

FIG. 1A

TGF-β2 (SEQ ID NO: 1) vs. mmTGF-β2-7M (SEQ ID NO: 3)

1. Heel Helix Deletion

2. Substitution of cysteine at interchain disulfide position with serine

3. Introduction of Basic Residues in Heel Helix region

4. Seven Modifications that partially convert TGF-β2 sequence into TGF-β1

SEQ ID NO: 1	ALDAAYCFRNVDNCCLRPLYIDFKRDLGWKWIHEPKGYNANFCAGACPYLMSSDTQHT	59
SEQ ID NO: 3	ALDAAYCFRNVDNCCLRPLYIDFKRDLGWKWIHEPKGYNANFCAGACPYR-----	52
	*****44*****311111111	
SEQ ID NO: 1	KVLSLYNTINPEASAPCCVSQDLEPLTILYYIGNTPKIEQLSNMIVKSKCS	112
SEQ ID NO: 3	-----ASKSPCVSQDLEPLTIVYVGRKPKVEQLSNMIVKSKCS	92
	11111111111**3**2*****44444*****	

TGF-β3-(TβRII)₂-(TβRI)₂ TGF-β3-TβRII

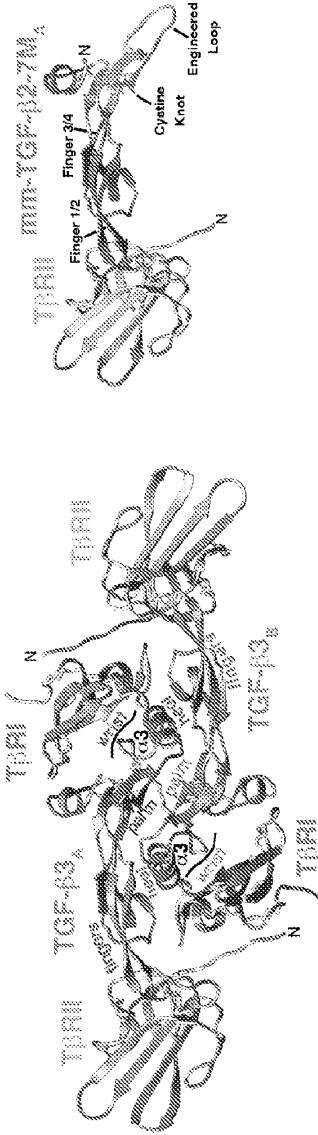


FIG. 1B

mmTGF-β2-7M (SEQ ID NO: 3) vs mmTGF-β2-7M2R (SEQ ID NO: 4)

- 5. Substitution of interchain disulfide position with arginine
- 6. Introduction of Basic Residue at dimer interface

SEQ ID NO: 3	ALDAAYCFRNVQDNCCLRPLYIDFRKDLGWKWIHEPKGYNANFCAGACPYRASKSPSCV	57 59
SEQ ID NO: 4	ALDAAYCFRNVQDNCCLRPLYIDFRKDLGWKWIHEPKGYNANFCAGACPYRASKSPICr	59
	*****5*6	
SEQ ID NO: 3	SQDLEPLTIVYYVGRKPKVEQLSNMIVKCKCS	92
SEQ ID NO: 4	SQDLEPLTIVYYVGRKPKVEQLSNMIVKCKCS	92

FIG. 1C

mmTGF- β 2-7M (SEQ ID NO: 3) vs mmTGF- β 2-2M-Del7-16 (SEQ ID NO: 5)

7. Elimination of cysteines that form the 7-16 disulfide
8. Modifications that revert TGF- β 1 sequence back to TGF- β 2

3/10

SEQ ID NO: 3	ALDAAYCFRNVQDNCCLRP ¹ LYIDFRKDLGWKWIHEPKGYNANFCAGACPYRASKSPSCV	59
SEQ ID NO: 5	ALDAAYVFRNVQDNCALRPLYIDFRRDLGWKWIHEPKGYNANFCAGACPYRASKSPSCV	59
	*****7*****8*****	
SEQ ID NO: 3	SQDLEPLTIVYVGRKPKVEQLSNMIVKSCCKS	92
SEQ ID NO: 5	SQDLEPLTILYVIGRTPKIEQLSNMIVKSCCKS	92
	*****8*****8*****	

FIG. 1D

mmTGF- β 2-7M (SEQ ID NO: 3) vs mmTGF- β 2-7M-PRDC (SEQ ID NO: 7)

9. Modification due to grafting with cystine-knot region of PRDC

Finger 1-2

SEQ ID NO: 3	-----ALDAAYCFRNVQDNCCLRPLYIDFRKDLGWKWIHEPKGYNANFCAGACPY 50
SEQ ID NO: 7	KEVLASSQEA LVTERKYLKSDWCKLRPLYIDFRKDLGWKWIHEPKGYNANFCYGCNS 59 999999999**99999999999*9*****99999999999*9*999

Finger 3-4

[illegible]

FIG. 1E

mmTGF- β 2-7M (SEQ ID NO: 3) vs mmTGF- β 2-7M2R-Del7-16 or var1 (SEQ ID NO: 6)

5. Substitution of interchain disulfide position with arginine
6. Introduction of Basic Residue at dimer interface
7. Elimination of cysteines that form the 7-16 disulfide

SEQ ID NO: 3	ALDAAYCFRNVQDNCCLRPLYIDFRKDLGWKWIHEPKGYNANFCAGACPYRASKSPSCV	59
SEQ ID NO: 6	ALDAAYVFRNVQDNCALRPLYIDFRKDLGWKWIHEPKGYNANFCAGACPYRASKSPYCr	59

```

SEQ ID NO: 3 SÖDLEPTIVYVGRKPKEÖLSNMIVKCKCS 92
SEQ ID NO: 6 SÖDLEPTIVYVGRKPKEÖLSNMIVKCKCS 92

```

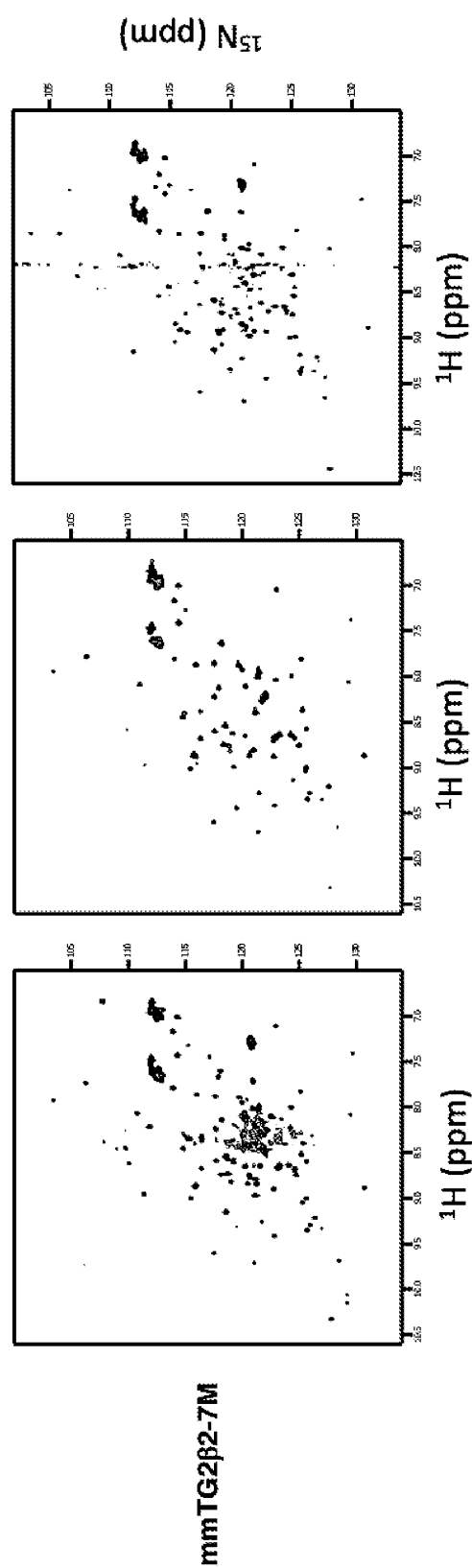
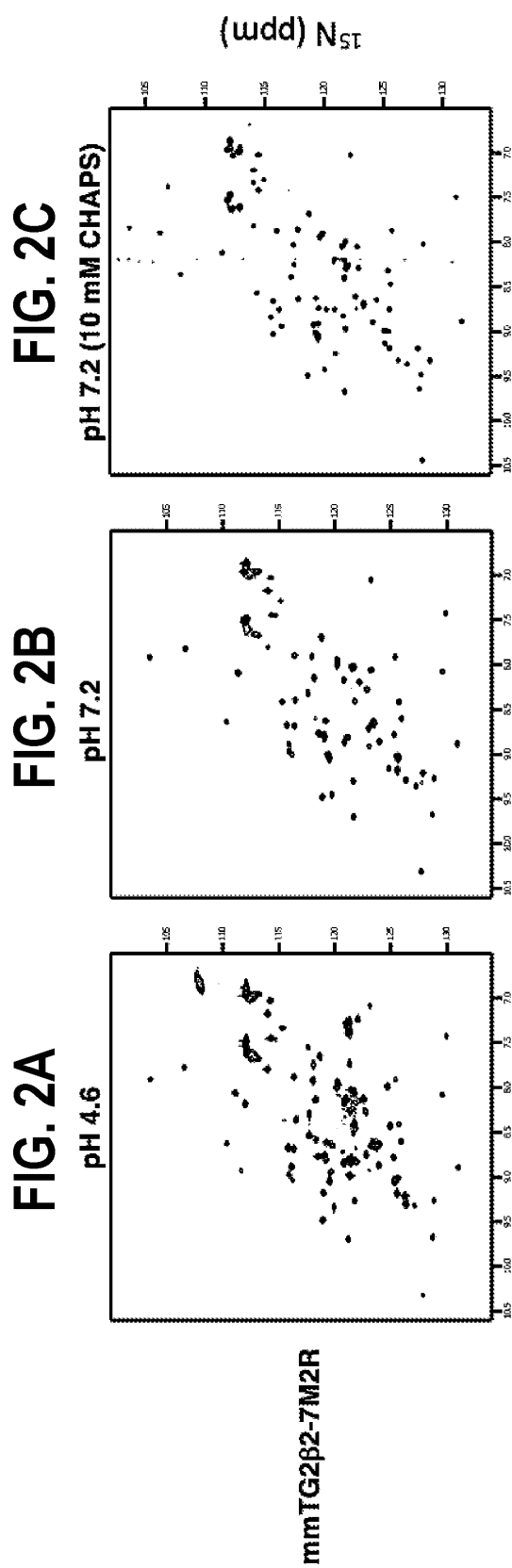


FIG. 3A

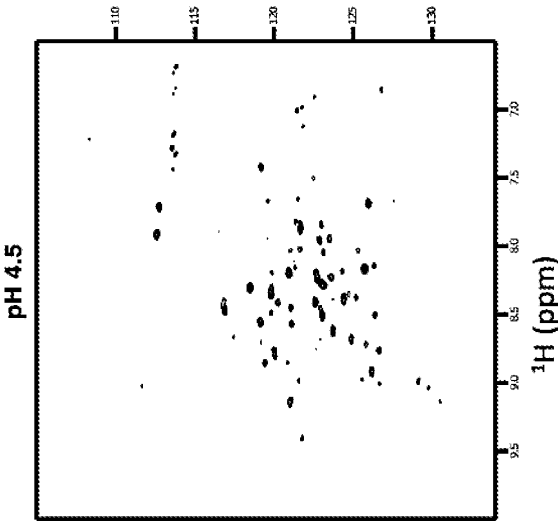


FIG. 3B

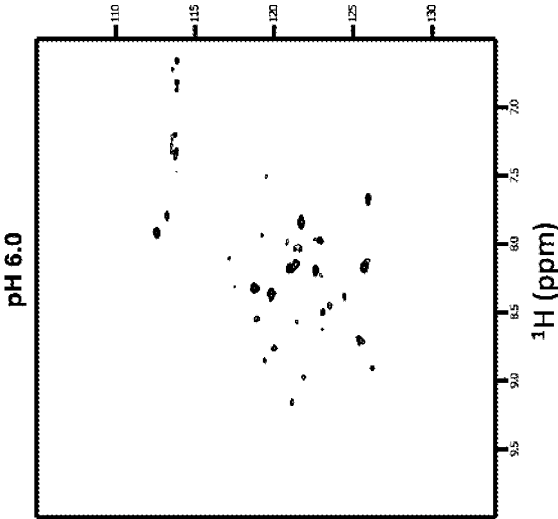


FIG. 3C

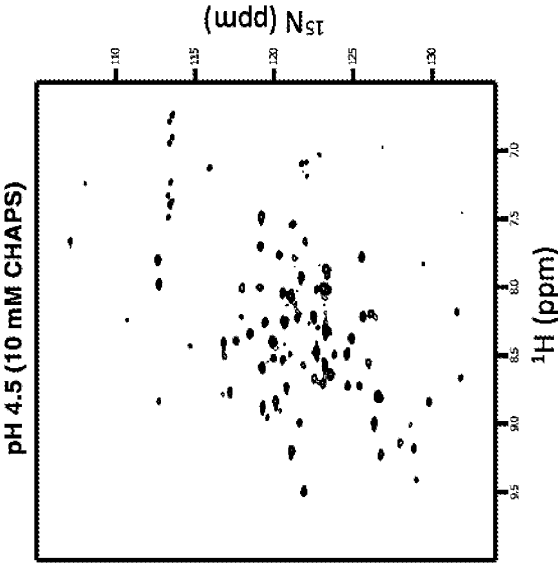


FIG. 4A

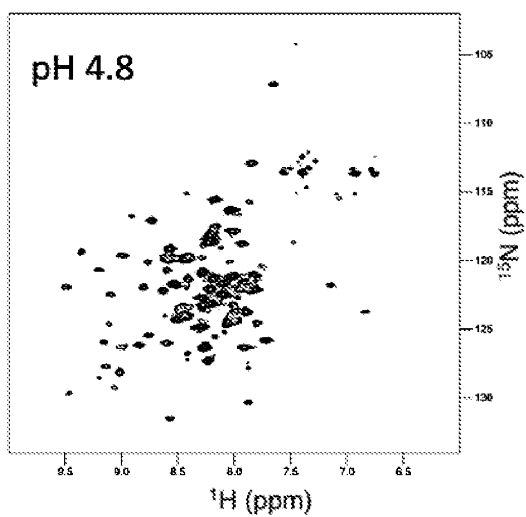


FIG. 4B

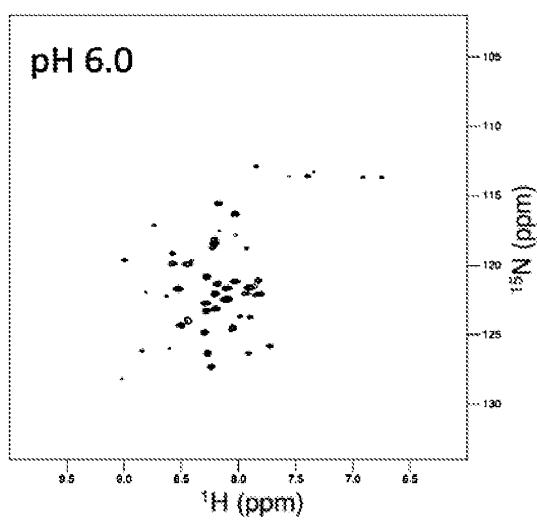
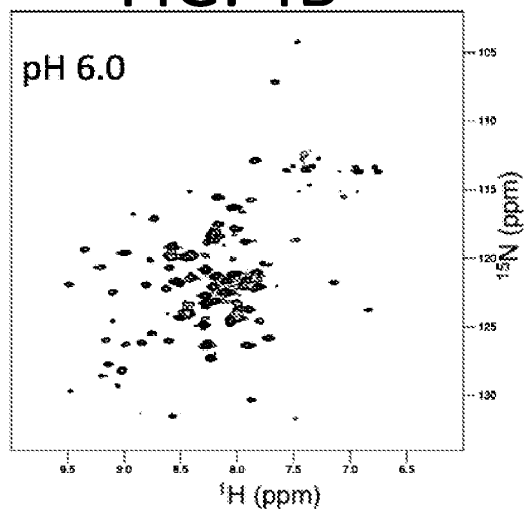


FIG. 4C

TβRII	+	+	+	+	+	+
7M		+B	+A			
7M2R				+A	+B	
7M-PRDC						+B



Ratios: A - 1:1, B - 2:1

FIG. 4D

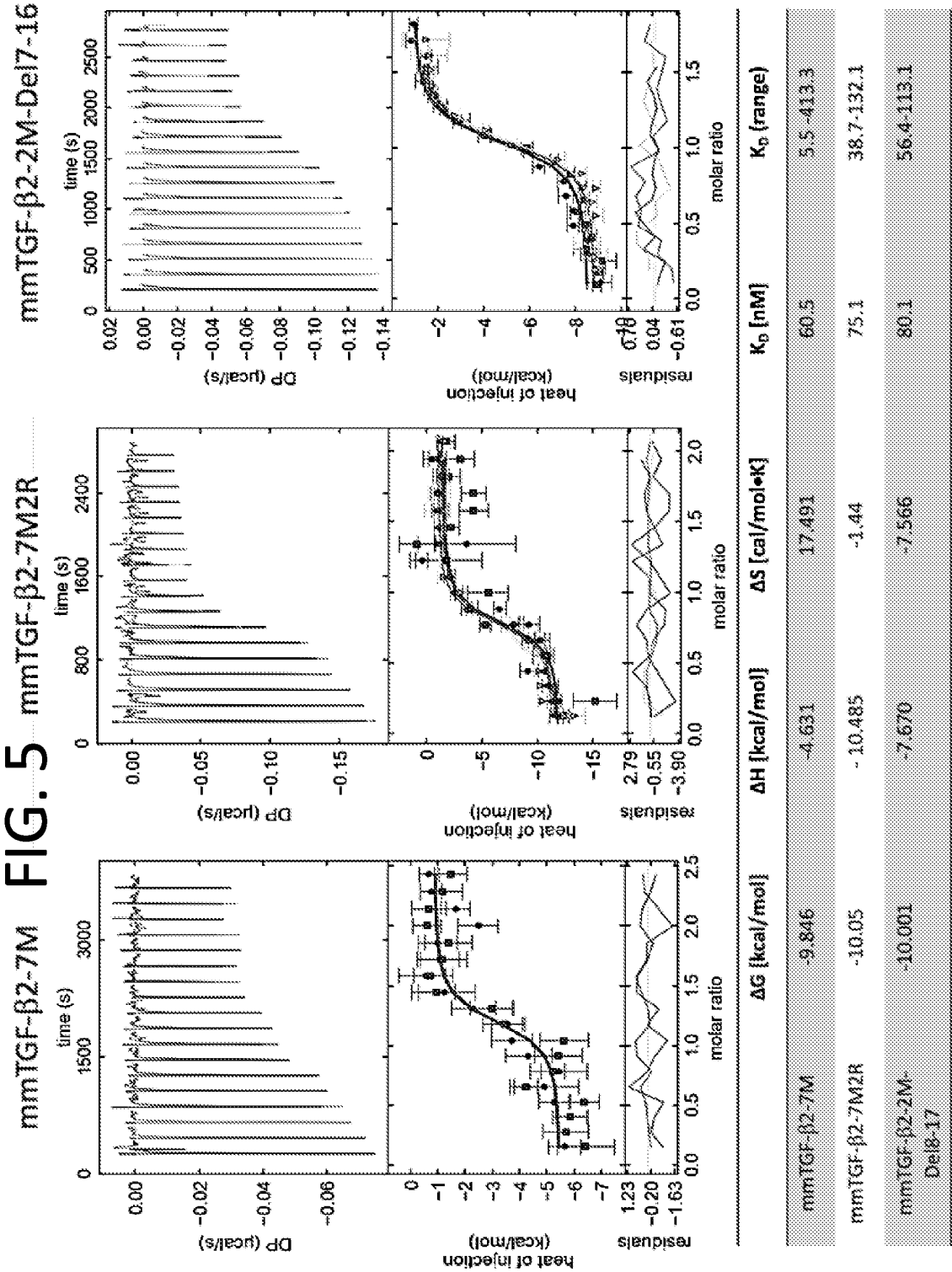


FIG. 6A

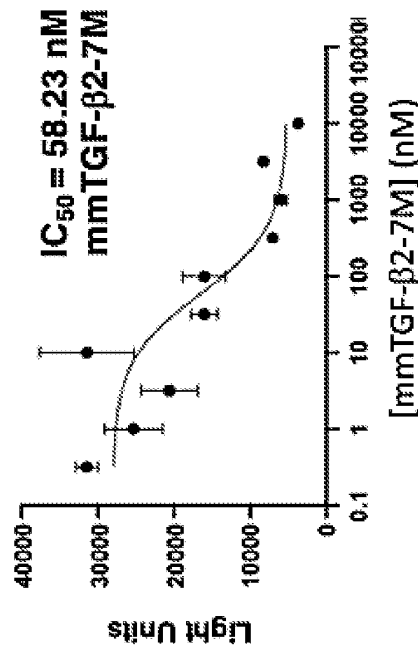


FIG. 6B

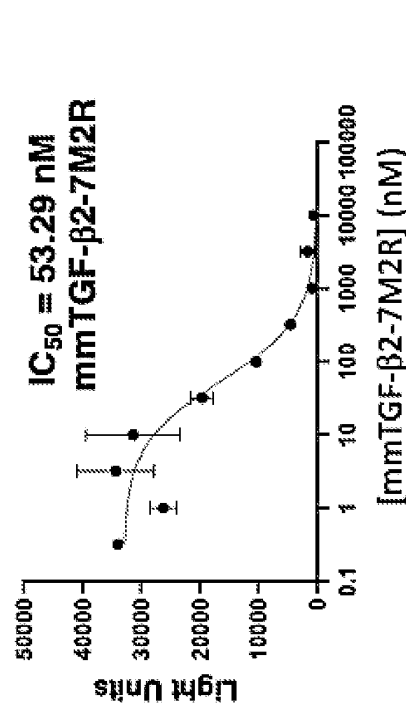


FIG. 6C

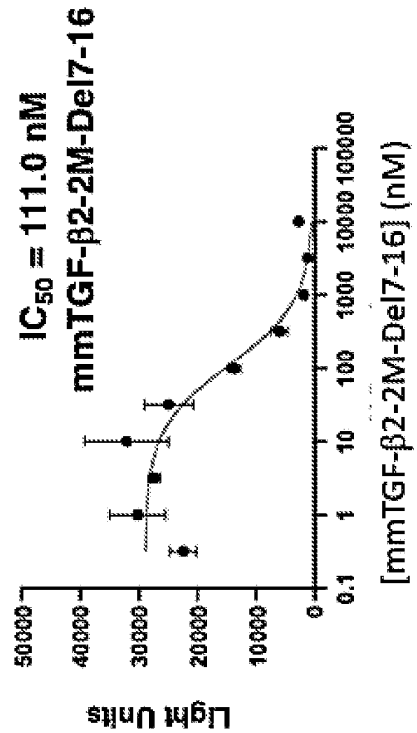


FIG. 6D

