

p115 RhoGEF, a GTPase Activating Protein for $G\alpha_{12}$ and $G\alpha_{13}$

Tohru Kozasa *et al.* 1998

Present by Liang
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Before this study ...

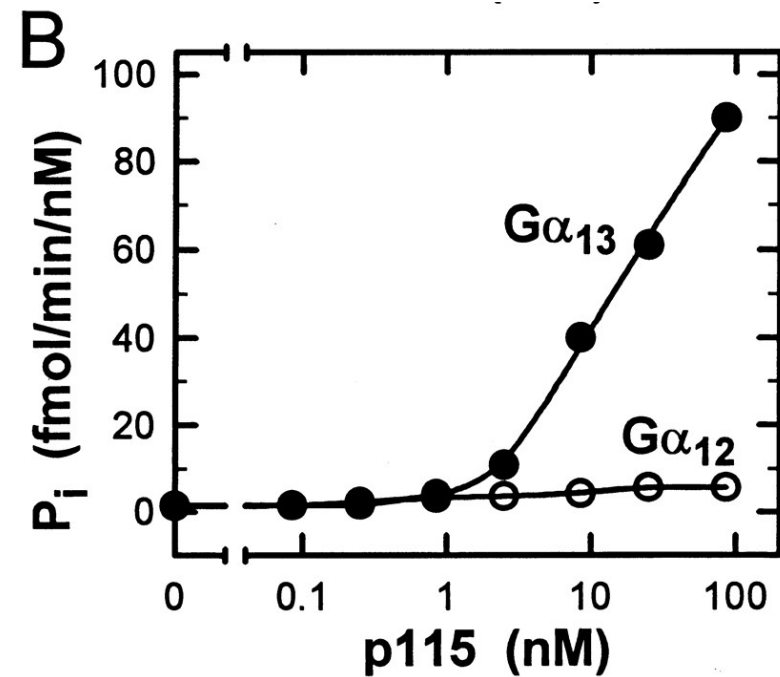
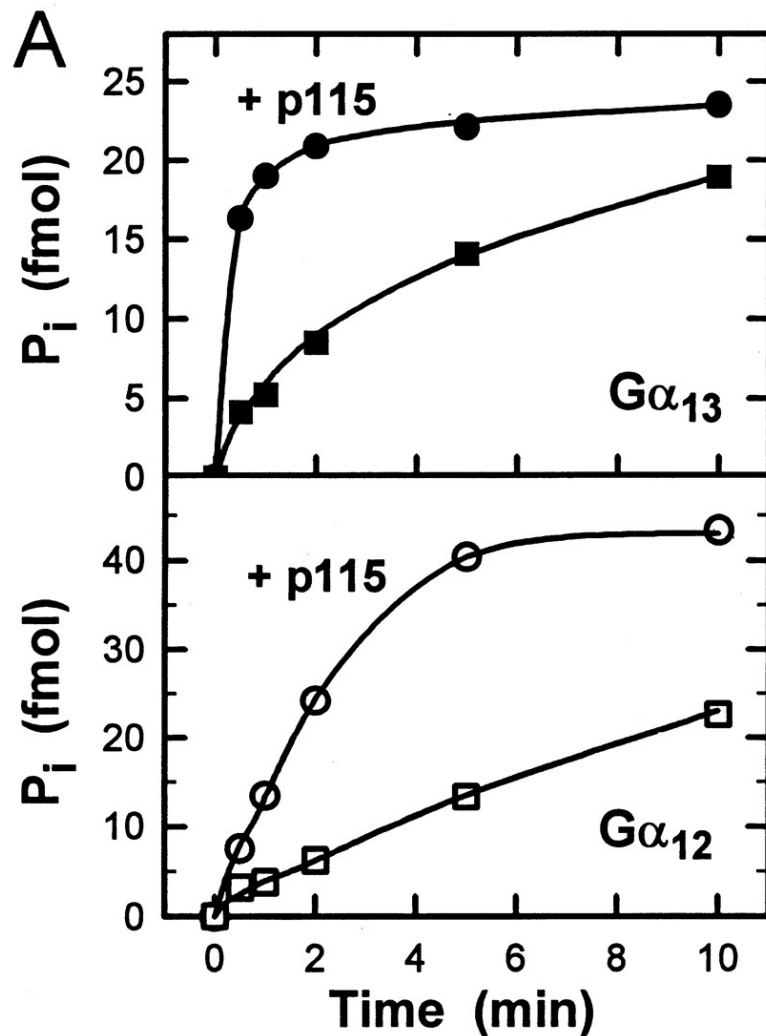
- GPCRs, heptahelical receptors, transduces signals for G proteins.
- Each heterotrimeric G protein has α , β , γ subunits.
- G α subunits are groups into four subfamilies: G_s, G_i, G_q & G₁₂.
- Rho, a small GTPase, mediates the formation of actin stress fibers and the assembly of focal adhesion complexes.

- Functional core (GTPase activating) of the RGS box contains nine alpha helices.
- P115 is a GEF specific for Rho.
- $G\alpha_{12}$ and $G\alpha_{13}$ activate Rho in vivo. A physical interaction between p115 and $G\alpha_{13}$ was detected.
- P115 RhoGEF stimulates only the intrinsic GTPase activity of $G\alpha_{12}$ and $G\alpha_{13}$, not other Gas.

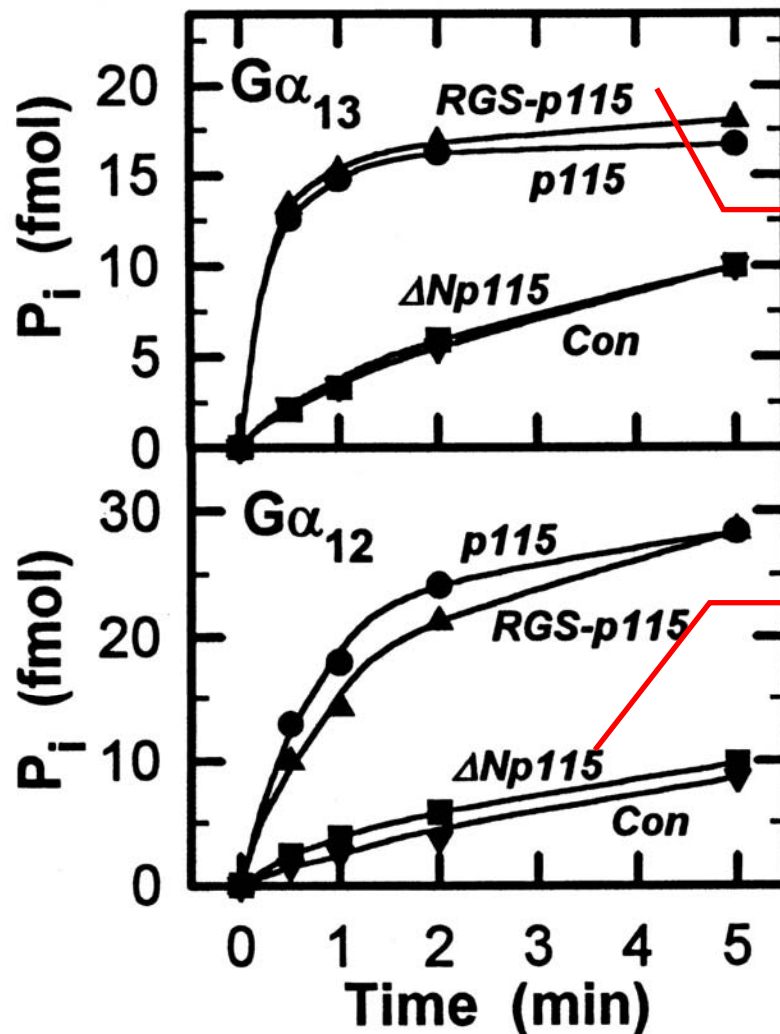
RGS sequence alignments

			$\alpha 1$	$\alpha 2$	$\alpha 3$	***	**	$\alpha 4$	
Rat	RGS4	(59)	W A E S L E N L I N H E C G L A A F K A F L K S E - - - Y S E E N I D F W I S C E E Y K K I						
Mouse	RGS2	(80)	W A E A F D E L L A S K Y G L A A F R A F L K S E - - - F C E E N I E F W L A C E D F K K T						
Human	GAIP	(87)	W A Q S F D K L M H S P A G R S V F R A F L R T E - - - Y S E E N M L F W L A C E E L K A E						
Rat	RGS12	(712)	W A V S F E R L L Q D P V G V R Y F S D F L R K E - - - F S E E N I L F W Q A C E C F S H V						
Rat	RGS14	(64)	W A Q S F E R L L Q D P R G L A Y F S D F L R K E - - - F S A E N V T F W Q A C E R F Q Q I						
Human	p115	(45)	Q F Q S L E Q V K R R P A H L M A L L Q H V A L Q - - - F E P G P L L C C L H A E M L G S L						
Mouse	Lsc	(43)	Q F Q S L E Q V K R R P A H L M A L L Q H V A L Q - - - F E P G P L L C C L H A E M L S S L						
Human	KIAA380	(310)	I F Q D L E K L K S R P A H L G V F L R Y I F S Q - - - A D P S P L L F Y L C A E V Y Q Q A						
Drosophila	DrhoGEF2	(924)	P F N N L T R L L - E A E N V T F L A I F L N Y V I S N S D P A P L L F Y L I T E L Y K E G						
					$\alpha 5$		**	*	$\alpha 6$
	RGS4	(102)	- - K S P S K L S P K A K K I Y N E F I S V - - - - Q A T K E - - - - V N L D S C T R E E						
	RGS2	(123)	- - K S P Q K L S S K A R K I Y T D F I E K - - - - E A P K E - - - - I N I D F Q T K S L						
	GAIP	(130)	- - A N Q H V V D E K A R L I Y E D Y V S I - - - - L S P K E - - - - V S L D S R V R E G						
	RGS12	(755)	P A H D K K E L S Y R A R E I F S K F L C S - - - - K A T T P - - - - V N I D S Q A Q L A						
	RGS14	(107)	P A S D T K Q L A Q E A H N I Y H E F L S S - - - - Q A L S P - - - - V N I D R Q A W L S						
	p115	(88)	- - - G P K E A K K A F L D F Y H S F L E K T A V L R - V P V P P N V A F E L D R T R A D L						
	Lsc	(86)	- - - G P K E A K K A F L D F Y H S F L E K T A V L R - V P V P P S V A F E L D R T R P D L						
	KIAA380	(353)	- - - S P K D S R S L G K D I W N I F L E K N A P L R - V K I P E M L Q A E I D S R L R N -						
	DrhoGEF2	(969)	- - - T S K D M R K W A Y E I H S T F L V P R A P L S W Y R Q D E S L A R E V D N V L Q L E						
			$\alpha 6$		$\alpha 7$	*	**	* $\alpha 8$	$\alpha 9$
	RGS4	(137)	T S R N M L E - - P T I T C F D E A Q K K I F N L M E K D S Y R R F L K S R F Y L D (176)						
	RGS2	(158)	I A Q N I Q E - - A T S G C F T T A Q K R V Y S L M E N N S Y P R F L E S E F Y Q D (197)						
	GAIP	(165)	I N K K M Q E - - P S A H T F D D A Q L Q I Y T L M H R D S Y P R F L S S P T Y R A (204)						
	RGS12	(792)	D D I L N A - - - P H P D M F K E Q Q L Q I F N L M K F D S Y T R F L K S Q L Y Q E (830)						
	RGS14	(144)	E E V L A Q - - - P R P D M F R A Q Q L Q I F N L M K F D S Y A R F V K S P L Y Q E (182)						
	p115	(130)	I S E D V Q - R R F V Q E V V Q S Q Q V A V G R Q L E D F R S K R L M G M T P W E Q (170)						
	Lsc	(128)	I S E D V Q - R R F I Q E V V Q S Q Q A A V S R Q L E D F R S K R L M G M T P W E Q (168)						
	KIAA380	(394)	- S E D A - - R G V L C E A Q E A A M P E I Q E Q I H D Y R T K R T L G L G S L Y G (432)						
	DrhoGEF2	(1012)	Y D K V E I L R T V F L R S R K R A K D L I S E Q L R E F Q Q K R T A G L G T I Y G (1053)						

GTPase activity stimulates by p115 RhoGEF



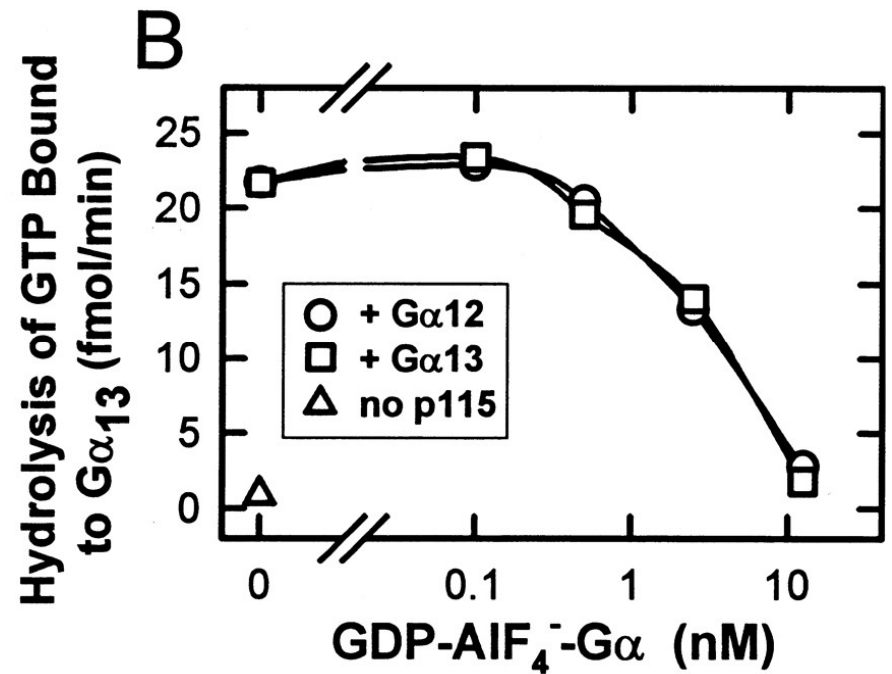
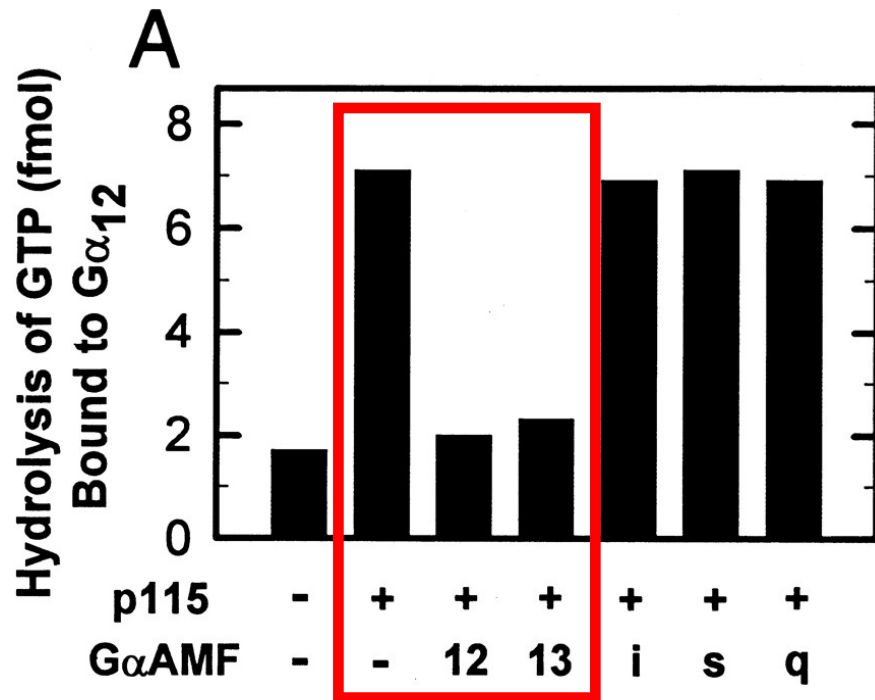
GTPase activity stimulates by the NH₂-terminus of p115 RhoGEF



Fusion protein contains the RGS region of p115, not the DH or PH domains.

P115 truncates at the N terminus to eliminate the RGS region.

Specific G α inhibits p115 RhoGEF GAP activity



RGS sequence alignments

		$\alpha 1$	$\alpha 2$	$\alpha 3$	***	**	$\alpha 4$
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Human	GAIP	(87)	W A Q S F D K L M H S P A G R S V F R A F L R T E - - - Y S E E N M L F W L A C E E L K A E				
Rat	RGS12	(712)	W A V S F E R L L Q D P V G V R Y F S D F L R K E - - - F S E E N I L F W Q A C E C F S H V				
Rat	RGS14	(64)	W A Q S F E R L L Q D P R G L A Y F S D F L K K E - - - F S A E N V T F W Q A C E R F Q Q I				
Human	p115	(45)	Q F Q S L E Q V K R R P A H L M A L L Q H V A L Q - - - F E P G P L L C C L H A E M L G S L				
Mouse	Lsc	(43)	Q F Q S L E Q V K R R P A H L M A L L Q H V A L Q - - - F E P G P L L C C L H A E M L S S L				
Human	KIAA380	(310)	I F Q D L E K L K S R P A H L G V F L R Y I F S Q - - - A D P S P L L F Y L C A E V Y Q Q A				
Drosophila	DrhoGEF2	(924)	P F N N L T R L L - E A E N V T F L A I F L N Y V I S N S D P A P L L F Y L I T E L Y K E G				

		$\alpha 5$	**	* <th>$\alpha 6$</th>	$\alpha 6$
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RGS2	(123)	- - K S P Q K L S S K A R K I Y T D F I E K - - - - E A P K E - - - - I N I D F Q T K S L			
GAIP	(130)	- - A N Q H V V D E K A R L I Y E D Y V S I - - - - L S P K E - - - - V S L D S R V R E G			
RGS12	(755)	P A H D K K E L S Y R A R E I F S K F L C S - - - - K A T T P - - - - V N I D S Q A Q L A			
RGS14	(107)	P A S D T K Q L A Q E A H N I Y H E F L S S - - - - Q A L S P - - - - V N I D R Q A W L S			
p115	(88)	- - - G P K E A K K A F L D F Y H S F L E K T A V L R - V P V P P N V A F E L D R T R A D L			
Lsc	(86)	- - - G P K E A K K A F L D F Y H S F L E K T A V L R - V P V P P S V A F E L D R T R P D L			
KIAA380	(353)	- - - S P K D S R S L G K D I W N I F L E K N A P L R - V K I P E M L Q A E I D S R L R N -			
DrhoGEF2	(969)	- - - T S K D M R K W A Y E I H S T F L V P R A P L S W Y R Q D E S L A R E V D N V L Q L E			

		$\alpha 6$	$\alpha 7$	* <th>**</th> <th>* $\alpha 8$</th> <th>$\alpha 9$</th>	**	* $\alpha 8$	$\alpha 9$
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RGS2	(158)	I A Q N I Q E - - A T S G C F T T A Q K R V Y S L M E N N S Y P R F L E S E F Y Q D (197)					
GAIP	(165)	I N K K M Q E - - P S A H T F D D A Q L Q I Y T L M H R D S Y P R F L S S P T Y R A (204)					
RGS12	(792)	D D I L N A - - P H P D M F K E Q Q L Q I F N L M K F D S Y T R F L K S Q L Y Q E (830)					
RGS14	(144)	E E V L A Q - - P R P D M F R A Q Q L Q I F N L M K F D S Y A R F V K S P L Y Q E (182)					
p115	(130)	I S E D V Q - R R F V Q E V V Q S Q Q V A V G R Q L E D F R S K R L M G M T P W E Q (170)					
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KIAA380	(394)	- S E D A - - R G V L C E A Q E A A M P E I Q E Q I H D Y R T K R T L G L G S L Y G (432)					
DrhoGEF2	(1012)	Y D K V E I L R T V F L R S R K R A K D L I S E Q L R E F Q Q K R T A G L G T I Y G (1053)					

Q & A

Thanks.