Supporting Materials

Osteogenesis Imperfecta Missense Mutations in Collagen: Structural consequences of glycine to alanine replacements

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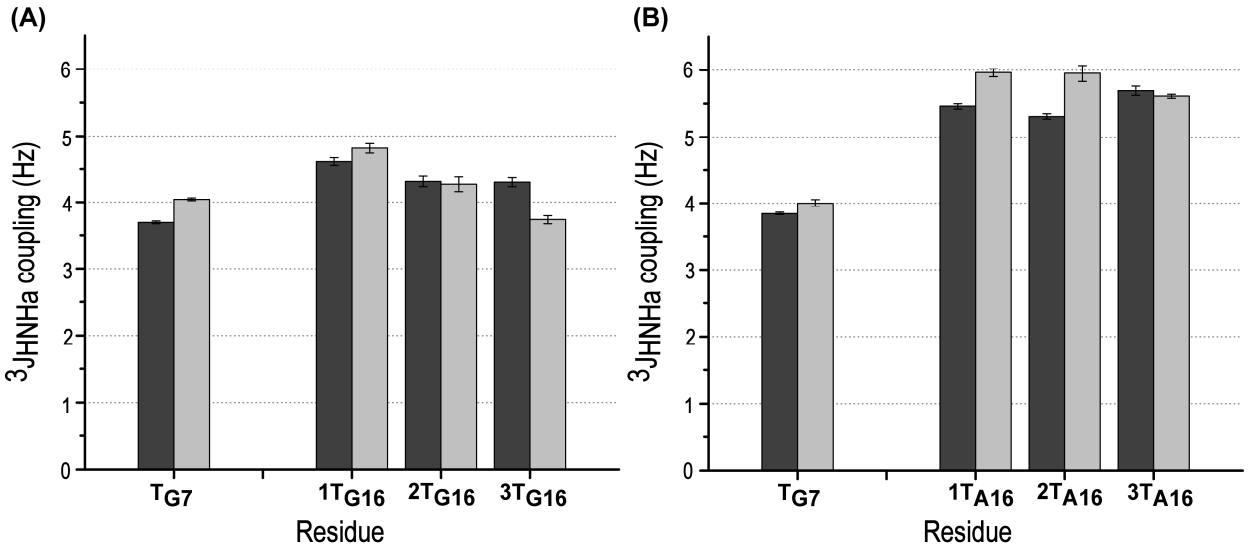

Figure S1. $^3J_{HNH\alpha}$-coupling values of peptide set T1-655. (A) $^3J_{HNH\alpha}$-coupling values of peptide T1-655 at pH 7 (black) and pH 3 (gray) at 15˚C; (B) $^3J_{HNH\alpha}$-coupling values of peptide T1-655[G16A] at pH 7 (black) and pH 3 (gray) at 15˚C. Residues in the triple helical conformation typically contain phi angles from -55 to -75 degrees and have a corresponding J coupling value of 4 to 6 Hz [1].

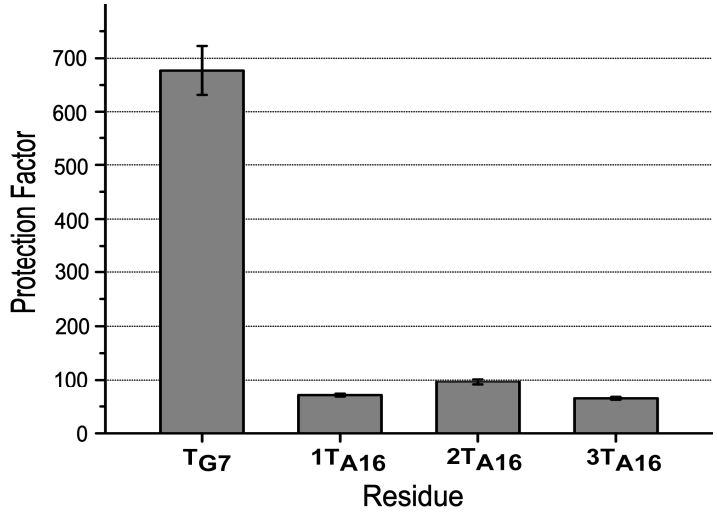

Figure S2. Protection factors of peptide T1-655[G16A] at pH 3 at 10˚C.

Table S1. List of Gly to Ala mutations leading to OI disease from the OI database [2], showing the surrounding sequence, OI phenotype and OI types for other Gly missense mutations at the same site. The mutation site is colored in red. Known binding sites are indicated with their sequences underlined.

Mutation site	Sequence	OI type	Other mutations	Nearby interaction site	Ref
Gly13Ala	GPMGPSGPRGLPGPPGAPGPQGFQGPPGEPGEP	I	D/OI IV		
Gly16Ala	GPSGPRGLPGPPGAPGPQGFQGPPGEPGEPGAS	I	R/OI I		
Gly106Ala	GFSGLDGAKGDAGPAGPKGEPGSPGENGAPGQM	I/IV	S/OI III	Integrin α1β1	[3-5]
Gly154Ala	GPAGARGNDGATGAAGPPGPTFPAGPPGFPGAV				
Gly187Ala	GAKGEAGPQGPRGSEGPQGVRGEPGPPGPAGAA	III/IV	V/OI II		
Gly199Ala	GSEGPQGVRGEPGPPGPAGAAGPAGNPGADGQP	III/IV			
Gly211Ala	GPPGPAGAAGPAGNPGADGQPGAKGANGAPGIA	I	S,R,C/OI I-IV		
Gly220Ala	GPAGNPGADGQPGAKGANGAPGIAGAPGFPGAR	IV	C, D/OI III, II	DDR2	[4-6]
Gly226Ala	GADGQPGAKGANGAPGIAGAPGFPGARGPSGPQ	IV,IV	S,C/OI III, IV	DDR2	[4-6]
Gly235Ala	GANGAPGIAGAPGFPGARGPSGPQGPGGPPGPK	III		DDR2	[4-6]
Gly244Ala	GAPGFPGARGPSGPQGPGGPPGPKGNSGEPGAP	III/IV	C/ OI II	DDR2	[4-6]
Gly304Ala	GKRGARGEPGPTGLPGPPGERGGPGSRGFPGAD	III	R/OI III	Integrin α1β1	[3-5]
Gly349Ala	GSPGPAGPKGSPGEAGRPGEAGLPGAKGLTGSP	I	C/OI IV		
Gly370Ala	GLPGAKGLTGSPGSPGPDGKTGPPGPAGQDGRP	II			
Gly376Ala	GLTGSPGSPGPDGKTGPPGPAGQDGRPGPPGPP	II			
Gly409Ala	GARGQAGVMGFPGPKGAAGEPGKAGERGVPGPP	IV	S/OI II	VWF, DDR2, SPARC	[4-8]
Gly481Ala	GLPGPAGPPGEAGKPGEQGVPGDLGAPGPSGAR	III			
Gly508Ala	GPSGARGERGFPGERGVQGPPGPAGPRGANGAP				
Gly 613Ala	GPAGDKGESGPSGPAGPTGARGAPGDRGEPGPP	III		COMP	[4]
Gly616Ala	GDKGESGPSGPAGPTGARGAPGDRGEPGPPGPA	OI			
Gly637Ala	GDRGEPGPPGPAGFAGPPGADGQPGAKGEPGDA	I	V/OI II		
Gly646Ala	GPAGFAGPPGADGQPGAKGEPGDAGAKGDAGPA	III,OI	R,C/OI II, I		
Gly658Ala	GQPGAKGEPGDAGAKGDAGPPGPAGPAGPPGPI	III		SPARC	[4, 7]
Gly682Ala	GPAGPPGPIGNVGAPGAKGARGSAGPPGATGFP	III/IV		COMP	[4]
Gly844Ala	GPPGESGREGAPGAEGSPGRDGSPGAKGDRGET	I/IV	S, V/OI III, II		
Gly886Ala	GAPGAPGPVGPAGKSGDRGETGPAGPAGPVGPV	IV			
Gly910Ala	GPAGPVGPVGARGPAGPQGPRGDKGETGEQGDR	II			
Gly928Ala	GPRGDKGETGEQGDRGIKGHRGFSGLQGPPGPP	II		CROSS-LINK	[4]
Gly955Ala	GPPGPPGSPGEQGPSGASGPAGPRGPPGSAGAP	IV,I			

Table S2. The effects of the Gly to Ala replacement in different contexts of collagen model peptides.

Peptide name	Tm (^{o}C) [§]	MRE_{225} (deg.cm^2.d mol^{-1}) [§]	Enthalpy (KJ/mol) [§]	$^3J_{HNH\alpha}$-coupling constants (Hz) [†]	NH temperature gradients (ppb/˚C) [†]
$(POG)_{10}$	57	4340	390	N/A	N/A
$(POG)_{10}$ (G-A)	26.5	4130	289	5.6, 8.6, 5.6[‡]	-12.2, -10.7, -4.3[‡]
T1-865[*]	35	4330	434	4.4, 4.6, 4.4[#]	N/A
T1-865 (G-A)	15.5	4140	301	5.5, 7.6, 6[#]	N/A
T1-655	55	3800	320	4.6, 4.3, 4.3	-3.6, -3.2, -4.2
T1-655[G16A]	30	3670	285	5.5, 5.3, 5.7	-5.1, -2.3, -10.5

[*] The amino acid sequence of T1-865: $GPO(GAO)_3GPV\underline{G}PAGAR(GPO)_4GY$ with the mutation site underlined.
[§] Tm, MRE_{225} and Enthalpy values of peptide sets $(POG)_{10}$ and T1-865 are measured by Bryan et al, 2011 [9].
[†] $^3J_{HNH\alpha}$-coupling constants and NH temperature gradients are for the Gly/Ala residue at the mutation site in the triple helix structure. The Gly/Ala has three values corresponding for three chains, respectively. Residues in the triple helical conformation typically contain phi angles from -55 to -75 degrees and have a corresponding J coupling value of 4 to 6 Hz [1]. Residues with NH temperature gradients less negative than a cut-off value of -4.6 ppb/˚C form hydrogen bonds [10].
[‡] Li et al, 2009 [11].
[#] Li Y., 2007 [12].

References:

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