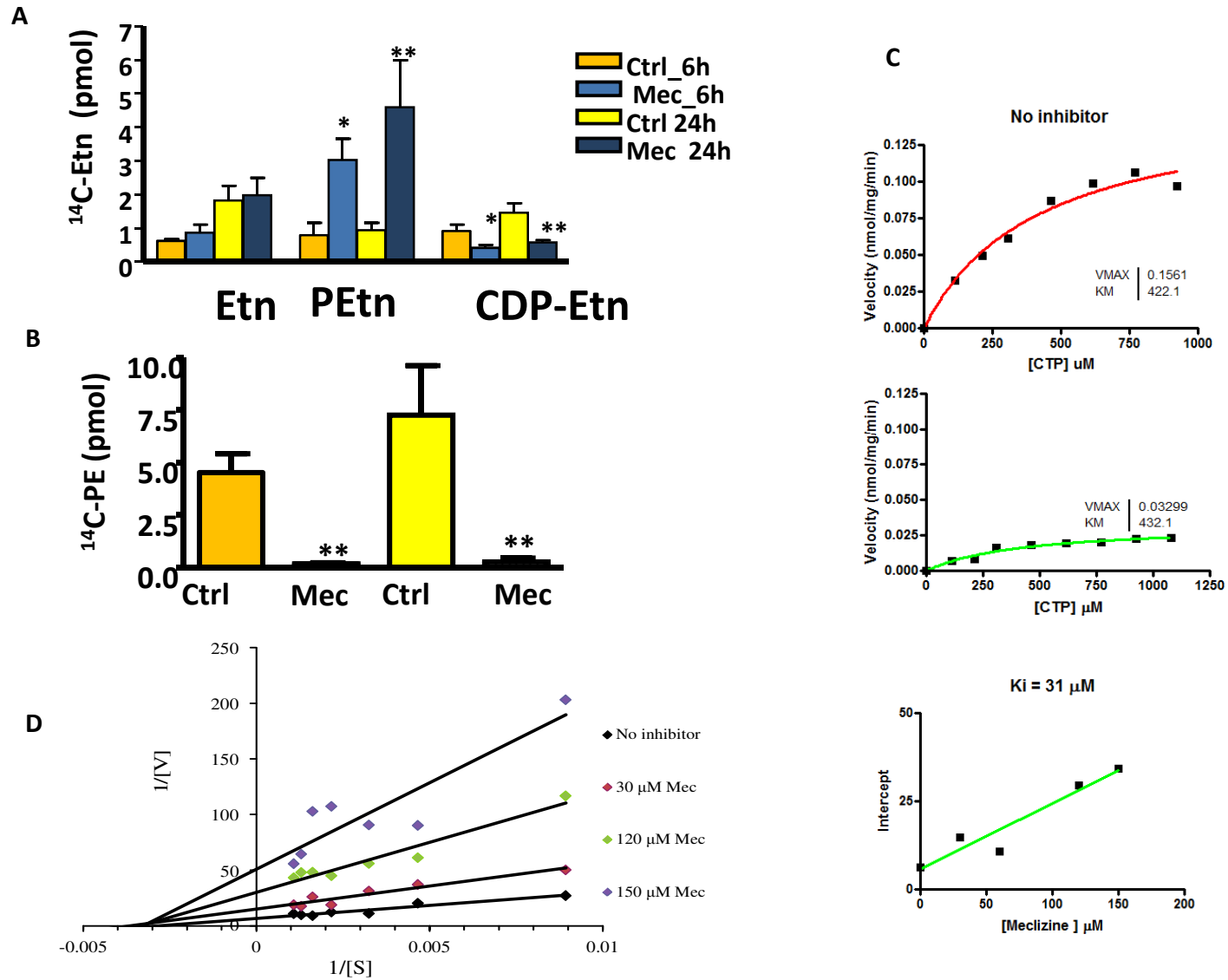
# Meclizine Story



**Meclizine**  
*(RS)*-1-[(4-chlorophenyl)(phenyl)methyl]-4-(3-methylbenzyl)piperazine



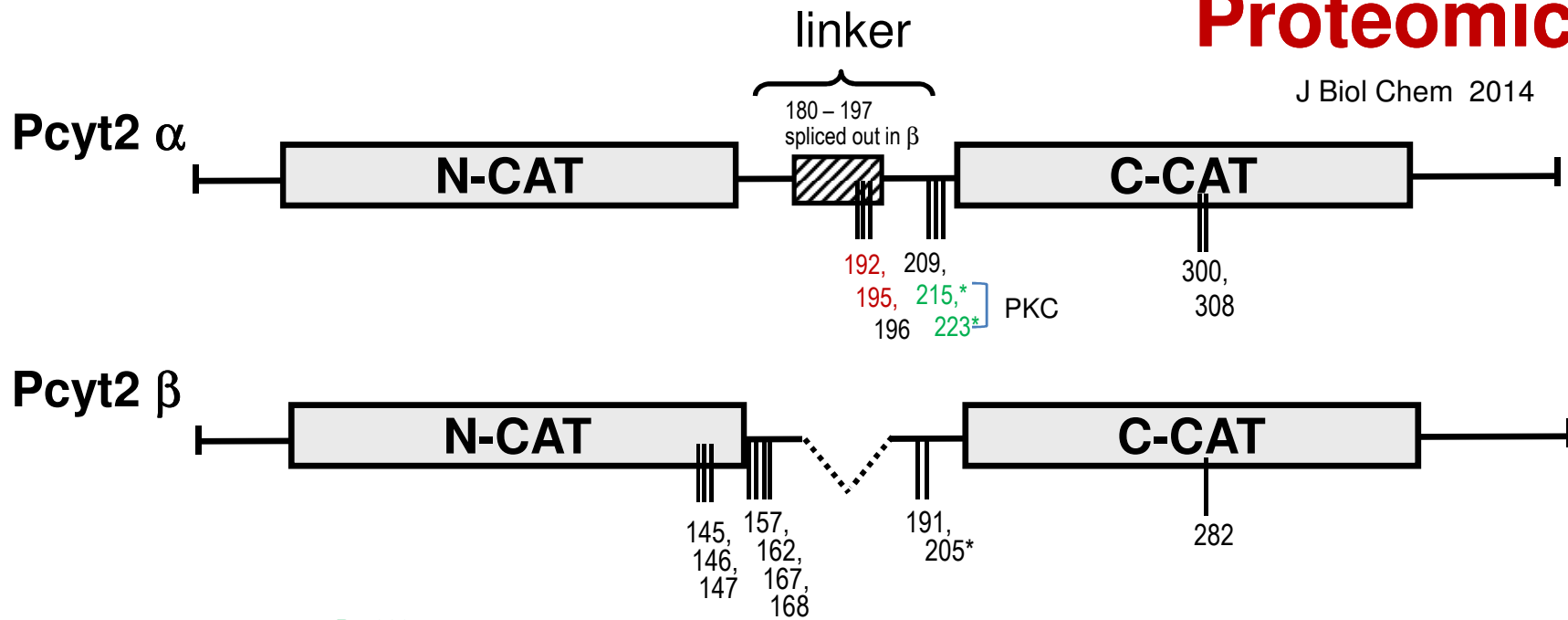
# Meclizine is a non-competitive inhibitor of Pcyt2 with respect to CTP



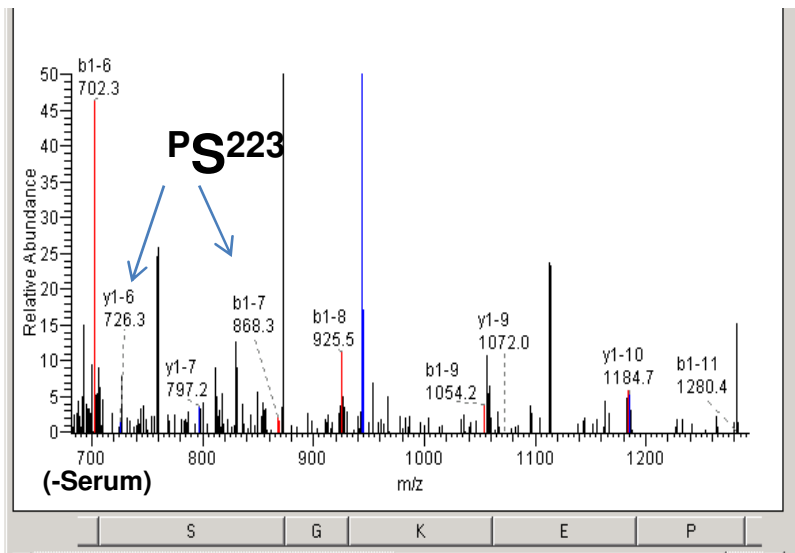


# Proteomics

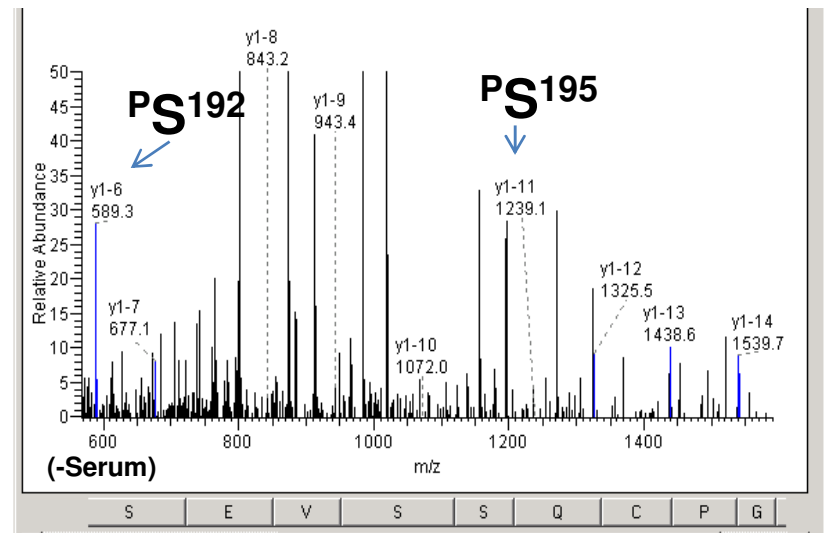
J Biol Chem 2014



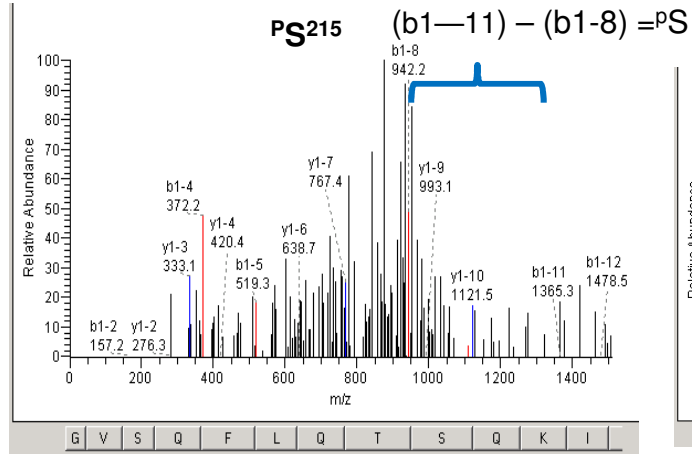
B. Pcyt2 $\alpha$  shared [PS<sup>223</sup>GKEP<sup>227</sup>]



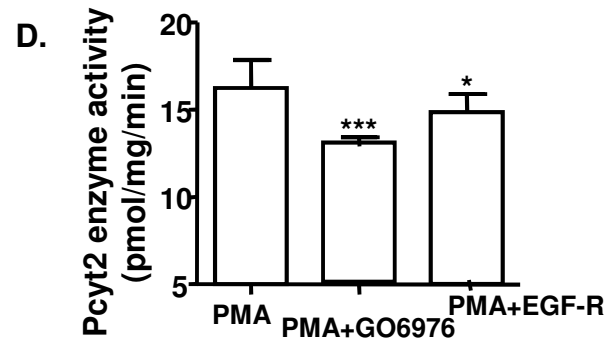
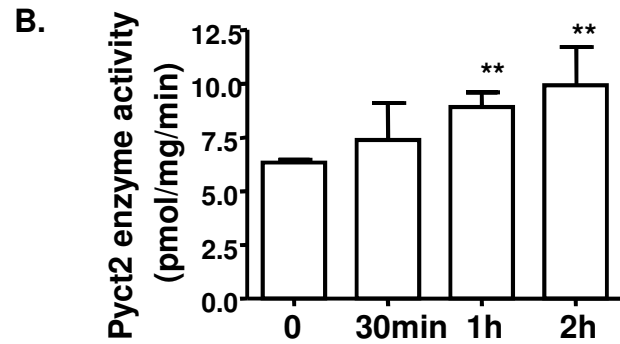
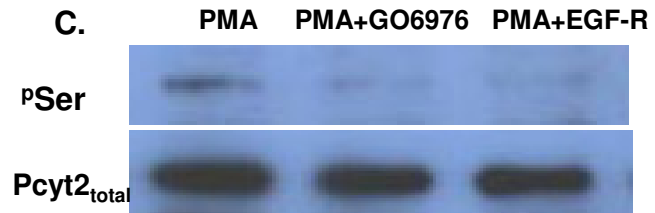
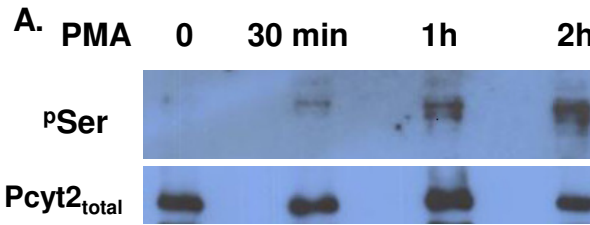
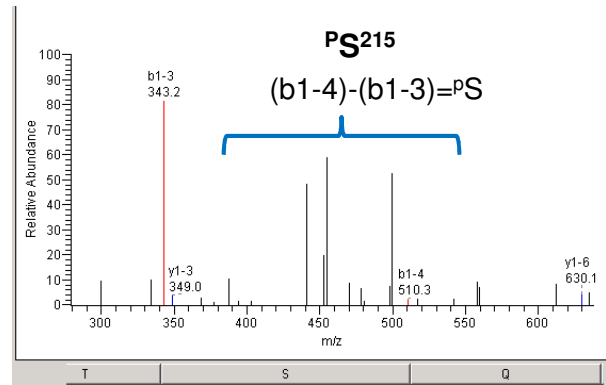
A. Pcyt2 $\alpha$  specific [PS<sup>192</sup>EVPS<sup>195</sup>SQCPG<sup>200</sup>]

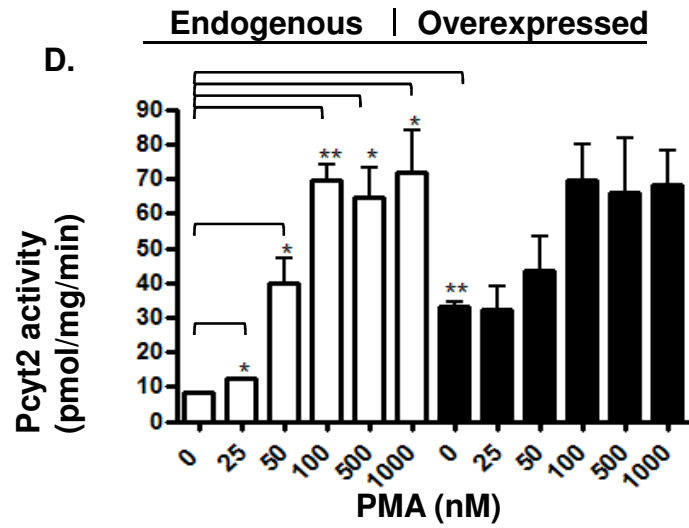
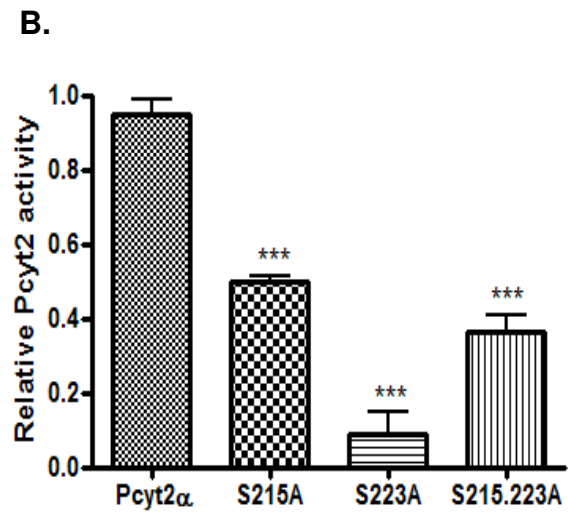
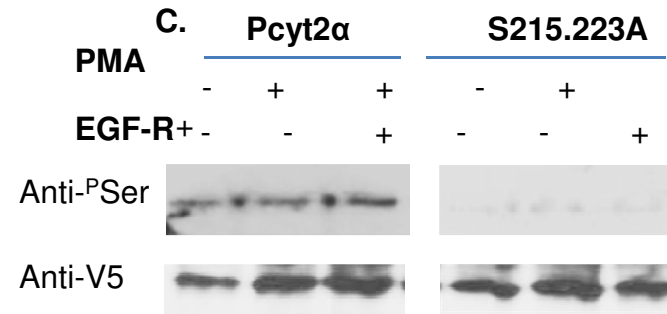
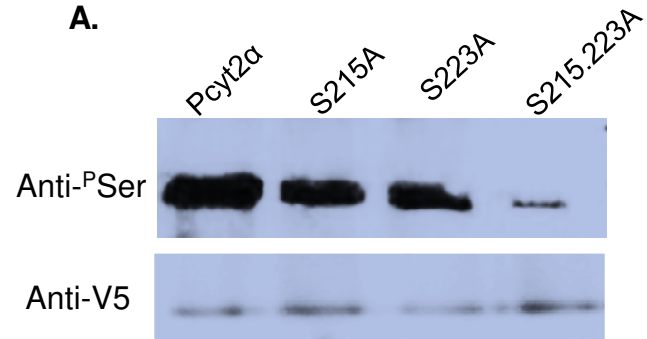


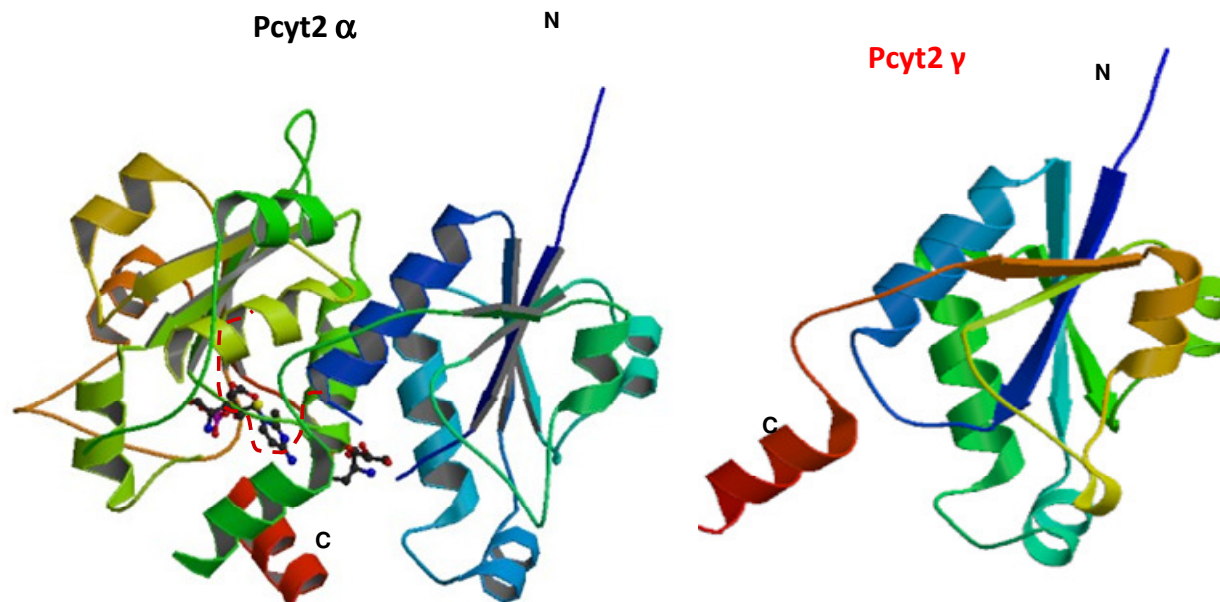
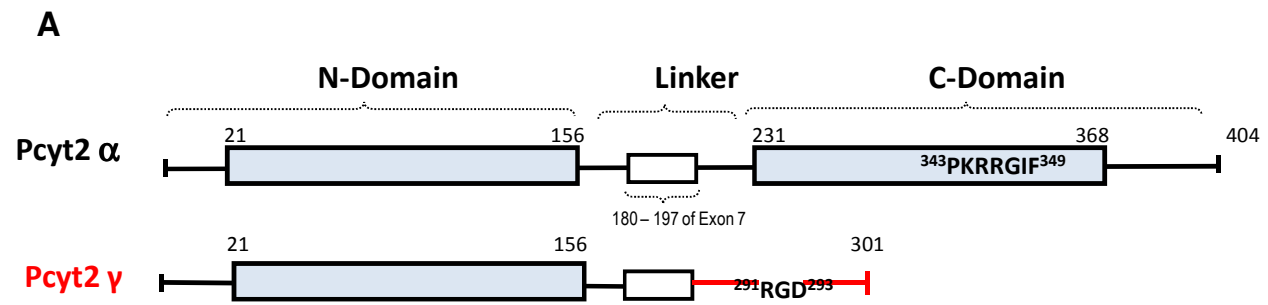
F. Pcyt2 $\alpha$  phosphorylation with PKC $\alpha$   
 $^{207}$ GVSQFLQT $^{\text{P}}\text{S}^{215}$ QKI $_{18}$



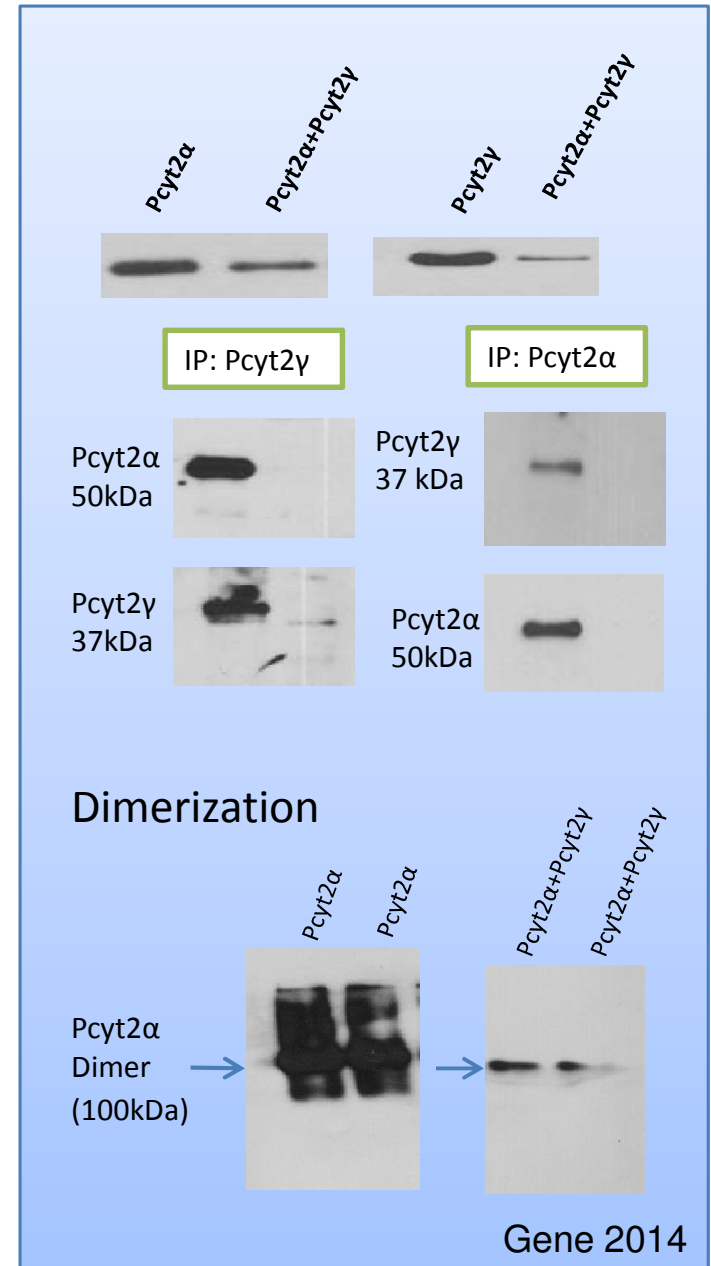
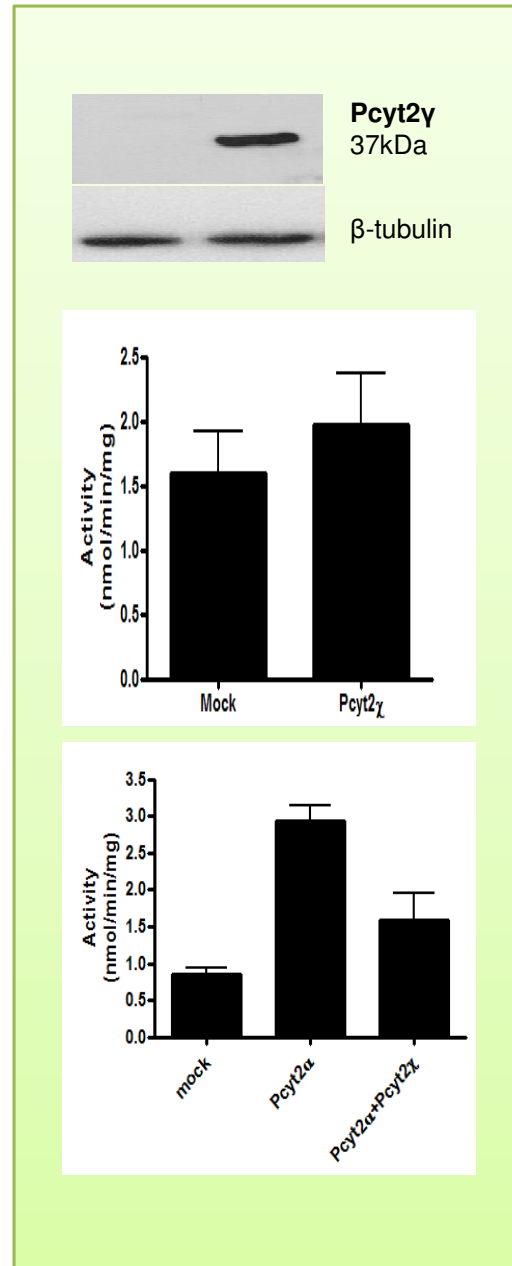
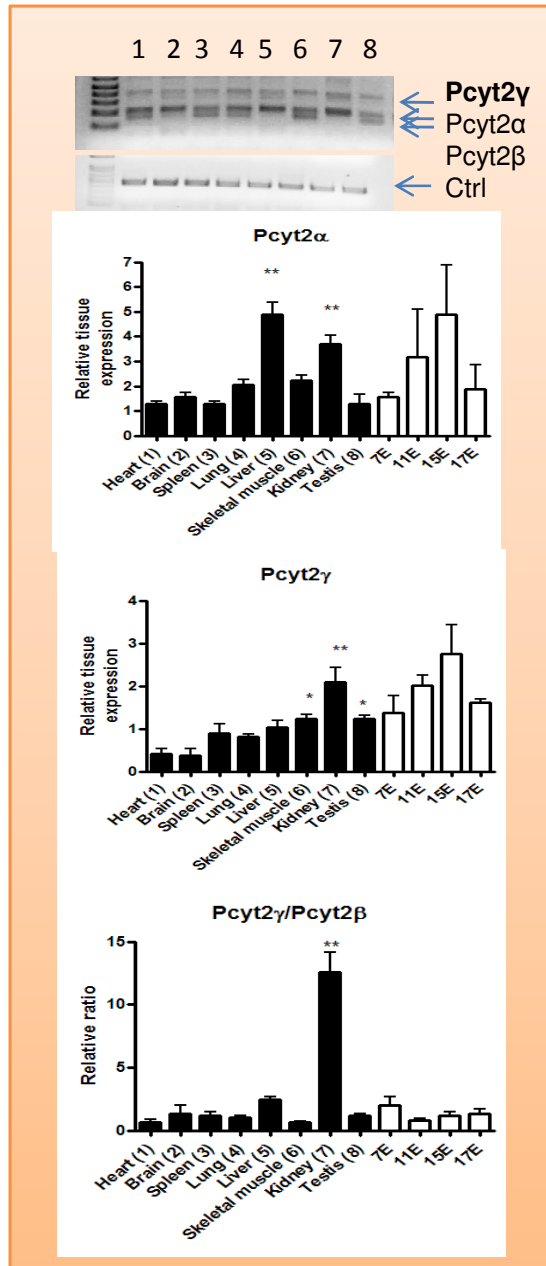
G. Pcyt2 $\alpha$  phosphorylation with PKC $\alpha$   
 $^{\text{P}}\text{S}^{215}$ Q



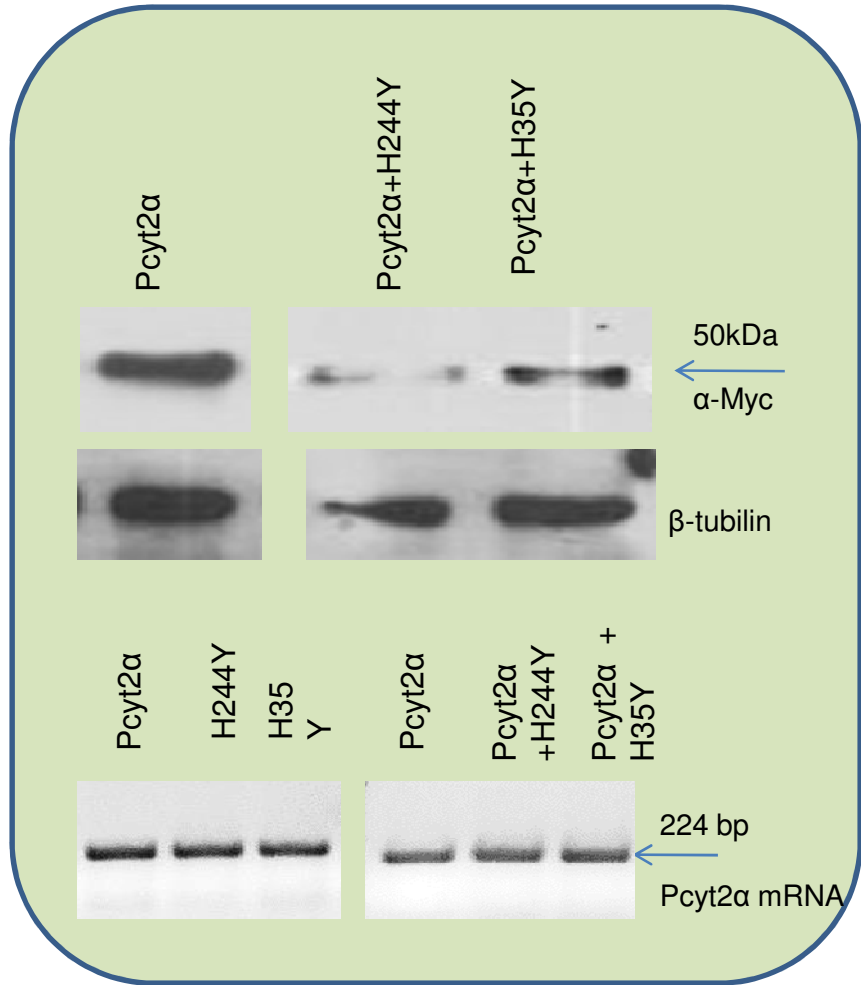




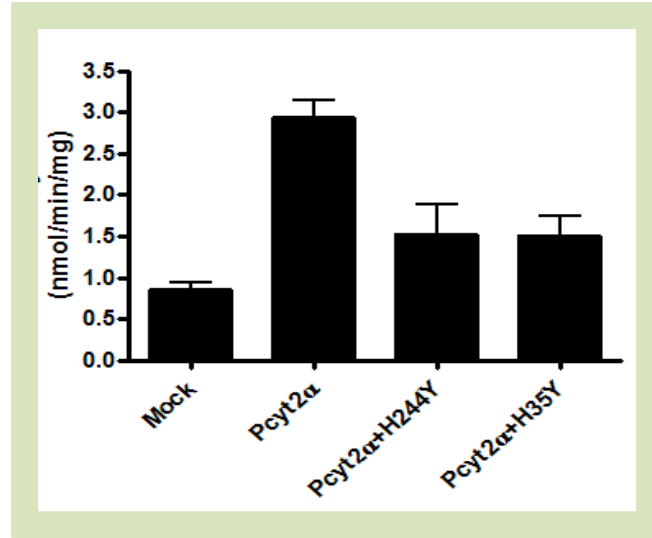
# Pcyt2 $\gamma$ is a dominant negative isoform



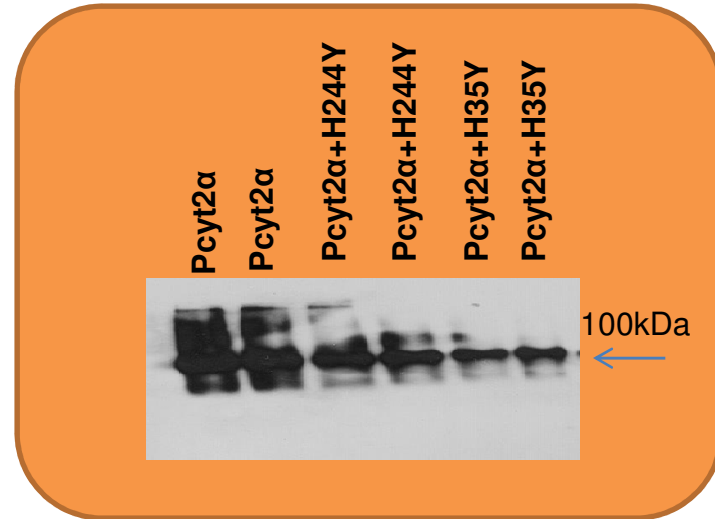
# Mutants of active isoforms are also inhibitors



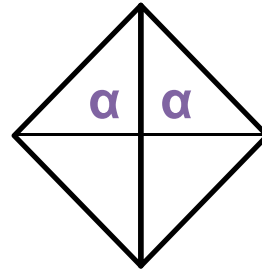
## Activity



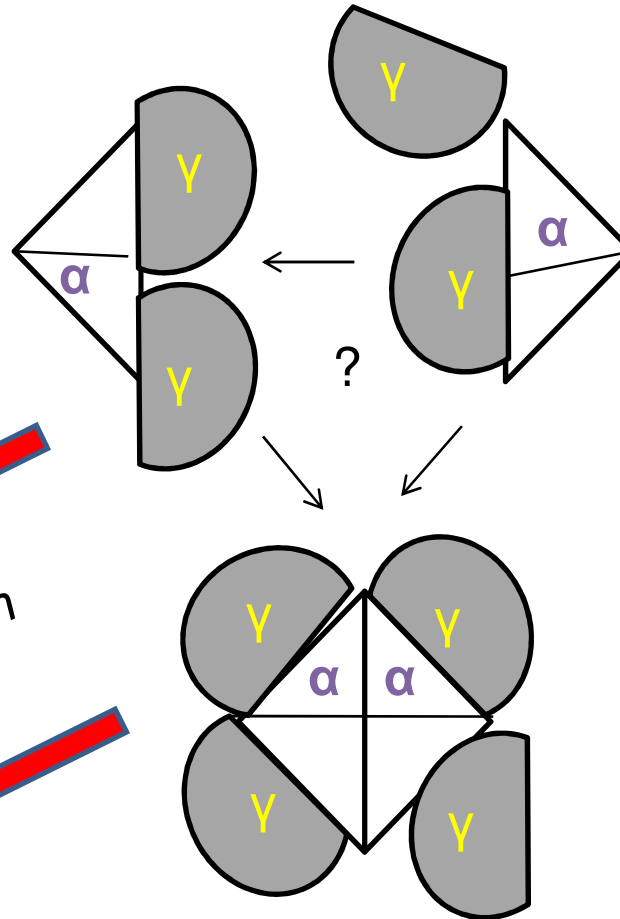
## Dimerization



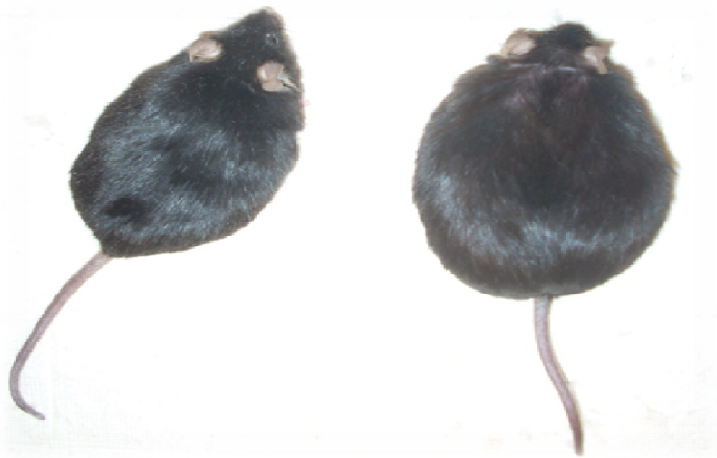
**Pcyt2 $\alpha$  homodimers are active**



**Heterodimers and aggregates are inactive**

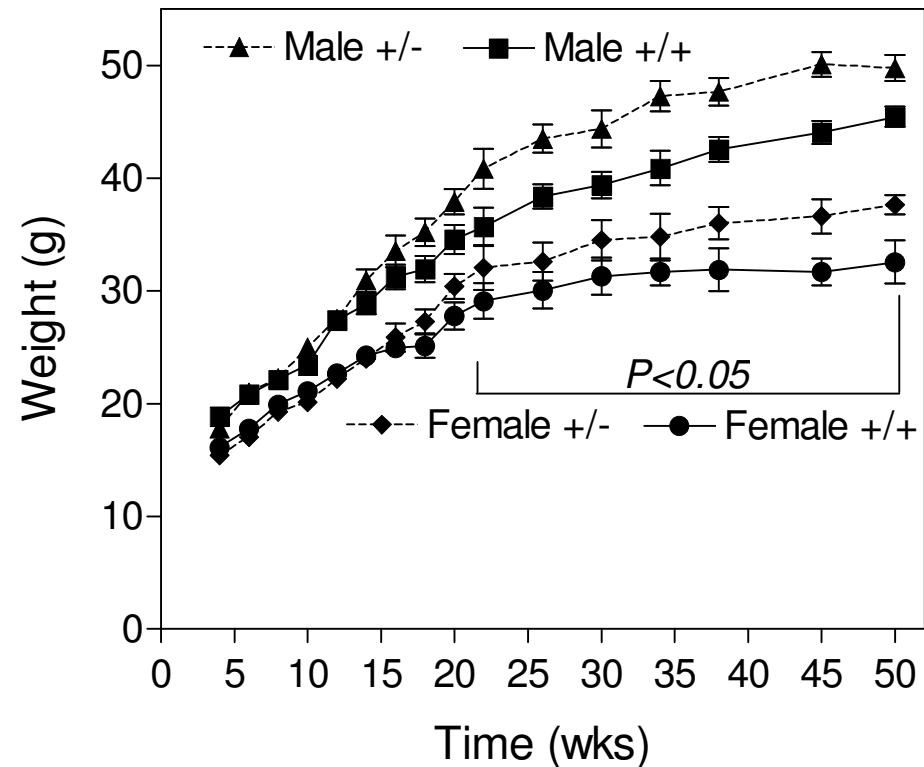


# Pcyt2 deficient mouse ETKO

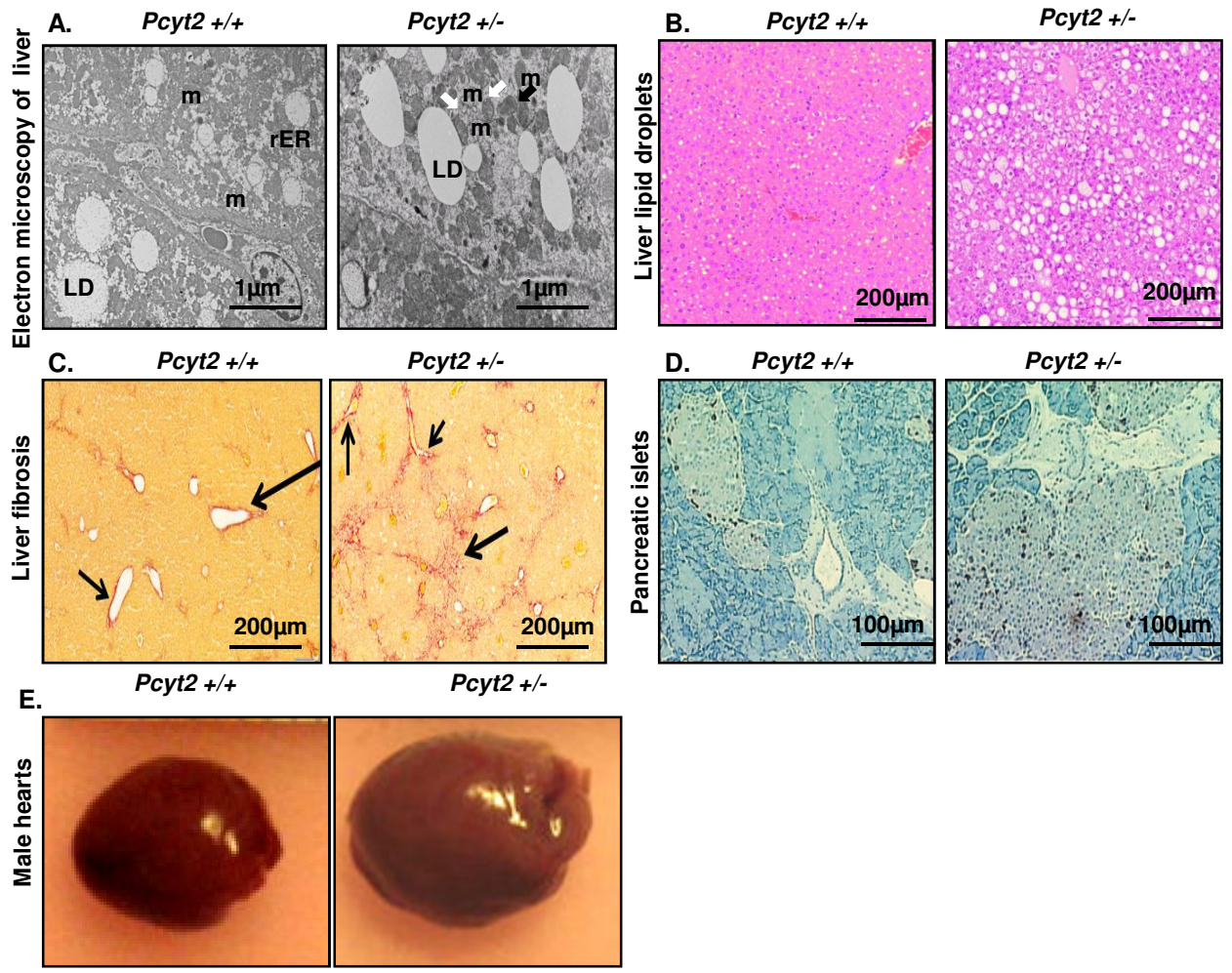


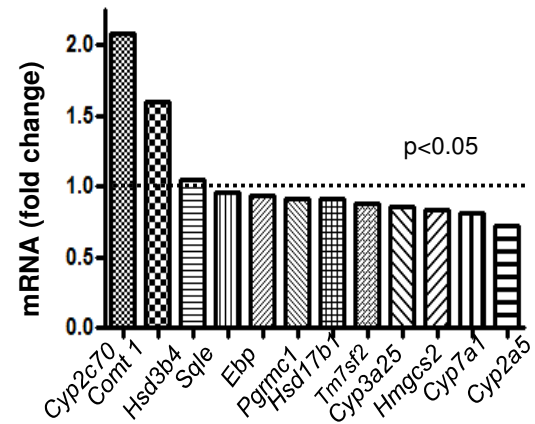
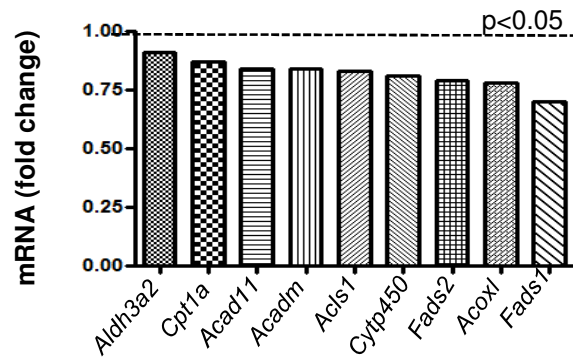
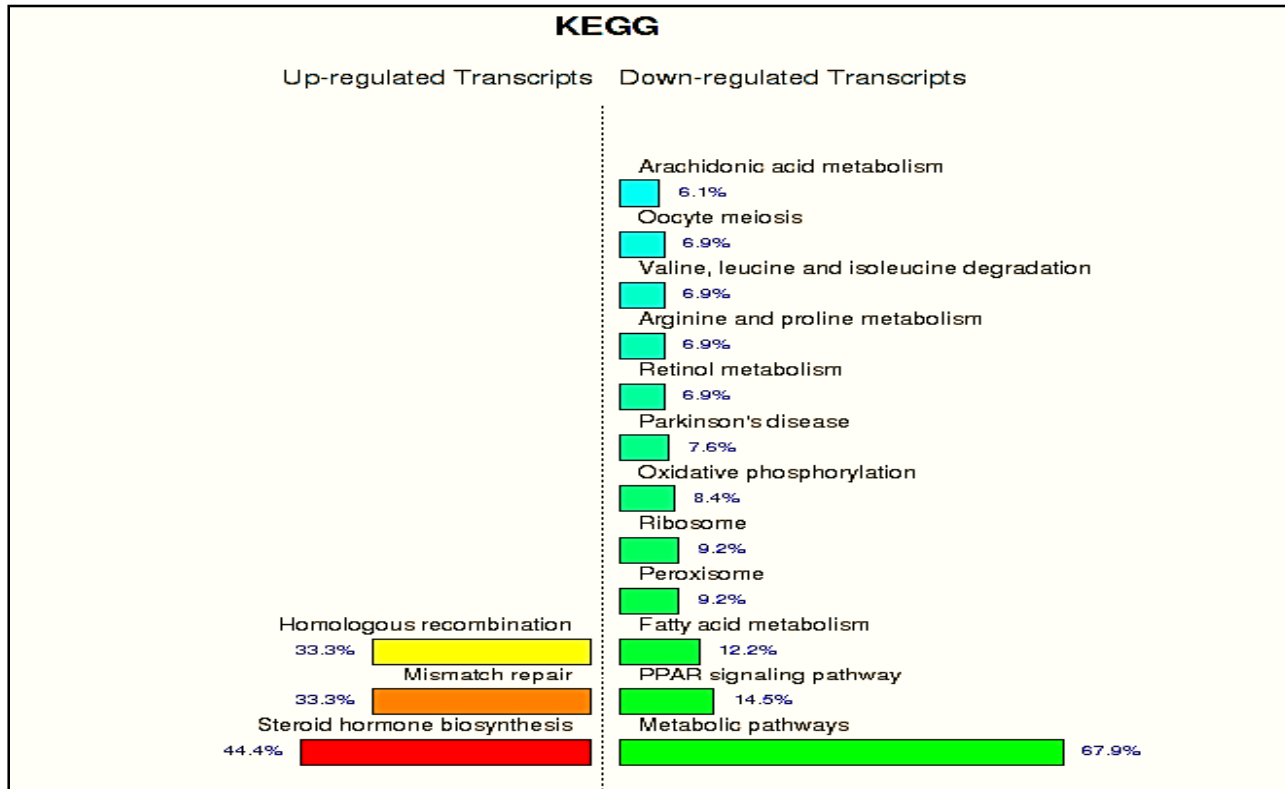
WT

Pcyt2<sup>+/-</sup>





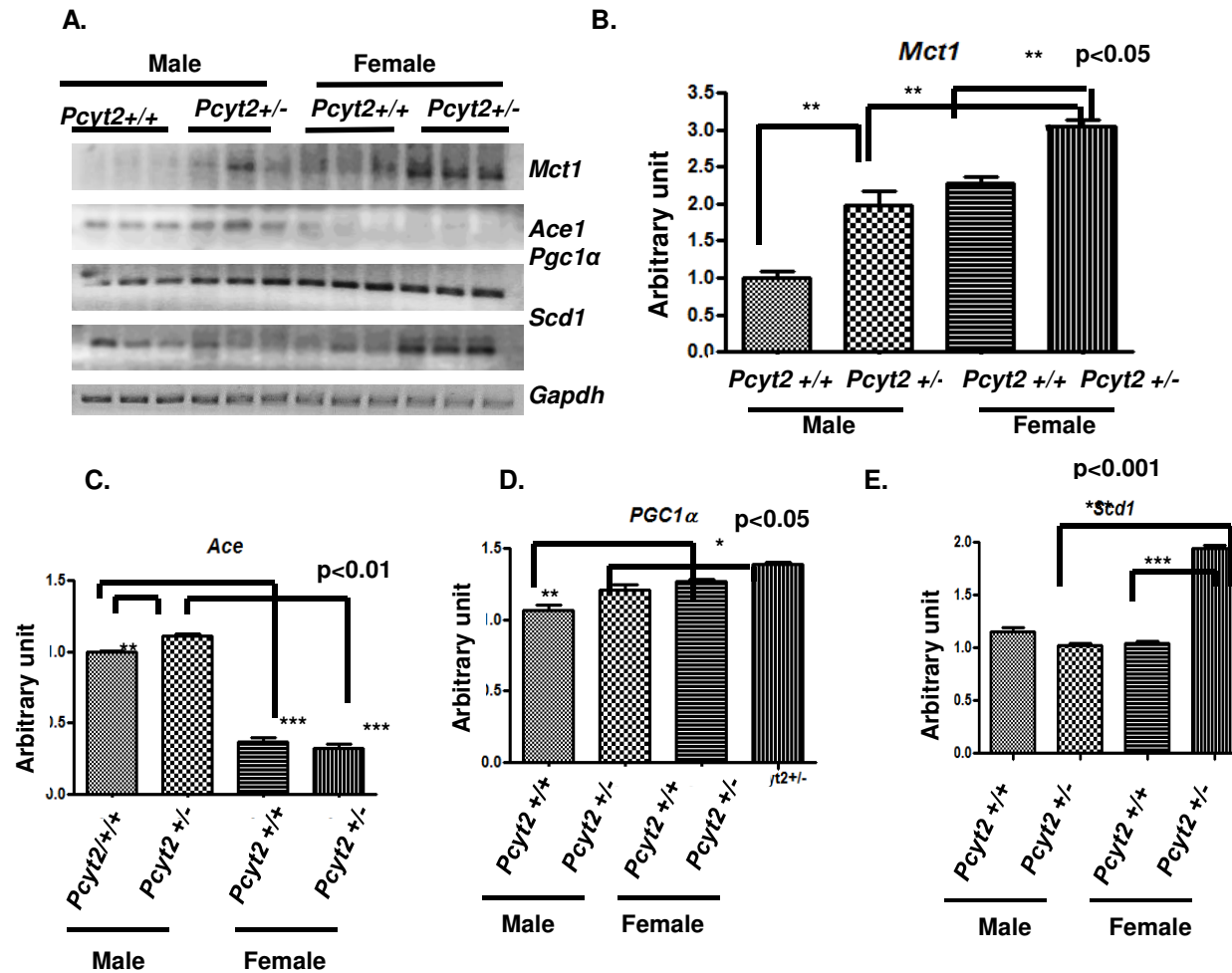


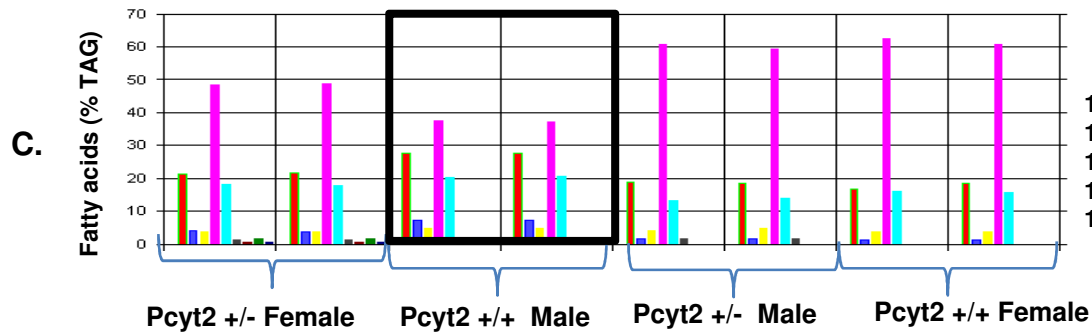
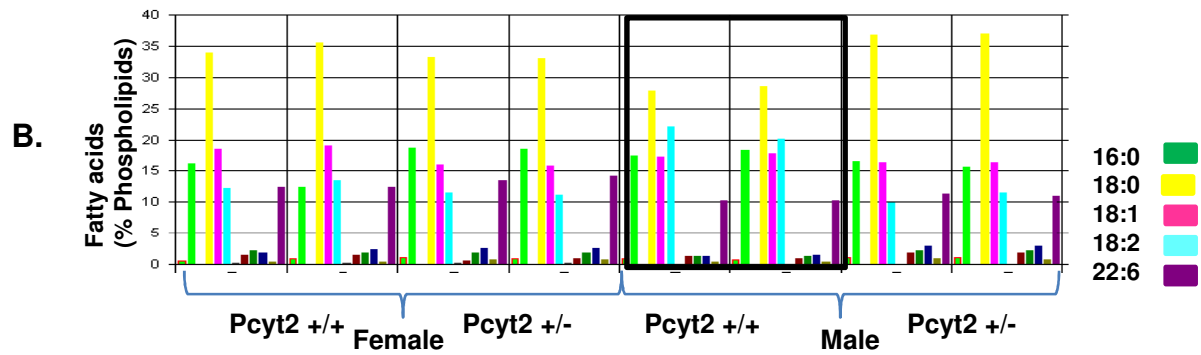
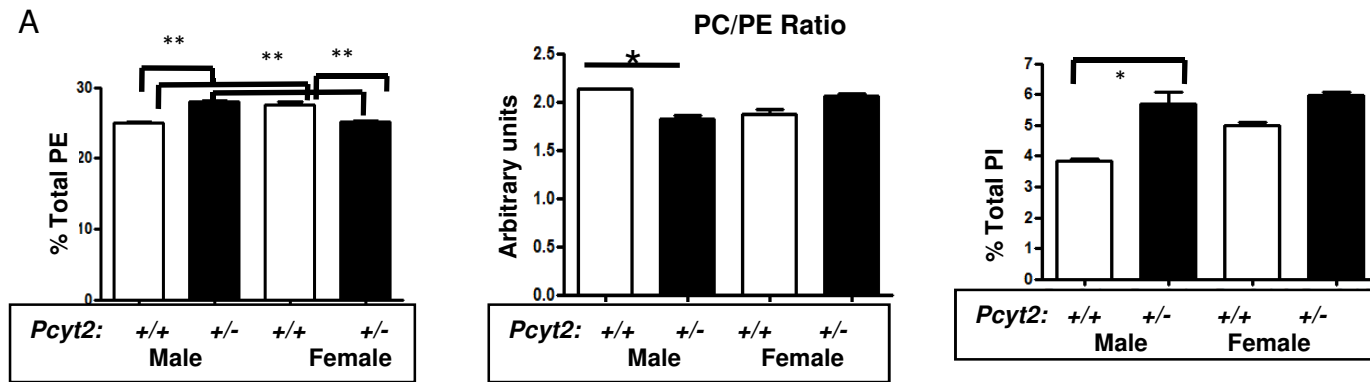


Microarray analysis

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# Gender effect on ETKO heart genes

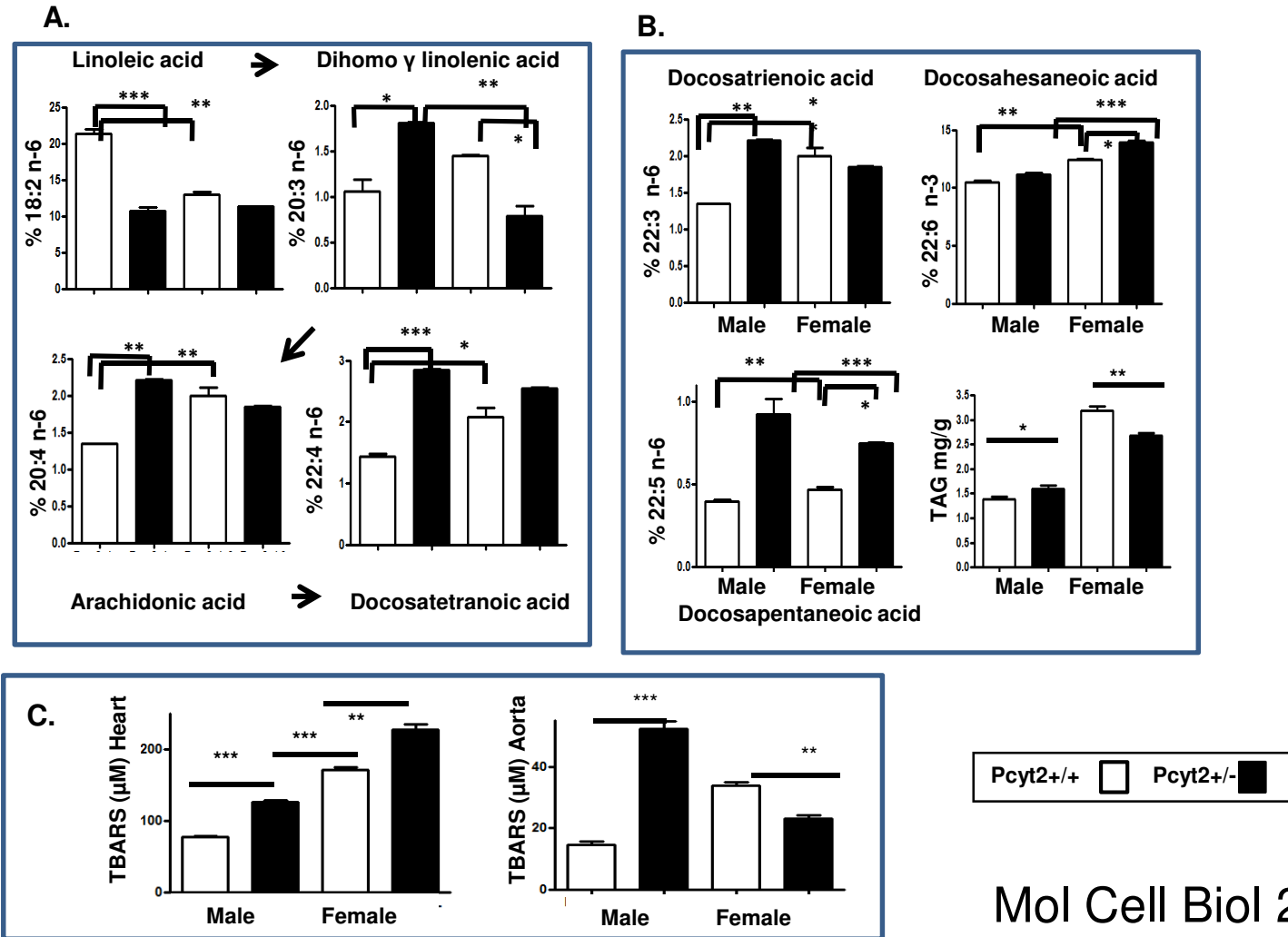


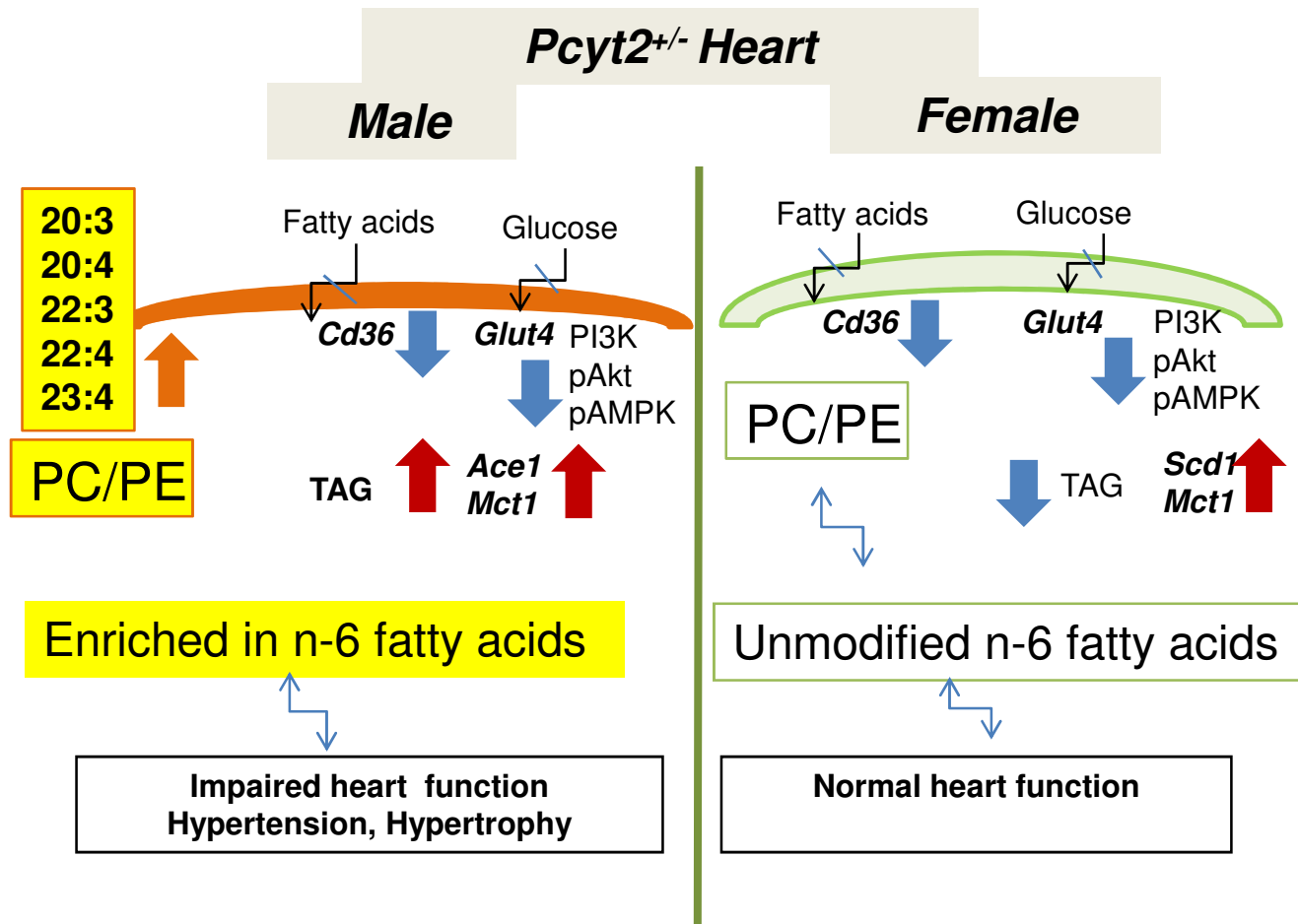


## Heart Lipid Dimorphism

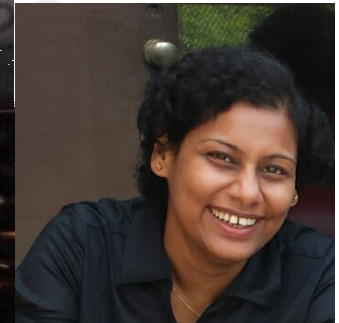
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# N-6 PUFA synthesis and oxidative stress





# Male-specific heart disease



*Pulami*



*Albert      Maida      Leanne      Zvezdan  
Ratnesh      Laila                      Sugash*

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