

FIG. 1

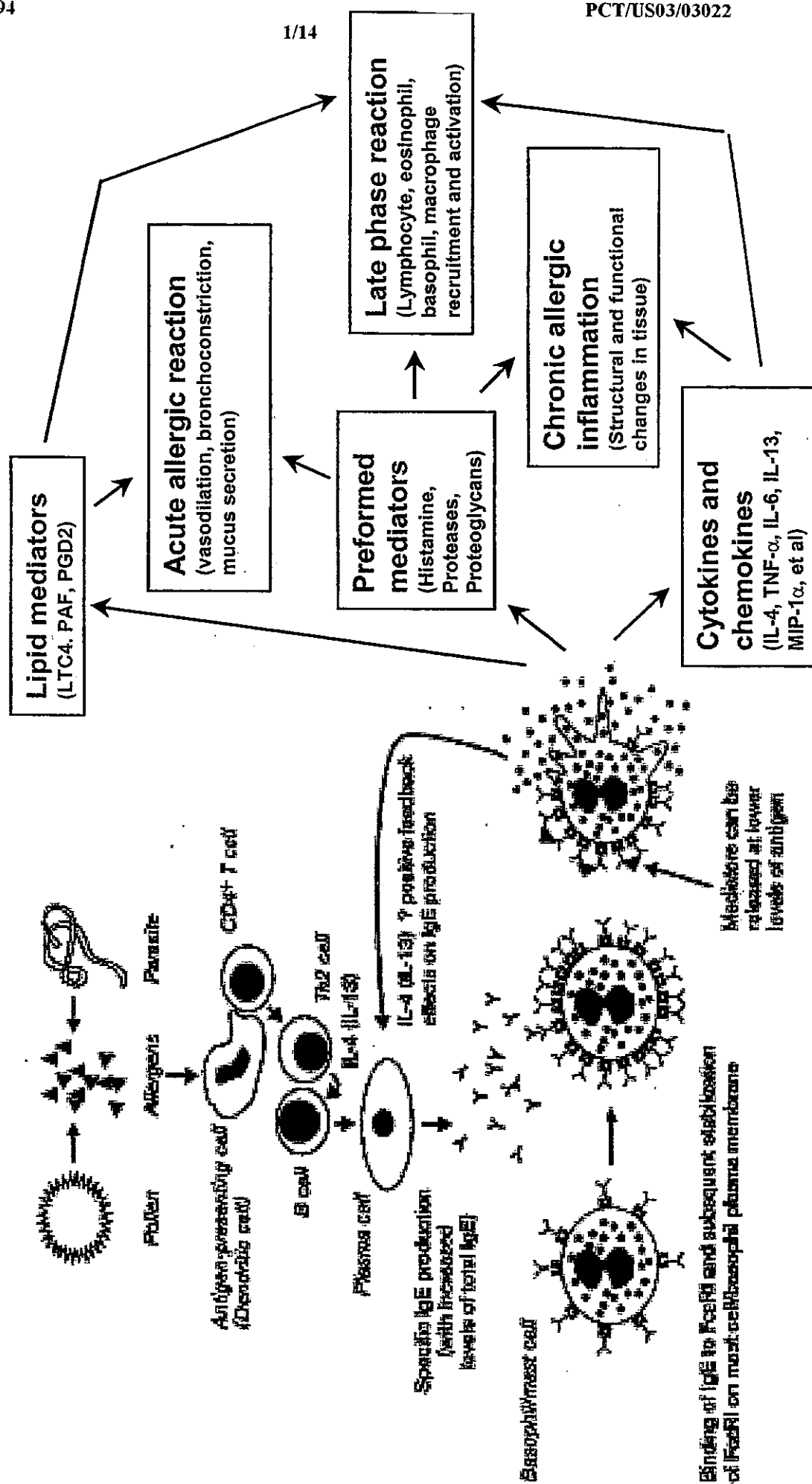


FIG. 2
Mast Cell FcεR1 Signaling Pathway

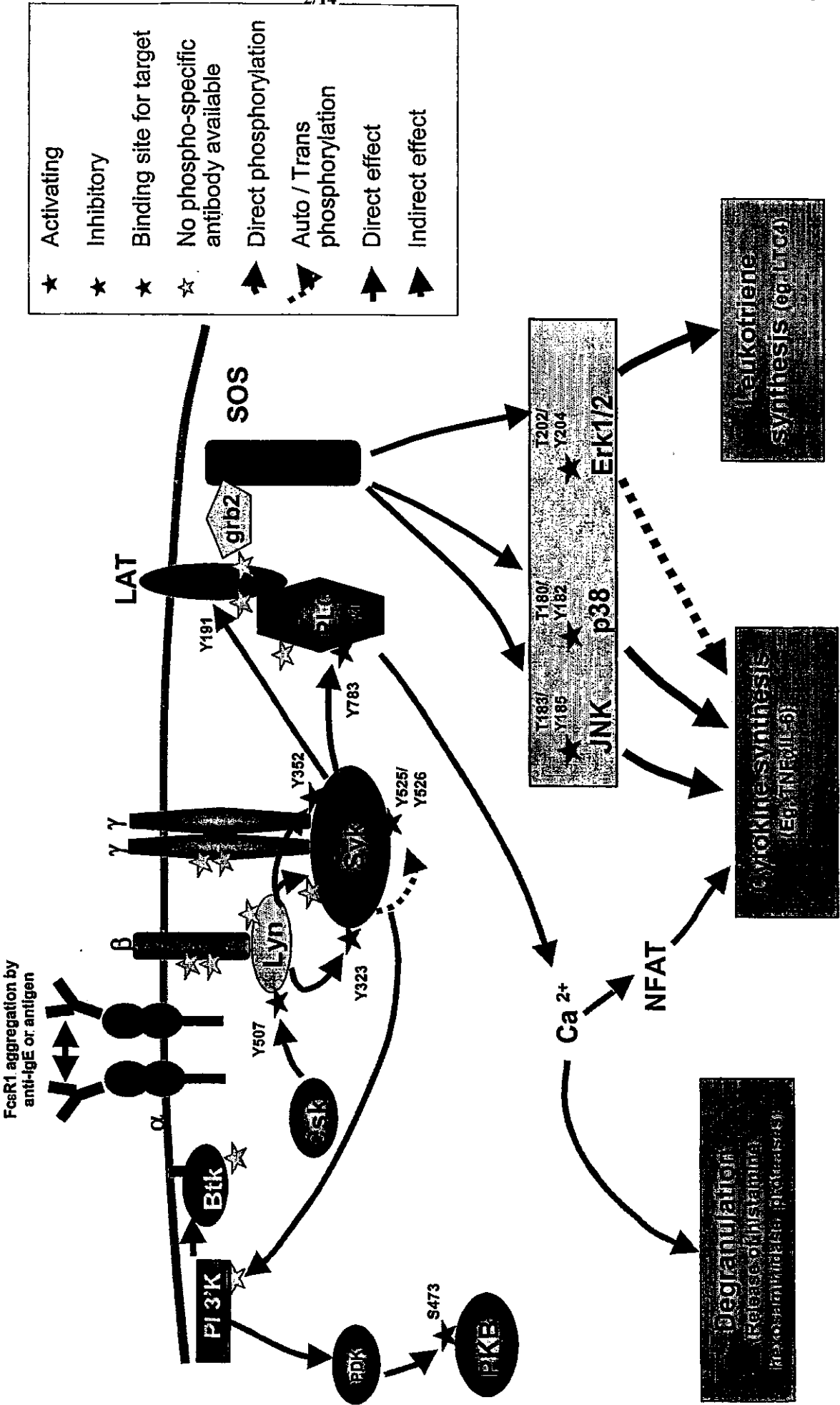


FIG. 3

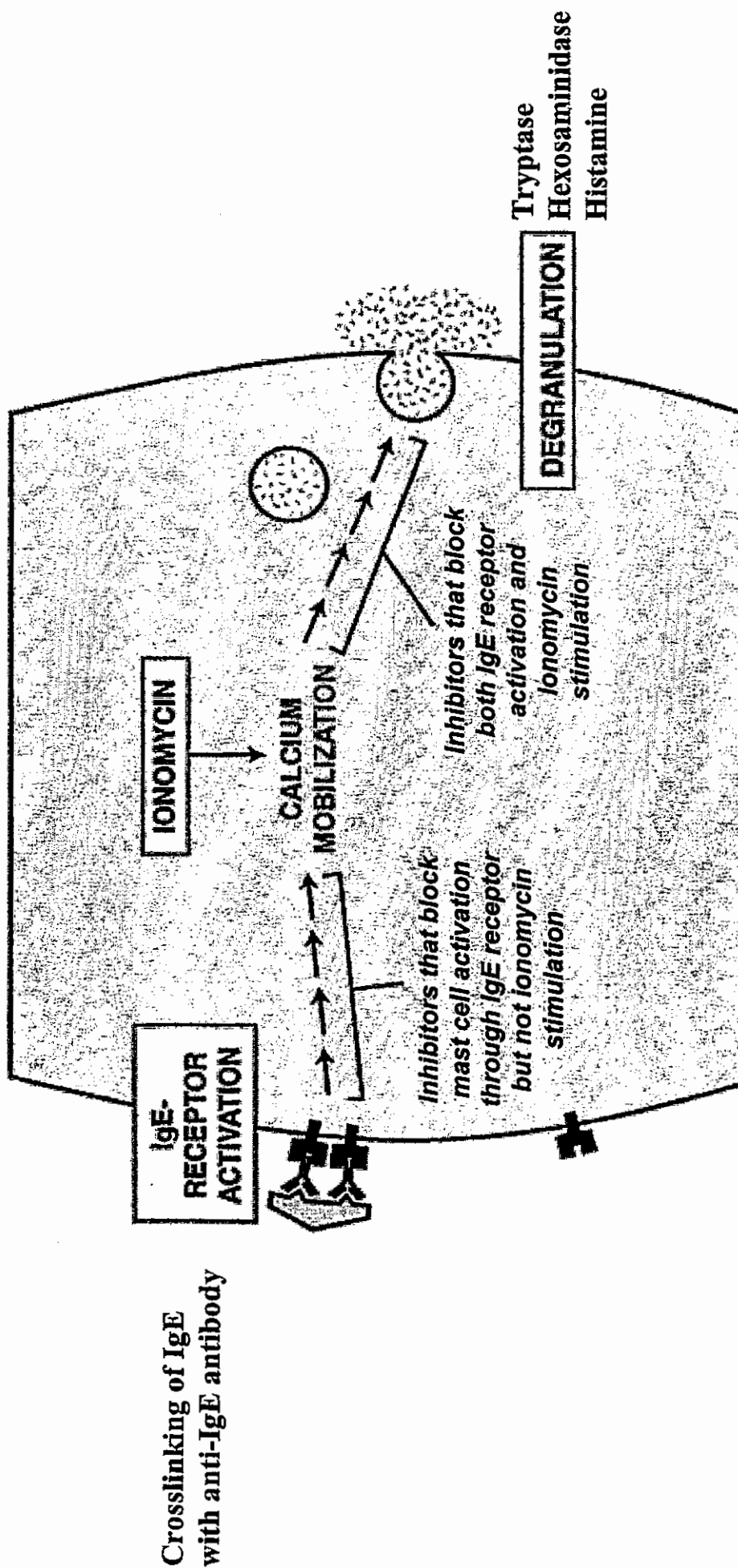


FIG. 4

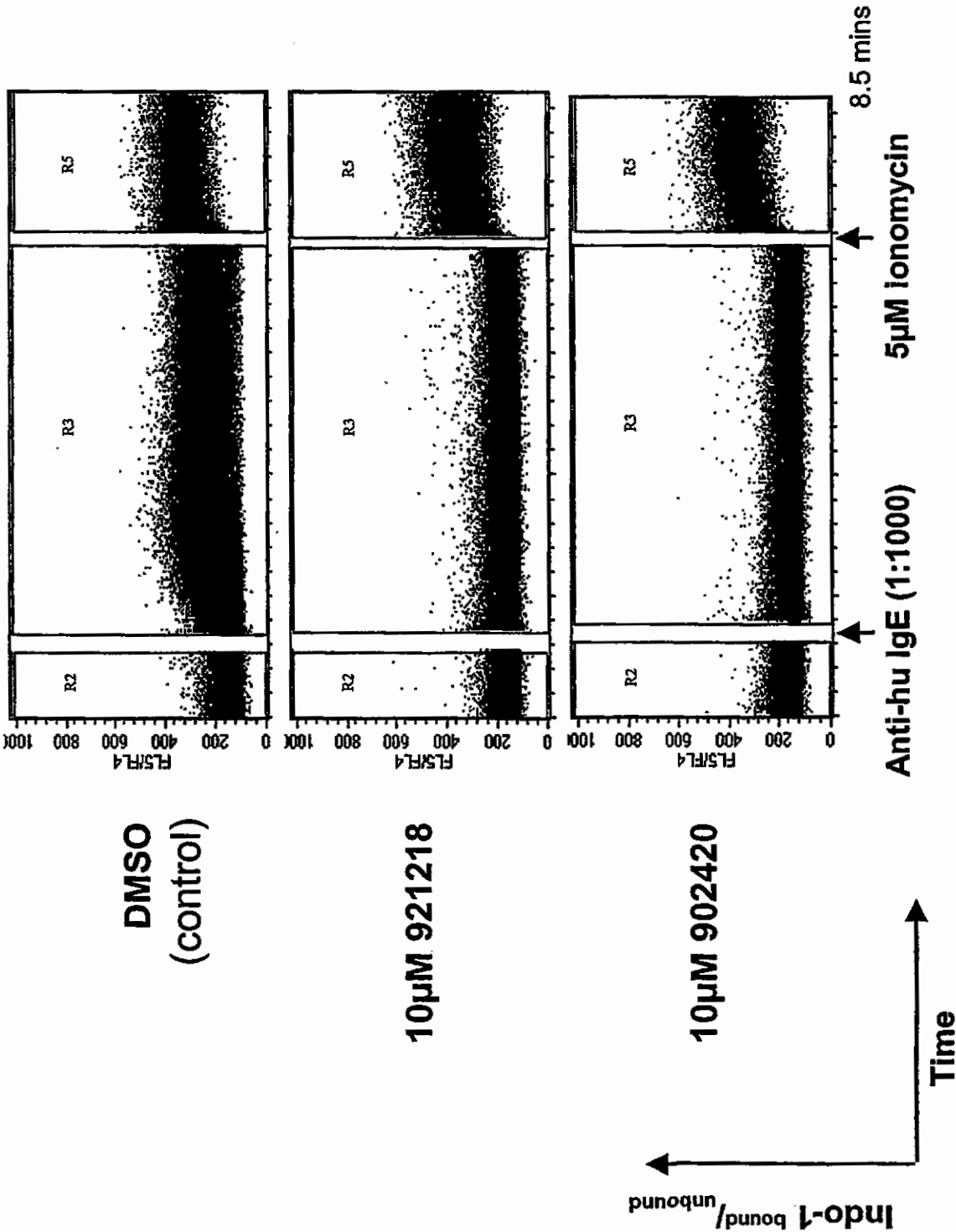


FIG. 5

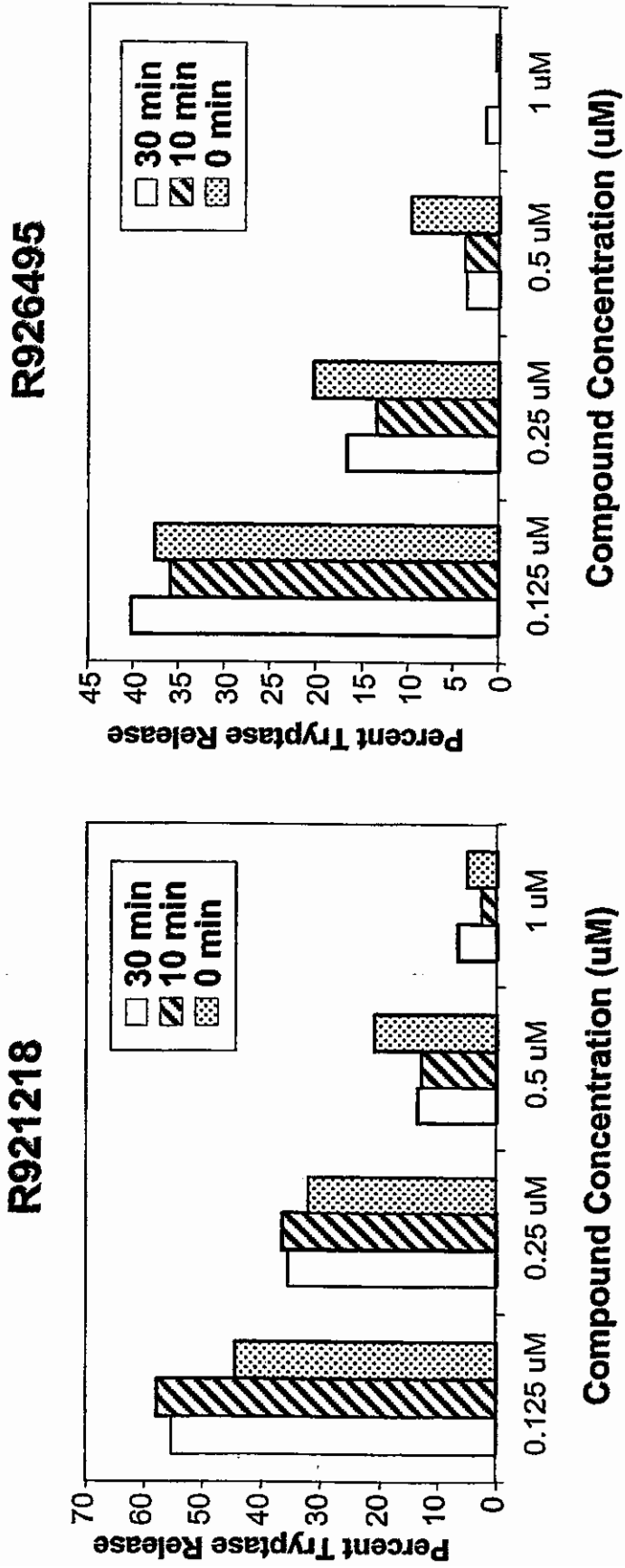


FIG. 6

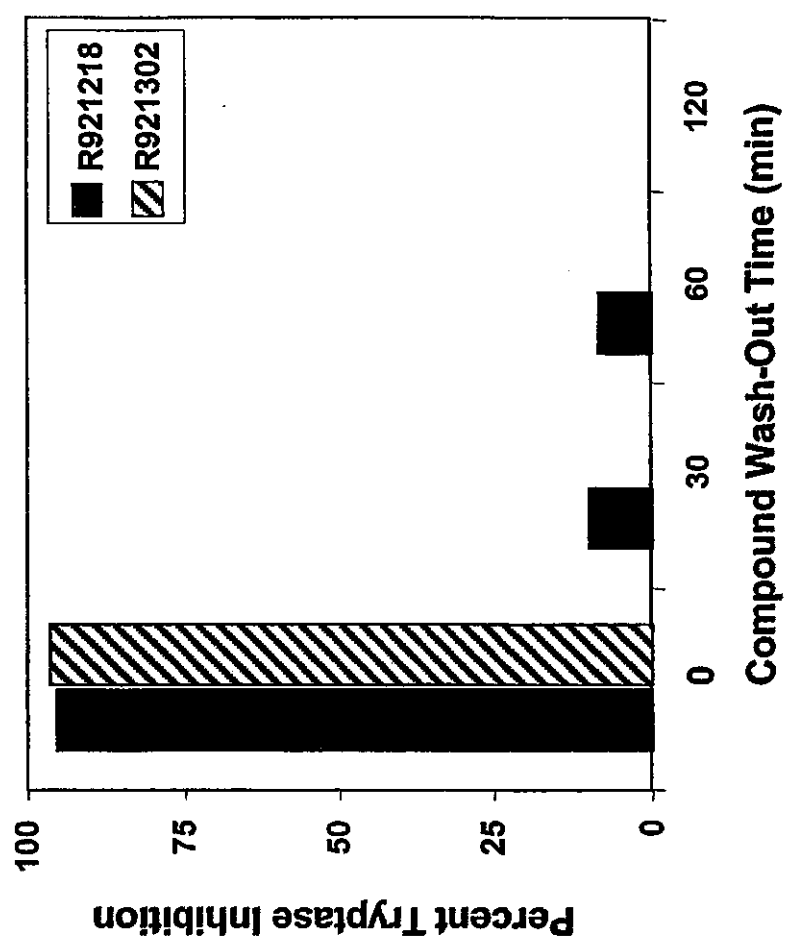


FIG. 7

Inhibition of Phosphorylation of Proteins Downstream of
Syk Kinase in Fce Receptor Activated BMMC Cells

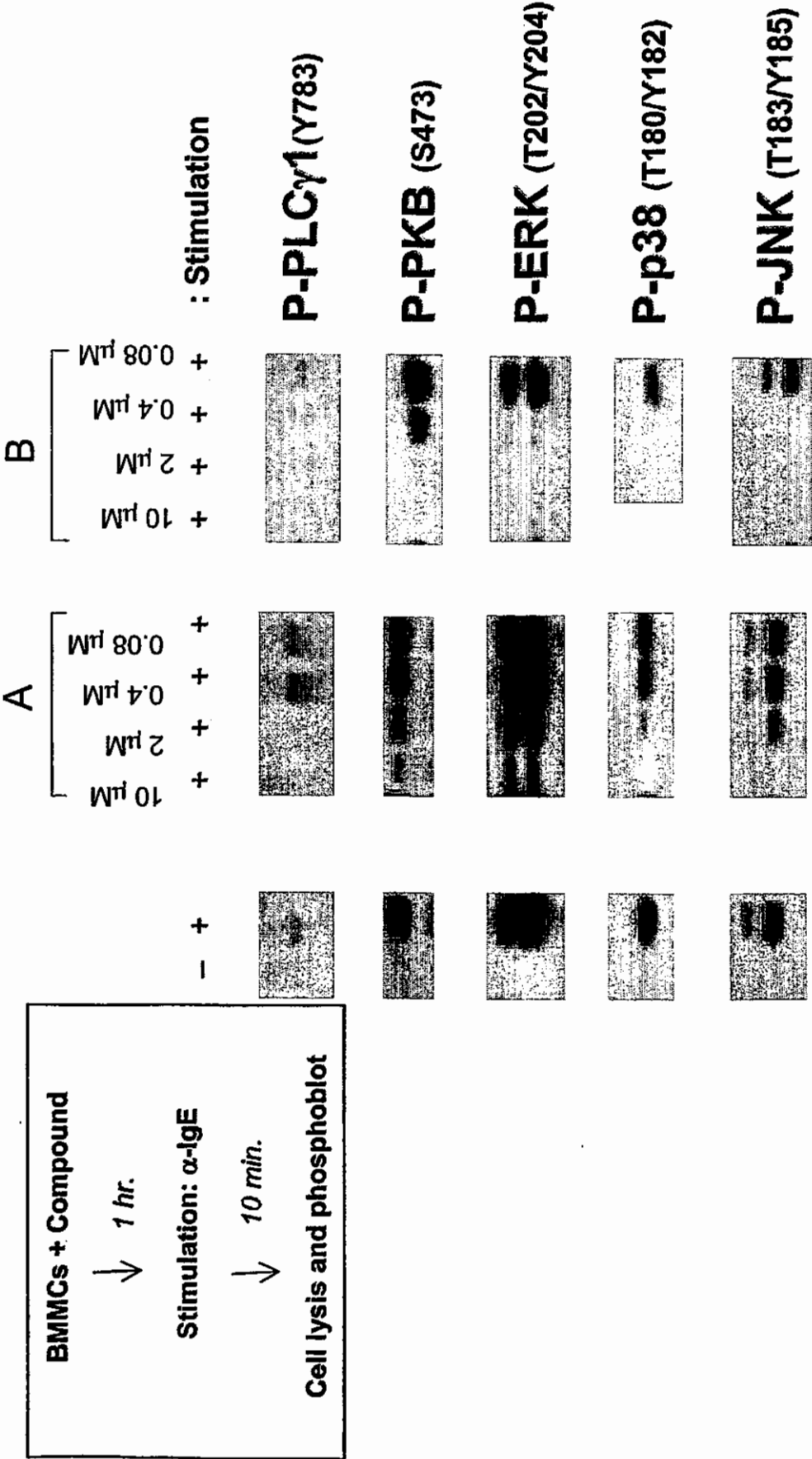
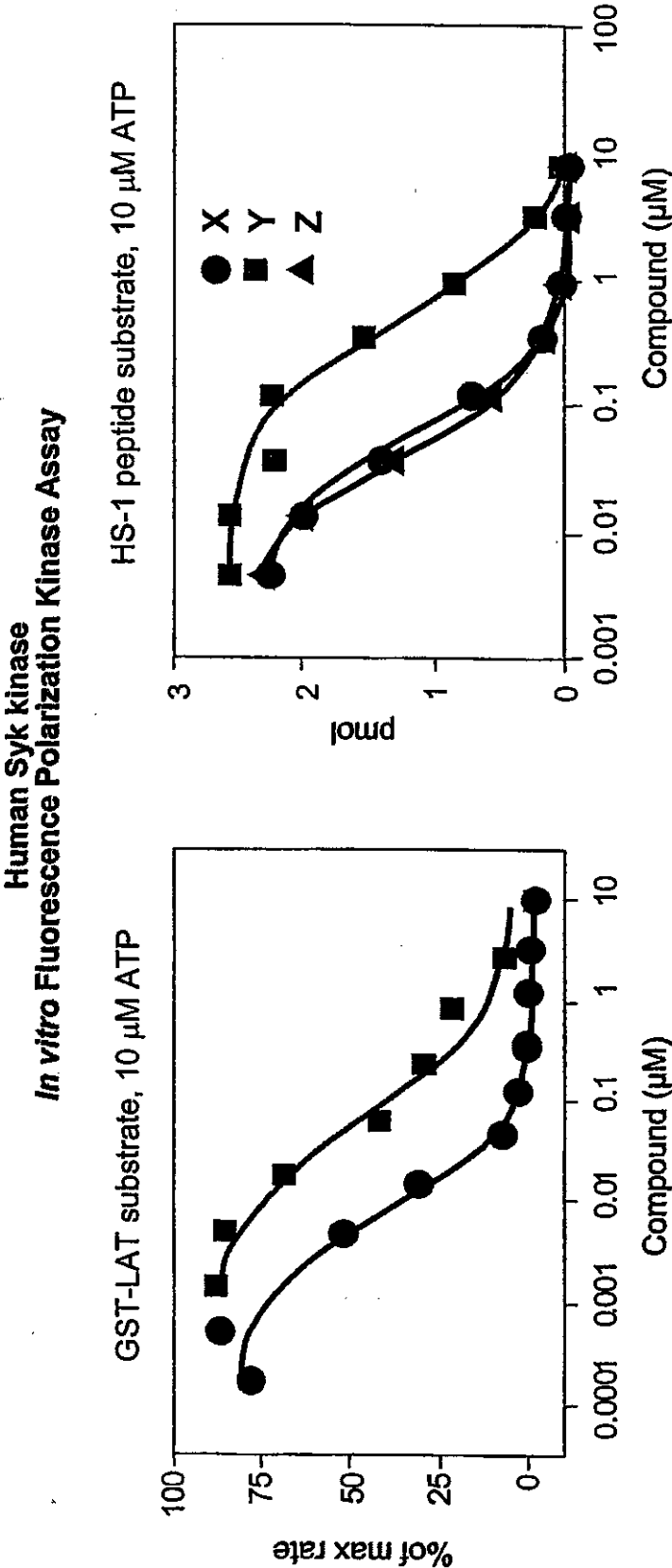
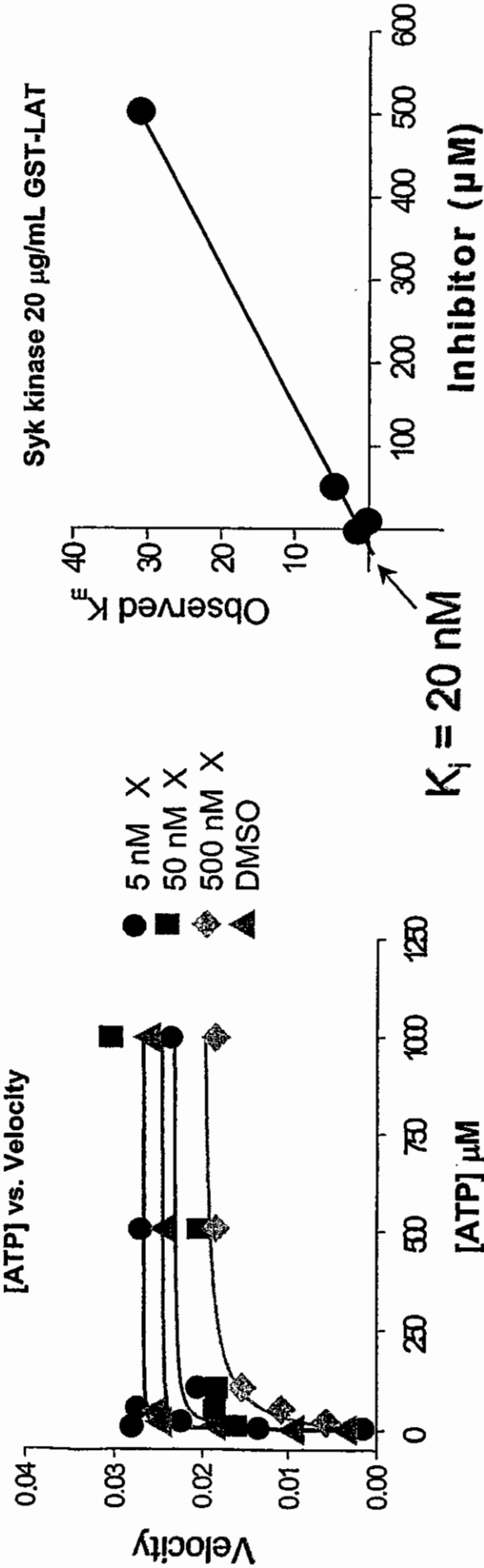


FIG. 8
The Disclosed Compounds Potently Inhibit the Activity of Syk Kinase



IC ₅₀ (nM)	
GST-LAT	HS-1
Y	200
X	10
Z	62
	43

FIG. 9
Compound Inhibition of Syk Is ATP Competitive



	DMSO	5 nM X	50 nM X	500 nM X
V_{max}	.025	0.027	.023	0.020
K_m	1.54	0.79	4.5	31

CHMC: Cultured human mast cells

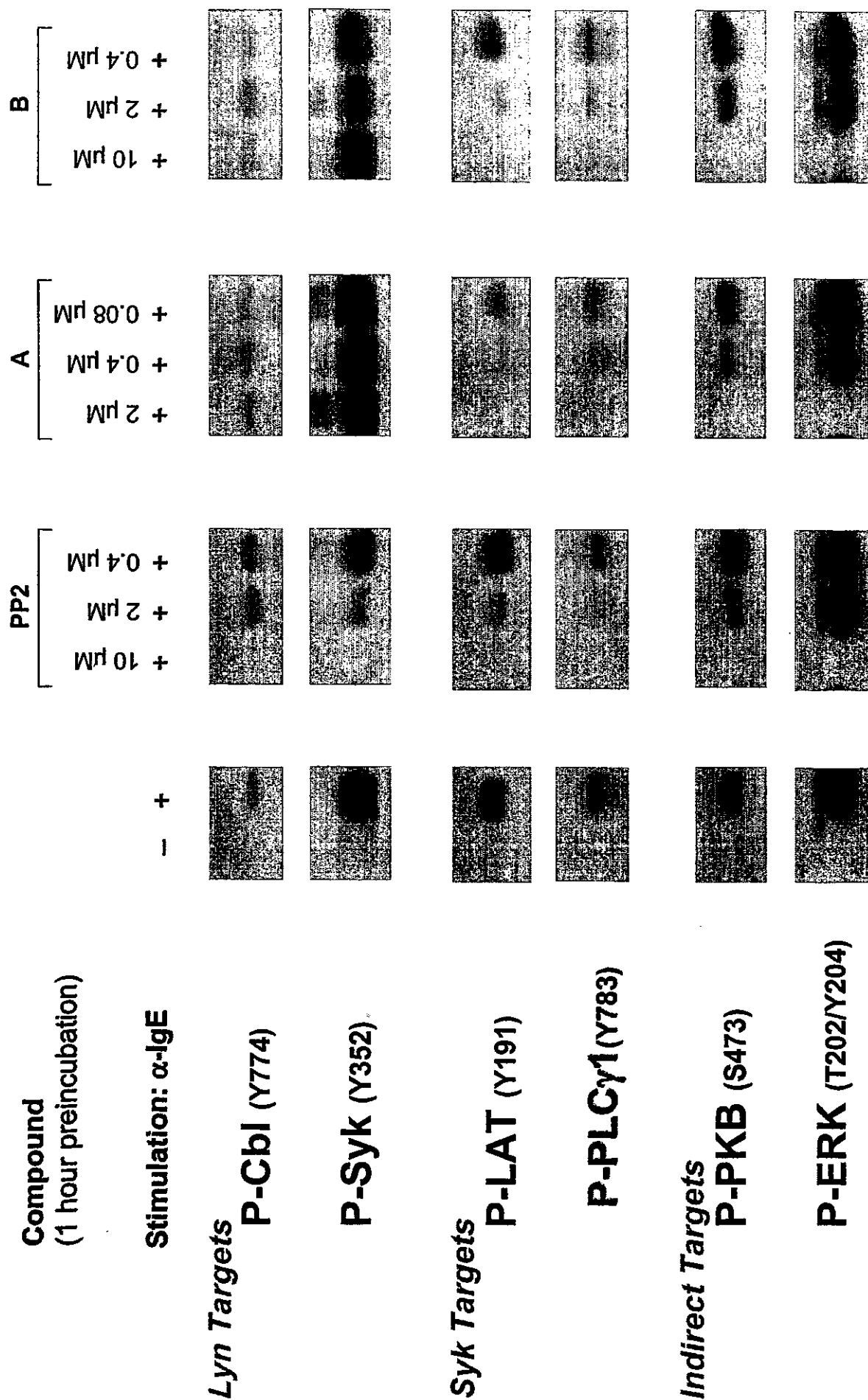
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FIG. 10



Inhibition of Phosphorylation of Proteins downstream of Syk in BMMC

	R921219						R921304						R940323						R935138					
	-	+	10 μ M	2 μ M	0.4 μ M	+ 0.08 μ M	-	+	10 μ M	2 μ M	0.4 μ M	+ 0.08 μ M	-	+	10 μ M	2 μ M	0.4 μ M	+ 0.08 μ M	-	+	10 μ M	2 μ M	0.4 μ M	+ 0.08 μ M
P-Syk ₃₅₂																								
P-Plc γ ₇₈₃																								
P-Lat ₁₉₁																								
P-ERK _{202/204}																								

FIG. 11B
Inhibition of Phosphorylation of Proteins downstream of Syk in BMMC

R921303				R940347				R926891				R920410			
+ 10 μ M				+ 10 μ M				+ 10 μ M				+ 10 μ M			
+ 2 μ M				+ 2 μ M				+ 2 μ M				+ 2 μ M			
+ 0.4 μ M				+ 0.4 μ M				+ 0.4 μ M				+ 0.4 μ M			
+ 0.08 μ M				+ 0.08 μ M				+ 0.08 μ M				+ 0.08 μ M			
-				-				-				-			
+				+				+				+			
P-Syk ₃₅₂															
P-PLC γ ₇₈₃															
P-Lat ₁₉₁															
P-ERK _{202/204}															

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FIG. 11C
Inhibition of Phosphorylation of Proteins downstream of Syk in BMMC

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R926321					R950368					R926594					R935310													
P-Syk ₃₅₂	-	+	10 μ M	+	2 μ M	+	0.4 μ M	+	0.08 μ M	-	+	10 μ M	+	2 μ M	+	0.4 μ M	+	0.08 μ M	-	+	10 μ M	+	2 μ M	+	0.4 μ M	+	0.08 μ M	
P-Plc γ ₇₈₃	-	+	10 μ M	+	2 μ M	+	0.4 μ M	+	0.08 μ M	-	+	10 μ M	+	2 μ M	+	0.4 μ M	+	0.08 μ M	-	+	10 μ M	+	2 μ M	+	0.4 μ M	+	0.08 μ M	
P-Lat ₁₉₁	-	+	10 μ M	+	2 μ M	+	0.4 μ M	+	0.08 μ M	-	+	10 μ M	+	2 μ M	+	0.4 μ M	+	0.08 μ M	-	+	10 μ M	+	2 μ M	+	0.4 μ M	+	0.08 μ M	
P-ERK _{202/204}	-	+	10 μ M	+	2 μ M	+	0.4 μ M	+	0.08 μ M	-	+	10 μ M	+	2 μ M	+	0.4 μ M	+	0.08 μ M	-	+	10 μ M	+	2 μ M	+	0.4 μ M	+	0.08 μ M	

Inhibition of Phosphorylation of Proteins downstream of Syk in BMMC

	R935237	R926813	R926839	R908712
P-Syk ³⁵²	+ 10 μM + 2 μM + 0.4 μM + 0.08 μM	+ 10 μM + 2 μM + 0.4 μM + 0.08 μM	+ 10 μM + 2 μM + 0.4 μM + 0.08 μM	+ 10 μM + 2 μM + 0.4 μM + 0.08 μM
	-	-	-	-
P-Plcγ ⁷⁸³	+ 10 μM + 2 μM + 0.4 μM + 0.08 μM	+ 10 μM + 2 μM + 0.4 μM + 0.08 μM	+ 10 μM + 2 μM + 0.4 μM + 0.08 μM	+ 10 μM + 2 μM + 0.4 μM + 0.08 μM
	-	-	-	-
P-Lat ¹⁹¹	+ 10 μM + 2 μM + 0.4 μM + 0.08 μM	+ 10 μM + 2 μM + 0.4 μM + 0.08 μM	+ 10 μM + 2 μM + 0.4 μM + 0.08 μM	+ 10 μM + 2 μM + 0.4 μM + 0.08 μM
	-	-	-	-
P-ERK ^{202/204}	+ 10 μM + 2 μM + 0.4 μM + 0.08 μM	+ 10 μM + 2 μM + 0.4 μM + 0.08 μM	+ 10 μM + 2 μM + 0.4 μM + 0.08 μM	+ 10 μM + 2 μM + 0.4 μM + 0.08 μM
	-	-	-	-