

1
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<110> F. Hoffmann-La Roche AG
Roche Diagnostics GmbH

<120> DNA Polymerases With Increased 3'-Mismatch Discrimination

<130> 26743 WO-HS

<140> Not yet assigned

<141> Not yet assigned

<150> 61/356,275

<151> 2010-06-18

<160> 42

<170> FastSEQ for windows Version 4.0

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<212> PRT

<213> Thermus sp.

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<223> Thermus sp. Z05 DNA polymerase (Z05)

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 Val Phe Asp Ala Lys Ala Pro Ser Phe Arg His Glu Ala Tyr Gly Gly
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 Tyr Lys Ala Gly Arg Ala Pro Thr Pro Glu Asp Phe Pro Arg Gln Leu
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 Val Pro Gly Tyr Glu Ala Asp Asp Val Leu Ala Ser Leu Ala Lys Lys
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 Ala Glu Lys Glu Gly Tyr Glu Val Arg Ile Leu Thr Ala Asp Lys Asp
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 Leu Tyr Gln Leu Leu Ser Asp Arg Ile His Val Leu His Pro Glu Gly
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 Tyr Leu Ile Thr Pro Ala Trp Leu Trp Glu Lys Tyr Gly Leu Arg Pro
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 Asp Gln Trp Ala Asp Tyr Arg Ala Leu Thr Gly Asp Glu Ser Asp Asn
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 Leu Pro Gly Val Lys Gly Ile Gly Glu Lys Thr Ala Arg Lys Leu Leu
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 Glu Glu Trp Gly Ser Leu Glu Ala Leu Leu Lys Asn Leu Asp Arg Leu
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 Glu Ser Pro Lys Ala Leu Glu Ala Pro Trp Pro Pro Glu Gly
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Val	Lys	Ser	Val	Arg	Glu	Ala	Ala	Glu	Arg	Met	Ala	Phe	Asn	Met	Pro
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<220>
 <223> Thermus filiformis DNA polymerase (Tfi)

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5

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Ala	Lys	Arg	Arg	Glu	Pro	Thr	Gly	Lys	Gly	Leu	Lys	Ala	Phe	Leu	Glu
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Ala	Leu	Ala	Gly	Ala	Lys	Glu	Gly	Arg	Val	His	Arg	Ala	Glu	Asp	Pro
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Asp	Asp	Pro	Met	Leu	Leu	Ala	Tyr	Leu	Leu	Asp	Pro	Gly	Asn	Thr	Asn
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Pro	Glu	Gly	Val	Ala	Arg	Arg	Tyr	Gly	Gly	Glu	Trp	Lys	Glu	Asp	Ala
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Ala	Ala	Arg	Ala	Leu	Ser	Glu	Arg	Leu	Trp	Gln	Ala	Leu	Tyr	Pro	
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Arg	Phe	Asn	Gln	Thr	Ala	Thr	Ala	Thr	Gly	Arg	Leu	Ser	Ser	Ser	Asp
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Arg	Lys	Ala	Phe	Ile	Ala	Glu	Glu	Gly	His	Leu	Leu	Val	Ala	Leu	Asp
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Tyr	Ser	Gln	Ile	Glu	Leu	Arg	Val	Leu	Ala	His	Leu	Ser	Gly	Asp	Glu
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Asn	Leu	Ile	Arg	Val	Phe	Arg	Glu	Gly	Lys	Asp	Ile	His	Thr	Glu	Thr
625					630					635					640
Ala	Ala	Trp	Met	Phe	Gly	Val	Pro	Pro	Glu	Gly	Val	Asp	Gly	Ala	Met

6

Arg	Arg	Ala	Ala	645 Lys	Thr	Val	Asn	Phe	650 Gly	Val	Leu	Tyr	Gly	655 Met	Ser
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Ala	Phe	675 Ile	Glu	Arg	Tyr	Phe	680 Gln	Ser	Phe	Pro	Lys	685 Val	Arg	Ala	Trp
Ile	Ala	Lys	Thr	Leu	Glu	Glu	Gly	Arg	Lys	Lys	Gly	Tyr	Val	Glu	Thr
705	Leu	Phe	Gly	Arg	710 Arg	Tyr	Val	Pro	Asp	715 Leu	Asn	Ala	Arg	Val	Lys
Ser	Val	Arg	Glu	725 Ala	Ala	Glu	Arg	Met	730 Ala	Phe	Asn	Met	Pro	735 Val	Gln
Gly	Thr	Ala	Ala	Asp	Leu	Met	Lys	745 Leu	Ala	Met	Val	Lys	Leu	Phe	Pro
Arg	Leu	Arg	Pro	Leu	Gly	Val	Arg	Ile	Leu	Leu	Gln	Val	His	Asp	Glu
770	Leu	Val	Leu	Glu	Ala	Pro	Lys	775 Ala	Arg	Ala	Glu	Ala	Ala	Gln	Leu
785	Ala	Lys	Glu	Thr	Met	Glu	Gly	Val	Tyr	Pro	Leu	Ser	Val	Pro	Leu
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<220>
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Thr	Thr	Ser	Arg	Gly	Glu	Pro	Val	Gln	Ala	Val	Tyr	Gly	Phe	Ala	Lys
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Phe	Asp	Ala	Lys	Ala	Pro	Ser	Phe	Arg	His	Glu	Ala	Tyr	Glu	Ala	Tyr
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Lys	Ala	Gly	Arg	Ala	Pro	Thr	Pro	Glu	Asp	Phe	Pro	Arg	Gln	Leu	Ala
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Tyr	Gln	Leu	Leu	Ser	Glu	Arg	Ile	Ala	Ile	Leu	His	Pro	Glu	Gly	Tyr
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Leu	Ile	Thr	Pro	Ala	Trp	Leu	Tyr	Glu	Lys	Tyr	Gly	Leu	Arg	Pro	Glu
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Gln	Trp	Val	Asp	Tyr	Arg	Ala	Leu	Ala	Gly	Asp	Pro	Ser	Asp	Asn	Ile
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Ser	Arg	Lys	Leu	Ser	Gln	Val	His	Thr	Asp	Leu	Pro	Leu	Glu	Val	Asp
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Phe	Gly	Arg	Arg	Arg	Thr	Pro	Asn	Leu	Glu	Gly	Leu	Arg	Ala	Phe	Leu
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Glu	Arg	Leu	Glu	Phe	Gly	Ser	Leu	Leu	His	Glu	Phe	Gly	Leu	Leu	Glu
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Gly	Pro	Lys	Ala	Ala	Glu	Glu	Ala	Pro	Trp	Pro	Pro	Pro	Glu	Gly	Ala
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Thr	Arg	Phe	Asn	Gln	Thr	Ala	Thr	Ala	Thr	Gly	Arg	Leu	Ser	Ser	Ser
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Ile	Arg	Arg	Ala	Phe	Val	Ala	Glu	Glu	Gly	Trp	Val	Leu	Val	Val	Leu
		595					600					605			
Asp	Tyr	Ser	Gln	Ile	Glu	Leu	Arg	Val	Leu	Ala	His	Leu	Ser	Gly	Asp
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Thr	Ala	Ser	Trp	Met	Phe	Gly	Val	Ser	Pro	Glu	Gly	Val	Asp	Pro	Leu
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Val	Ala	Phe	Ile	Glu	Arg	Tyr	Phe	Gln	Ser	Tyr	Pro	Lys	Val	Arg	Ala
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Thr	Leu	Phe	Gly	Arg	Arg	Arg	Tyr	Val	Pro	Asp	Leu	Asn	Ala	Arg	Val
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Lys	Ser	Val	Arg	Glu	Ala	Ala	Glu	Arg	Met	Ala	Phe	Asn	Met	Pro	Val
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Gln	Gly	Thr	Ala	Ala	Asp	Leu	Met	Lys	Leu	Ala	Met	Val	Arg	Leu	Phe
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Pro	Arg	Leu	Gln	Glu	Leu	Gly	Ala	Arg	Met	Leu	Leu	Gln	Val	His	Asp
	770					775					780				
Glu	Leu	Val	Leu	Glu	Ala	Pro	Lys	Asp	Arg	Ala	Glu	Arg	Val	Ala	Ala
785					790					795					800
Leu	Ala	Lys	Glu	Val	Met	Glu	Gly	Val	Trp	Pro	Leu	Gln	Val	Pro	Leu
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Leu Lys Ala Leu Lys Glu Asp Gly Glu Val Ala Ile Val Val Phe Asp
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Ala Lys Ala Pro Ser Phe Arg His Glu Ala Tyr Glu Ala Tyr Lys Ala
65 70 75 80
Gly Arg Ala Pro Thr Pro Glu Asp Phe Pro Arg Gln Leu Ala Leu Ile
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Lys Glu Leu Val Asp Leu Leu Gly Leu Val Arg Leu Glu Val Pro Gly
100 105 110
Phe Glu Ala Asp Asp Val Leu Ala Thr Leu Ala Lys Lys Ala Glu Arg
115 120 125
Glu Gly Tyr Glu Val Arg Ile Leu Ser Ala Asp Arg Asp Leu Tyr Gln
130 135 140
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145 150 155 160
Thr Pro Gly Trp Leu Gln Glu Arg Tyr Gly Leu Ser Pro Glu Arg Trp
165 170 175
Val Glu Tyr Arg Ala Leu Val Gly Asp Pro Ser Asp Asn Leu Pro Gly
180 185 190
Val Pro Gly Ile Gly Glu Lys Thr Ala Leu Lys Leu Lys Glu Trp
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Arg Leu Glu Phe Gly Ser Leu Leu His Glu Phe Gly Leu Leu Glu Ala
275 280 285
Pro Lys Glu Ala Glu Glu Ala Pro Trp Pro Pro Gly Gly Ala Phe
290 295 300
Leu Gly Phe Leu Leu Ser Arg Pro Glu Pro Met Trp Ala Glu Leu Leu
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325 330 335
Val Gly Ala Leu Lys Asp Leu Lys Glu Ile Arg Gly Leu Leu Ala Lys
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Asp Leu Ser Val Leu Ala Leu Arg Glu Gly Arg Glu Ile Pro Pro Gly
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Asp Asp Pro Met Leu Leu Ala Tyr Leu Leu Asp Pro Gly Asn Thr Asn
370 375 380
Pro Glu Gly Val Ala Arg Arg Tyr Gly Gly Glu Trp Lys Glu Asp Ala
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Ala Ala Arg Ala Leu Leu Ser Glu Arg Leu Trp Gln Ala Leu Tyr Pro
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Arg	Ile	Leu	Glu	Tyr	Arg	Glu	Leu	Met	Lys	Leu	Lys	Ser	Thr	Tyr	Ile
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Asn	Leu	Ile	Arg	Val	Phe	Arg	Glu	Gly	Lys	Asp	Ile	His	Thr	Glu	Thr
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Ala	Ala	Trp	Met	Phe	Gly	Val	Pro	Pro	Glu	Gly	Val	Asp	Gly	Ala	Met
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Ile	Ala	Lys	Thr	Leu	Glu	Gly	Arg	Lys	Lys	Gly	Tyr	Val	Glu	Thr	
705					710									720	
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				725					730					735	
Ser	Val	Arg	Glu	Ala	Ala	Glu	Arg	Met	Ala	Phe	Asn	Met	Pro	Val	Gln
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Gly	Thr	Ala	Ala	Asp	Leu	Met	Lys	Leu	Ala	Met	Val	Lys	Leu	Phe	Pro
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Arg	Leu	Arg	Pro	Leu	Gly	Val	Arg	Ile	Leu	Leu	Gln	Val	His	Asp	Glu
	770					775					780				
Leu	Val	Leu	Glu	Ala	Pro	Lys	Ala	Arg	Ala	Glu	Glu	Ala	Ala	Gln	Leu
785					790					795					800
Ala	Lys	Glu	Thr	Met	Glu	Gly	Val	Tyr	Pro	Leu	Ser	Val	Pro	Leu	Glu
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Leu	Thr	Thr	Ser	Arg	Gly	Glu	Pro	Val	Gln	Ala	Val	Tyr	Gly	Phe	Ala
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Lys	Ser	Leu	Leu	Lys	Ala	Leu	Lys	Glu	Asp	Gly	Tyr	Lys	Ala	Val	Phe
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Leu	Ala	Leu	Ile 100	Lys	Glu	Leu	Val	Asp 105	Leu	Leu	Gly	Phe	Thr 110	Arg	Leu
Glu	Val	Pro 115	Gly	Tyr	Glu	Ala	Asp 120	Asp	Val	Leu	Ala	Thr 125	Leu	Ala	Lys
Lys	Ala 130	Glu	Lys	Glu	Gly	Tyr 135	Glu	Val	Arg	Ile	Leu 140	Thr	Ala	Asp	Arg
Asp 145	Leu	Tyr	Gln	Leu	Val 150	Ser	Asp	Arg	Val	Ala 155	Val	Leu	His	Pro	Glu 160
Gly	His	Leu	Ile	Thr 165	Pro	Glu	Trp	Leu	Trp 170	Glu	Lys	Tyr	Gly	Leu 175	Arg
Pro	Glu	Gln	Trp 180	Val	Asp	Phe	Arg	Ala 185	Leu	Val	Gly	Asp	Pro 190	Ser	Asp
Asn	Leu	Pro 195	Gly	Val	Lys	Gly	Ile 200	Gly	Glu	Lys	Thr	Ala 205	Leu	Lys	Leu
Leu	Lys 210	Glu	Trp	Gly	Ser	Leu 215	Glu	Asn	Leu	Leu	Lys 220	Asn	Leu	Asp	Arg
Val 225	Lys	Pro	Glu	Asn	Val 230	Arg	Glu	Lys	Ile	Lys 235	Ala	His	Leu	Glu	Asp 240
Leu	Arg	Leu	Ser	Leu 245	Glu	Leu	Ser	Arg	Val 250	Arg	Thr	Asp	Leu	Pro 255	Leu
Glu	Val	Asp	Leu 260	Ala	Gln	Gly	Arg	Glu 265	Pro	Asp	Arg	Glu	Gly 270	Leu	Arg
Ala	Phe	Leu	Glu	Arg	Leu	Glu	Phe 280	Gly	Ser	Leu	Leu	His 285	Glu	Phe	Gly
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Glu 305	Gly	Ala	Phe	Val	Gly 310	Phe	Val	Leu	Ser	Arg 315	Pro	Glu	Pro	Met	Trp 320
Ala	Glu	Leu	Lys	Ala 325	Leu	Ala	Ala	Cys	Arg 330	Asp	Gly	Arg	Val	His 335	Arg
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Leu	Leu	Ala 355	Lys	Asp	Leu	Ala	Val 360	Leu	Ala	Ser	Arg	Glu 365	Gly	Leu	Asp
Leu	Val 370	Pro	Gly	Asp	Asp	Pro 375	Met	Leu	Leu	Ala	Tyr 380	Leu	Leu	Asp	Pro
Ser 385	Asn	Thr	Thr	Pro	Glu 390	Gly	Val	Ala	Arg	Arg 395	Tyr	Gly	Gly	Glu	Trp 400
Thr	Glu	Asp	Ala	Ala 405	His	Arg	Ala	Leu	Leu 410	Ser	Glu	Arg	Leu	His 415	Arg
Asn	Leu	Leu	Lys 420	Arg	Leu	Glu	Gly	Glu 425	Glu	Lys	Leu	Leu	Trp 430	Leu	Tyr
His	Glu	Val 435	Glu	Lys	Pro	Leu	Ser 440	Arg	Val	Leu	Ala	His 445	Met	Glu	Ala
Thr	Gly 450	Val	Arg	Arg	Asp	Val 455	Ala	Tyr	Leu	Gln	Ala 460	Leu	Ser	Leu	Glu
Leu 465	Ala	Glu	Glu	Ile	Arg 470	Arg	Leu	Glu	Glu	Glu 475	Val	Phe	Arg	Leu	Ala 480
Gly	His	Pro	Phe	Asn 485	Leu	Asn	Ser	Arg	Asp 490	Gln	Leu	Glu	Arg	Val 495	Leu
Phe	Asp	Glu	Leu 500	Arg	Leu	Pro	Ala	Leu 505	Gly	Lys	Thr	Gln	Lys 510	Thr	Gly
Lys	Arg	Ser 515	Thr	Ser	Ala	Ala	Val 520	Leu	Glu	Ala	Leu	Arg 525	Glu	Ala	His
Pro	Ile 530	Val	Glu	Lys	Ile	Leu 535	Gln	His	Arg	Glu	Leu 540	Thr	Lys	Leu	Lys
Asn 545	Thr	Tyr	Val	Asp	Pro 550	Leu	Pro	Ser	Leu	Val 555	His	Pro	Arg	Thr	Gly 560
Arg	Leu	His	Thr	Arg 565	Phe	Asn	Gln	Thr	Ala 570	Thr	Ala	Thr	Gly	Arg 575	Leu
Ser	Ser	Ser	Asp 580	Pro	Asn	Leu	Gln	Asn 585	Ile	Pro	Val	Arg	Thr 590	Pro	Leu
Gly	Gln	Arg 595	Ile	Arg	Arg	Ala	Phe 600	Val	Ala	Glu	Ala	Gly 605	Trp	Ala	Leu

11

Val	Ala	Leu	Asp	Tyr	Ser	Gln	Ile	Glu	Leu	Arg	Val	Leu	Ala	His	Leu
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His	Thr	Gln	Thr	Ala	Ser	Trp	Met	Phe	Gly	Val	Pro	Pro	Glu	Ala	Val
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Asp	Pro	Leu	Met	Arg	Arg	Ala	Ala	Lys	Thr	Val	Asn	Phe	Gly	Val	Leu
			660					665					670		
Tyr	Gly	Met	Ser	Ala	His	Arg	Leu	Ser	Gln	Glu	Leu	Ala	Ile	Pro	Tyr
		675					680					685			
Glu	Glu	Ala	Val	Ala	Phe	Ile	Glu	Arg	Tyr	Phe	Gln	Ser	Phe	Pro	Lys
	690					695					700				
Val	Arg	Ala	Trp	Ile	Glu	Lys	Thr	Leu	Glu	Glu	Gly	Arg	Lys	Arg	Gly
705					710					715					720
Tyr	Val	Glu	Thr	Leu	Phe	Gly	Arg	Arg	Arg	Tyr	Val	Pro	Asp	Leu	Asn
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Ala	Arg	Val	Lys	Ser	Val	Arg	Glu	Ala	Ala	Glu	Arg	Met	Ala	Phe	Asn
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Met	Pro	Val	Gln	Gly	Thr	Ala	Ala	Asp	Leu	Met	Lys	Leu	Ala	Met	Val
		755					760					765			
Lys	Leu	Phe	Pro	Arg	Leu	Arg	Glu	Met	Gly	Ala	Arg	Met	Leu	Leu	Gln
	770					775				780					
Val	His	Asp	Glu	Leu	Leu	Leu	Glu	Ala	Pro	Gln	Ala	Arg	Ala	Glu	Glu
785					790					795					800
Val	Ala	Ala	Leu	Ala	Lys	Glu	Ala	Met	Glu	Lys	Ala	Tyr	Pro	Leu	Ala
			805						810					815	
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Asn	Pro	Glu	Lys	Glu	Gly	Tyr	Glu	Val	Arg	Ile	Leu	Thr	Ala	Asp	Arg
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Asp	Leu	Asp	Gln	Leu	Val	Ser	Asp	Arg	Val	Ala	Val	Leu	His	Pro	Glu
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Gly	His	Leu	Ile	Thr	Pro	Glu	Trp	Leu	Trp	Gln	Lys	Tyr	Gly	Leu	Lys
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Pro	Glu	Gln	Trp	Val	Asp	Phe	Arg	Ala	Leu	Val	Gly	Asp	Pro	Ser	Asp
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Asn	Leu	Pro	Gly	Val	Lys	Gly	Ile	Gly	Glu	Lys	Thr	Ala	Leu	Lys	Leu
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Leu	Lys	Glu	Trp	Gly	Ser	Leu	Glu	Asn	Leu	Leu	Lys	Asn	Leu	Asp	Arg
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Glu	Val	Asp	Leu 260	Ala	Gln	Gly	Arg	Glu 265	Pro	Asp	Arg	Glu	Gly 270	Leu	Arg
Ala	Phe	Leu 275	Glu	Arg	Leu	Glu	Phe 280	Gly	Ser	Leu	Leu	His 285	Glu	Phe	Gly
Leu	Leu 290	Glu	Ala	Pro	Ala	Pro 295	Leu	Glu	Glu	Ala	Pro 300	Trp	Pro	Pro	Pro
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Ala	Ala	Asp	Pro 340	Leu	Ala	Gly	Leu	Lys 345	Asp	Leu	Lys	Glu	Val 350	Arg	Gly
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His	Glu	Val 435	Glu	Lys	Pro	Leu	Ser 440	Arg	Val	Leu	Ala	His 445	Met	Glu	Ala
Thr	Gly	Val	Arg	Leu	Asp	Val 455	Ala	Tyr	Leu	Gln	Ala 460	Leu	Ser	Leu	Glu
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Lys	Arg	Ser 515	Thr	Ser	Ala	Ala	Val 520	Leu	Glu	Ala	Leu	Arg 525	Glu	Ala	His
Pro	Ile 530	Val	Glu	Lys	Ile	Leu 535	Gln	His	Arg	Glu	Leu 540	Thr	Lys	Leu	Lys
Asn 545	Thr	Tyr	Val	Asp	Pro 550	Leu	Pro	Ser	Leu	Val 555	His	Pro	Asn	Thr	Gly 560
Arg	Leu	His	Thr	Arg 565	Phe	Asn	Gln	Thr	Ala 570	Thr	Ala	Thr	Gly	Arg 575	Leu
Ser	Ser	Ser	Asp 580	Pro	Asn	Leu	Gln	Asn 585	Ile	Pro	Val	Arg	Thr 590	Pro	Leu
Gly	Gln	Arg 595	Ile	Arg	Arg	Ala	Phe 600	Val	Ala	Glu	Ala	Gly 605	Trp	Ala	Leu
Val	Ala	Leu	Asp	Tyr	Ser	Gln 615	Ile	Glu	Leu	Arg	Val 620	Leu	Ala	His	Leu
Ser 625	Gly	Asp	Glu	Asn	Leu 630	Ile	Arg	Val	Phe	Gln 635	Glu	Gly	Lys	Asp	Ile 640
His	Thr	Gln	Thr	Ala 645	Ser	Trp	Met	Phe	Gly 650	Val	Pro	Pro	Glu	Ala 655	Val
Asp	Pro	Leu	Met 660	Arg	Arg	Ala	Ala	Lys 665	Thr	Val	Asn	Phe	Gly 670	Val	Leu
Tyr	Gly	Met 675	Ser	Ala	His	Arg	Leu 680	Ser	Gln	Glu	Leu	Ala 685	Ile	Pro	Tyr
Glu	Glu	Ala	Val	Ala	Phe	Ile 695	Glu	Arg	Tyr	Phe	Gln 700	Ser	Phe	Pro	Lys
Val 705	Arg	Ala	Trp	Ile	Glu 710	Lys	Thr	Leu	Glu	Glu 715	Gly	Arg	Lys	Arg	Gly 720
Tyr	Val	Glu	Thr	Leu 725	Phe	Gly	Arg	Arg	Arg 730	Tyr	Val	Pro	Asp	Leu 735	Asn
Ala	Arg	Val	Lys 740	Ser	Val	Arg	Glu	Ala 745	Ala	Glu	Arg	Met	Ala 750	Phe	Asn
Met	Pro	Val 755	Gln	Gly	Thr	Ala	Ala 760	Asp	Leu	Met	Lys	Leu 765	Ala	Met	Val

Lys Leu Phe Pro Arg Leu Arg Glu Met Gly Ala Arg Met Leu Leu Gln
 770 775 780
 Val His Asp Glu Leu Leu Leu Glu Ala Pro Gln Ala Gly Ala Glu Glu
 785 790 795 800
 Val Ala Ala Leu Ala Lys Glu Ala Met Glu Lys Ala Tyr Pro Leu Ala
 805 810 815
 Val Pro Leu Glu Val Glu Val Gly Met Gly Glu Asp Trp Leu Ser Ala
 820 825 830
 Lys Gly

<210> 8
 <211> 15
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> synthetic DNA polymerase domain motif

<220>
 <221> VARIANT
 <222> (1)...(1)
 <223> Xaa = Met or Gln

<220>
 <221> VARIANT
 <222> (4)...(4)
 <223> Xaa = Ala, Val or Gln

<220>
 <221> VARIANT
 <222> (5)...(5)
 <223> Xaa = Ala or Gly

<220>
 <221> VARIANT
 <222> (7)...(7)
 <223> Xaa = Thr, Met or Ala

<220>
 <221> VARIANT
 <222> (8)...(8)
 <223> Xaa = any amino acid other than Val or Ile

<220>
 <221> VARIANT
 <222> (11)...(11)
 <223> Xaa = Gly, Ser or Ala

<220>
 <221> VARIANT
 <222> (12)...(12)
 <223> Xaa = Val or Ile

<220>
 <221> VARIANT
 <222> (13)...(13)
 <223> Xaa = Leu, Ile or Val

<400> 8
 Xaa Arg Arg Xaa Xaa Lys Xaa Xaa Asn Phe Xaa Xaa Xaa Tyr Gly
 1 5 10 15

<210> 9
 <211> 15
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> synthetic DNA polymerase domain motif

<220>
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 <222> (5)...(5)
 <223> Xaa = Ala or Gly

<220>
 <221> VARIANT
 <222> (7)...(7)
 <223> Xaa = Thr or Met

<220>
 <221> VARIANT
 <222> (8)...(8)
 <223> Xaa = any amino acid other than Val or Ile

<220>
 <221> VARIANT
 <222> (11)...(11)
 <223> Xaa = Gly or Ser

<220>
 <221> VARIANT
 <222> (12)...(12)
 <223> Xaa = Val or Ile

<220>
 <221> VARIANT
 <222> (13)...(13)
 <223> Xaa = Leu or Ile

<400> 9
 Met Arg Arg Ala Xaa Lys Xaa Xaa Asn Phe Xaa Xaa Xaa Tyr Gly
 1 5 10 15

<210> 10
 <211> 15
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> synthetic DNA polymerase domain motif

<220>
 <221> VARIANT
 <222> (8)...(8)
 <223> Xaa = any amino acid other than Val or Ile

<400> 10
 Met Arg Arg Ala Ala Lys Thr Xaa Asn Phe Gly Val Leu Tyr Gly
 1 5 10 15

<210> 11
 <211> 15
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> synthetic DNA polymerase domain motif

<400> 11
 Met Arg Arg Ala Ala Lys Thr Glu Asn Phe Gly Val Leu Tyr Gly
 1 5 10 15

<210> 12
 <211> 38
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> synthetic region from polymerase domain of Thermus
 sp. Z05 DNA polymerase (Z05)

<400> 12
 Trp Met Phe Gly Val Ser Pro Glu Ala Val Asp Pro Leu Met Arg Arg
 1 5 10 15
 Ala Ala Lys Thr Val Asn Phe Gly Val Leu Tyr Gly Met Ser Ala His
 20 25 30
 Arg Leu Ser Gln Glu Leu
 35

<210> 13
 <211> 38
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> synthetic region from polymerase domain of Thermus
 aquaticus DNA polymerase (Taq)

<400> 13
 Trp Met Phe Gly Val Pro Arg Glu Ala Val Asp Pro Leu Met Arg Arg
 1 5 10 15
 Ala Ala Lys Thr Ile Asn Phe Gly Val Leu Tyr Gly Met Ser Ala His
 20 25 30
 Arg Leu Ser Gln Glu Leu
 35

<210> 14
 <211> 38
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> synthetic region from polymerase domain of Thermus
 filiformus DNA polymerase (Tfi)

<400> 14
 Trp Met Phe Gly Val Pro Pro Glu Gly Val Asp Gly Ala Met Arg Arg
 1 5 10 15
 Ala Ala Lys Thr Val Asn Phe Gly Val Leu Tyr Gly Met Ser Ala His
 20 25 30
 Arg Leu Ser Gln Glu Leu
 35

<210> 15
 <211> 38
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> synthetic region from polymerase domain of Thermus
 flavus DNA polymerase (Tfl)

<400> 15
 Trp Met Phe Gly Val Ser Pro Glu Gly Val Asp Pro Leu Met Arg Arg
 1 5 10 15

Ala Ala Lys Thr Ile Asn Phe Gly Val¹⁶ Leu Tyr Gly Met Ser Ala His
 20 25 30
 Arg Leu Ser Gly Glu Leu
 35

<210> 16
 <211> 38
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> synthetic region from polymerase domain of Thermus
 sp. Sps17 DNA polymerase (Sps17)

<400> 16
 Trp Met Phe Gly Val Pro Pro Glu Gly Val Asp Gly Ala Met Arg Arg
 1 5 10 15
 Ala Ala Lys Thr Val Asn Phe Gly Val Leu Tyr Gly Met Ser Ala His
 20 25 30
 Arg Leu Ser Gln Glu Leu
 35

<210> 17
 <211> 38
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> synthetic region from polymerase domain of Thermus
 thermophilus DNA polymerase (Tth)

<400> 17
 Trp Met Phe Gly Val Pro Pro Glu Ala Val Asp Pro Leu Met Arg Arg
 1 5 10 15
 Ala Ala Lys Thr Val Asn Phe Gly Val Leu Tyr Gly Met Ser Ala His
 20 25 30
 Arg Leu Ser Gln Glu Leu
 35

<210> 18
 <211> 38
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> synthetic region from polymerase domain of Thermus
 caldophilus DNA polymerase (Tca)

<400> 18
 Trp Met Phe Gly Val Pro Pro Glu Ala Val Asp Pro Leu Met Arg Arg
 1 5 10 15
 Ala Ala Lys Thr Val Asn Phe Gly Val Leu Tyr Gly Met Ser Ala His
 20 25 30
 Arg Leu Ser Gln Glu Leu
 35

<210> 19
 <211> 38
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> synthetic region from polymerase domain of
 Thermotoga maritima DNA polymerase (Tma)

<400> 19
 Arg Ile Phe Asn Val Lys Pro Glu Glu Val Thr Glu Glu Met Arg Arg
 1 5 10 15
 Ala Gly Lys Met Val Asn Phe Ser Ile Ile Tyr Gly Val Thr Pro Tyr
 20 25 30
 Gly Leu Ser Val Arg Leu
 35

<210> 20
 <211> 38
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> synthetic region from polymerase domain of
 Thermotoga neopolitana DNA polymerase (Tne)

<400> 20
 Arg Ile Tyr Asn Val Lys Pro Glu Glu Val Asn Glu Glu Met Arg Arg
 1 5 10 15
 Val Gly Lys Met Val Asn Phe Ser Ile Ile Tyr Gly Val Thr Pro Tyr
 20 25 30
 Gly Leu Ser Val Arg Leu
 35

<210> 21
 <211> 38
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> synthetic region from polymerase domain of
 Thermosipho africanus DNA polymerase (Taf)

<400> 21
 Lys Ile Phe Gly Val Ser Glu Met Phe Val Ser Glu Gln Met Arg Arg
 1 5 10 15
 Val Gly Lys Met Val Asn Phe Ala Ile Ile Tyr Gly Val Ser Pro Tyr
 20 25 30
 Gly Leu Ser Lys Arg Ile
 35

<210> 22

<400> 22
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<210> 23
 <211> 38
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> synthetic region from polymerase domain of
 Deinococcus radiodurans DNA polymerase (Dra)

<400> 23
 Gln Val Leu Gly Leu Asp Glu Ala Thr Val Asp Ala Asn Gln Arg Arg
 1 5 10 15
 Ala Ala Lys Thr Val Asn Phe Gly Val Leu Tyr Gly Met Ser Ala His
 20 25 30
 Arg Leu Ser Asn Asp Leu
 35

<210> 24
 <211> 38
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> synthetic region from polymerase domain of
 Bacillus stearothermophilus DNA polymerase (Bst)

<400> 24
 Asp Ile Phe His Val Ser Glu Glu Asp Val Thr Ala Asn Met Arg Arg
 1 5 10 15
 Gln Ala Lys Ala Val Asn Phe Gly Ile Val Tyr Gly Ile Ser Asp Tyr
 20 25 30
 Gly Leu Ala Gln Asn Leu
 35

<210> 25
 <211> 38
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> synthetic region from polymerase domain of
 Bacillus caldotenax DNA polymerase (Bca)

<400> 25
 Asp Ile Phe Gln Val Ser Glu Asp Glu Val Thr Pro Asn Met Arg Arg
 1 5 10 15
 Gln Ala Lys Ala Val Asn Phe Gly Ile Val Tyr Gly Ile Ser Asp Tyr
 20 25 30
 Gly Leu Ala Gln Asn Leu
 35

<210> 26
 <211> 15
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> synthetic consensus sequence for region from
 polymerase domain of bacterial DNA polymerase

<220>
 <221> VARIANT
 <222> (1)...(1)
 <223> Xaa = Met or Gln

<220>
 <221> VARIANT
 <222> (4)...(4)
 <223> Xaa = Ala, Val or Gln

<220>
 <221> VARIANT
 <222> (5)...(5)
 <223> Xaa = Ala or Gly

<220>
 <221> VARIANT
 <222> (7)...(7)
 <223> Xaa = Thr, Met or Ala

<220>

<221> VARIANT
 <222> (8)...(8)
 <223> Xaa = Val or Ile

<220>
 <221> VARIANT
 <222> (11)...(11)
 <223> Xaa = Gly, Ser or Ala

<220>
 <221> VARIANT
 <222> (12)...(12)
 <223> Xaa = Val or Ile

<220>
 <221> VARIANT
 <222> (13)...(13)
 <223> Xaa = Leu, Ile or Val

<400> 26
 Xaa Arg Arg Xaa Xaa Lys Xaa Xaa Asn Phe Xaa Xaa Xaa Tyr Gly
 1 5 10 15

<210> 27
 <211> 13
 <212> PRT
 <213> Artificial sequence

<220>
 <223> synthetic polymerase motif corresponding to the
 D580X mutation of Z05, modified Z05 D580 motif

<220>
 <221> VARIANT
 <222> (7)...(7)
 <223> Xaa = Ser or Thr

<220>
 <221> VARIANT
 <222> (8)...(8)
 <223> Xaa = any amino acid other than Asp or Glu

<400> 27
 Thr Gly Arg Leu Ser Ser Xaa Xaa Pro Asn Leu Gln Asn
 1 5 10

<210> 28
 <211> 8
 <212> PRT
 <213> Artificial sequence

<220>
 <223> synthetic conserved DNA polymerase active site
 motif A

<400> 28
 Asp Tyr Ser Gln Ile Glu Leu Arg
 1 5

<210> 29
 <211> 893
 <212> PRT
 <213> Artificial sequence

<220>

<223> synthetic chimeric CS5 DNA polymerase derived from
N-terminal 5'-nuclease domain of *Thermus* sp. Z05
and C-terminal 3'-5' exonuclease and polymerase
domains of *Thermotoga maritima* DNA polymerases

<400> 29

Met	Lys	Ala	Met	Leu	Pro	Leu	Phe	Glu	Pro	Lys	Gly	Arg	Val	Leu	Leu
1				5					10					15	
Val	Asp	Gly	His	His	Leu	Ala	Tyr	Arg	Thr	Phe	Phe	Ala	Leu	Lys	Gly
			20					25					30		
Leu	Thr	Thr	Ser	Arg	Gly	Glu	Pro	Val	Gln	Ala	Val	Tyr	Gly	Phe	Ala
		35					40					45			
Lys	Ser	Leu	Leu	Lys	Ala	Leu	Lys	Glu	Asp	Gly	Tyr	Lys	Ala	Val	Phe
	50					55					60				
Val	Val	Phe	Asp	Ala	Lys	Ala	Pro	Ser	Phe	Arg	His	Glu	Ala	Tyr	Glu
65					70					75					80
Ala	Tyr	Lys	Ala	Gly	Arg	Ala	Pro	Thr	Pro	Glu	Asp	Phe	Pro	Arg	Gln
				85					90					95	
Leu	Ala	Leu	Ile	Lys	Glu	Leu	Val	Asp	Leu	Leu	Gly	Phe	Thr	Arg	Leu
			100					105					110		
Glu	Val	Pro	Gly	Phe	Glu	Ala	Asp	Asp	Val	Leu	Ala	Thr	Leu	Ala	Lys
		115					120					125			
Lys	Ala	Glu	Arg	Glu	Gly	Tyr	Glu	Val	Arg	Ile	Leu	Thr	Ala	Asp	Arg
	130					135					140				
Asp	Leu	Tyr	Gln	Leu	Val	Ser	Asp	Arg	Val	Ala	Val	Leu	His	Pro	Glu
145					150					155					160
Gly	His	Leu	Ile	Thr	Pro	Glu	Trp	Leu	Trp	Glu	Lys	Tyr	Gly	Leu	Lys
				165					170					175	
Pro	Glu	Gln	Trp	Val	Asp	Phe	Arg	Ala	Leu	Val	Gly	Asp	Pro	Ser	Asp
			180					185					190		
Asn	Leu	Pro	Gly	Val	Lys	Gly	Ile	Gly	Glu	Lys	Thr	Ala	Leu	Lys	Leu
		195					200					205			
Leu	Lys	Glu	Trp	Gly	Ser	Leu	Glu	Asn	Ile	Leu	Lys	Asn	Leu	Asp	Arg
	210					215					220				
Val	Lys	Pro	Glu	Ser	Val	Arg	Glu	Arg	Ile	Lys	Ala	His	Leu	Glu	Asp
225					230					235					240
Leu	Lys	Leu	Ser	Leu	Glu	Leu	Ser	Arg	Val	Arg	Ser	Asp	Leu	Pro	Leu
				245					250					255	
Glu	Val	Asp	Phe	Ala	Arg	Arg	Arg	Glu	Pro	Asp	Arg	Glu	Gly	Leu	Arg
			260					265					270		
Ala	Phe	Leu	Glu	Arg	Leu	Glu	Phe	Gly	Ser	Leu	Leu	His	Glu	Phe	Gly
		275					280					285			
Leu	Leu	Glu	Glu	Ser	Glu	Pro	Val	Gly	Tyr	Arg	Ile	Val	Lys	Asp	Leu
	290					295					300				
Val	Glu	Phe	Glu	Lys	Leu	Ile	Glu	Lys	Leu	Arg	Glu	Ser	Pro	Ser	Phe
305					310					315					320
Ala	Ile	Asp	Leu	Glu	Thr	Ser	Ser	Leu	Asp	Pro	Phe	Asp	Cys	Asp	Ile
				325					330					335	
Val	Gly	Ile	Ser	Val	Ser	Phe	Lys	Pro	Lys	Glu	Ala	Tyr	Tyr	Ile	Pro
			340					345					350		
Leu	His	His	Arg	Asn	Ala	Gln	Asn	Leu	Asp	Glu	Lys	Glu	Val	Leu	Lys
		355					360					365			
Lys	Leu	Lys	Glu	Ile	Leu	Glu	Asp	Pro	Gly	Ala	Lys	Ile	Val	Gly	Gln
	370					375					380				
Asn	Leu	Lys	Phe	Asp	Tyr	Lys	Val	Leu	Met	Val	Lys	Gly	Val	Glu	Pro
385					390					395					400
Val	Pro	Pro	Tyr	Phe	Asp	Thr	Met	Ile	Ala	Ala	Tyr	Leu	Leu	Glu	Pro
				405					410					415	
Asn	Glu	Lys	Lys	Phe	Asn	Leu	Asp	Asp	Leu	Ala	Leu	Lys	Phe	Leu	Gly
			420					425					430		
Tyr	Lys	Met	Thr	Ser	Tyr	Gln	Glu	Leu	Met	Ser	Phe	Ser	Phe	Pro	Leu
		435					440					445			
Phe	Gly	Phe	Ser	Phe	Ala	Asp	Val	Pro	Val	Glu	Lys	Ala	Ala	Asn	Tyr
	450					455					460				
Ser	Cys	Glu	Asp	Ala	Asp	Ile	Thr	Tyr	Arg	Leu	Tyr	Lys	Thr	Leu	Ser
465					470					475					480
Leu	Lys	Leu	His	Glu	Ala	Asp	Leu	Glu	Asn	Val	Phe	Tyr	Lys	Ile	Glu
				485					490					495	

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Met	Pro	Leu	Val	Asn	Val	Leu	Ala	Arg	Met	Glu	Leu	Asn	Gly	Val	Tyr
			500					505					510		
Val	Asp	Thr	Glu	Phe	Leu	Lys	Lys	Leu	Ser	Glu	Glu	Tyr	Gly	Lys	Lys
		515					520					525			
Leu	Glu	Glu	Leu	Ala	Glu	Glu	Ile	Tyr	Arg	Ile	Ala	Gly	Glu	Pro	Phe
	530					535					540				
Asn	Ile	Asn	Ser	Pro	Lys	Gln	Val	Ser	Arg	Ile	Leu	Phe	Glu	Lys	Leu
545					550					555					560
Gly	Ile	Lys	Pro	Arg	Gly	Lys	Thr	Thr	Lys	Thr	Gly	Asp	Tyr	Ser	Thr
				565					570					575	
Arg	Ile	Glu	Val	Leu	Glu	Glu	Leu	Ala	Gly	Glu	His	Glu	Ile	Ile	Pro
			580					585					590		
Leu	Ile	Leu	Glu	Tyr	Arg	Lys	Ile	Gln	Lys	Leu	Lys	Ser	Thr	Tyr	Ile
		595					600					605			
Asp	Ala	Leu	Pro	Lys	Met	Val	Asn	Pro	Lys	Thr	Gly	Arg	Ile	His	Ala
	610					615					620				
Ser	Phe	Asn	Gln	Thr	Gly	Thr	Ala	Thr	Gly	Arg	Leu	Ser	Ser	Ser	Asp
625					630					635					640
Pro	Asn	Leu	Gln	Asn	Leu	Pro	Thr	Lys	Ser	Glu	Glu	Gly	Lys	Glu	Ile
				645					650					655	
Arg	Lys	Ala	Ile	Val	Pro	Gln	Asp	Pro	Asn	Trp	Trp	Ile	Val	Ser	Ala
			660					665					670		
Asp	Tyr	Ser	Gln	Ile	Glu	Leu	Arg	Ile	Leu	Ala	His	Leu	Ser	Gly	Asp
		675					680					685			
Glu	Asn	Leu	Leu	Arg	Ala	Phe	Glu	Glu	Gly	Ile	Asp	Val	His	Thr	Leu
	690					695					700				
Thr	Ala	Ser	Arg	Ile	Phe	Asn	Val	Lys	Pro	Glu	Glu	Val	Thr	Glu	Glu
705					710					715					720
Met	Arg	Arg	Ala	Gly	Lys	Met	Val	Asn	Phe	Ser	Ile	Ile	Tyr	Gly	Val
				725					730					735	
Thr	Pro	Tyr	Gly	Leu	Ser	Val	Arg	Leu	Gly	Val	Pro	Val	Lys	Glu	Ala
			740					745					750		
Glu	Lys	Met	Ile	Val	Asn	Tyr	Phe	Val	Leu	Tyr	Pro	Lys	Val	Arg	Asp
		755					760					765			
Tyr	Ile	Gln	Arg	Val	Val	Ser	Glu	Ala	Lys	Glu	Lys	Gly	Tyr	Val	Arg
	770					775					780				
Thr	Leu	Phe	Gly	Arg	Lys	Arg	Asp	Ile	Pro	Gln	Leu	Met	Ala	Arg	Asp
785					790					795					800
Arg	Asn	Thr	Gln	Ala	Glu	Gly	Glu	Arg	Ile	Ala	Ile	Asn	Thr	Pro	Ile
				805					810					815	
Gln	Gly	Thr	Ala	Ala	Asp	Ile	Ile	Lys	Leu	Ala	Met	Ile	Glu	Ile	Asp
			820					825					830		
Arg	Glu	Leu	Lys	Glu	Arg	Lys	Met	Arg	Ser	Lys	Met	Ile	Ile	Gln	Val
		835					840					845			
His	Asp	Glu	Leu	Val	Phe	Glu	Val	Pro	Asn	Glu	Glu	Lys	Asp	Ala	Leu
	850					855					860				
Val	Glu	Leu	Val	Lys	Asp	Arg	Met	Thr	Asn	Val	Val	Lys	Leu	Ser	Val
865					870					875					880
Pro	Leu	Glu	Val	Asp	Val	Thr	Ile	Gly	Lys	Thr	Trp	Ser			
				885					890						

<210> 30

<211> 893

<212> PRT

<213> Artificial Sequence

<220>

<223> synthetic chimeric CS6 DNA polymerase derived from
N-terminal 5'-nuclease domain of *Thermus* sp. Z05
and C-terminal 3'-5' exonuclease and polymerase
domains of *Thermotoga maritima* DNA polymerases

<400> 30

Met	Lys	Ala	Met	Leu	Pro	Leu	Phe	Glu	Pro	Lys	Gly	Arg	Val	Leu	Leu
1				5					10					15	
Val	Asp	Gly	His	His	Leu	Ala	Tyr	Arg	Thr	Phe	Phe	Ala	Leu	Lys	Gly
			20					25					30		

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Leu	Thr	Thr	Ser	Arg	Gly	Glu	Pro	Val	Gln	Ala	Val	Tyr	Gly	Phe	Ala
Lys	Ser	Leu	Leu	Lys	Ala	Leu	Lys	Glu	Asp	Gly	Tyr	Lys	Ala	Val	Phe
Val	Val	Phe	Asp	Ala	Lys	Ala	Pro	Ser	Phe	Arg	His	Glu	Ala	Tyr	Glu
65	Ala	Tyr	Lys	Ala	Gly	Arg	Ala	Pro	Thr	Pro	Glu	Asp	Phe	Pro	Arg
				85					90					95	Gln
Leu	Ala	Leu	Ile	Lys	Glu	Leu	Val	Asp	Leu	Leu	Gly	Phe	Thr	Arg	Leu
			100					105					110		
Glu	Val	Pro	Gly	Phe	Glu	Ala	Asp	Asp	Val	Leu	Ala	Thr	Leu	Ala	Lys
		115					120					125			
Lys	Ala	Glu	Arg	Glu	Gly	Tyr	Glu	Val	Arg	Ile	Leu	Thr	Ala	Asp	Arg
	130					135					140				
Asp	Leu	Tyr	Gln	Leu	Val	Ser	Asp	Arg	Val	Ala	Val	Leu	His	Pro	Glu
145				150						155					160
Gly	His	Leu	Ile	Thr	Pro	Glu	Trp	Leu	Trp	Glu	Lys	Tyr	Gly	Leu	Lys
			165					170						175	
Pro	Glu	Gln	Trp	Val	Asp	Phe	Arg	Ala	Leu	Val	Gly	Asp	Pro	Ser	Asp
		180						185					190		
Asn	Leu	Pro	Gly	Val	Lys	Gly	Ile	Gly	Glu	Lys	Thr	Ala	Leu	Lys	Leu
		195					200					205			
Leu	Lys	Glu	Trp	Gly	Ser	Leu	Glu	Asn	Ile	Leu	Lys	Asn	Leu	Asp	Arg
	210					215					220				
Val	Lys	Pro	Glu	Ser	Val	Arg	Glu	Arg	Ile	Lys	Ala	His	Leu	Glu	Asp
225				230						235					240
Leu	Lys	Leu	Ser	Leu	Glu	Leu	Ser	Arg	Val	Arg	Ser	Asp	Leu	Pro	Leu
				245					250					255	
Glu	Val	Asp	Phe	Ala	Arg	Arg	Arg	Glu	Pro	Asp	Arg	Glu	Gly	Leu	Arg
		260						265					270		
Ala	Phe	Leu	Glu	Arg	Leu	Glu	Phe	Gly	Ser	Leu	Leu	His	Glu	Phe	Gly
	275						280					285			
Leu	Leu	Glu	Glu	Ser	Glu	Pro	Val	Gly	Tyr	Arg	Ile	Val	Lys	Asp	Leu
	290					295					300				
Val	Glu	Phe	Glu	Lys	Leu	Ile	Glu	Lys	Leu	Arg	Glu	Ser	Pro	Ser	Phe
305				310						315					320
Ala	Ile	Ala	Leu	Ala	Thr	Ser	Ser	Leu	Asp	Pro	Phe	Asp	Cys	Asp	Ile
				325					330					335	
Val	Gly	Ile	Ser	Val	Ser	Phe	Lys	Pro	Lys	Glu	Ala	Tyr	Tyr	Ile	Pro
		340						345					350		
Leu	His	His	Arg	Asn	Ala	Gln	Asn	Leu	Asp	Glu	Lys	Glu	Val	Leu	Lys
	355						360					365			
Lys	Leu	Lys	Glu	Ile	Leu	Glu	Asp	Pro	Gly	Ala	Lys	Ile	Val	Gly	Gln
	370					375					380				
Asn	Leu	Lys	Phe	Asp	Tyr	Lys	Val	Leu	Met	Val	Lys	Gly	Val	Glu	Pro
385				390						395					400
Val	Pro	Pro	Tyr	Phe	Asp	Thr	Met	Ile	Ala	Ala	Tyr	Leu	Leu	Glu	Pro
				405					410					415	
Asn	Glu	Lys	Lys	Phe	Asn	Leu	Asp	Asp	Leu	Ala	Leu	Lys	Phe	Leu	Gly
		420						425					430		
Tyr	Lys	Met	Thr	Ser	Tyr	Gln	Glu	Leu	Met	Ser	Phe	Ser	Phe	Pro	Leu
	435						440					445			
Phe	Gly	Phe	Ser	Phe	Ala	Asp	Val	Pro	Val	Glu	Lys	Ala	Ala	Asn	Tyr
	450					455					460				
Ser	Cys	Glu	Asp	Ala	Asp	Ile	Thr	Tyr	Arg	Leu	Tyr	Lys	Thr	Leu	Ser
465				470						475					480
Leu	Lys	Leu	His	Glu	Ala	Asp	Leu	Glu	Asn	Val	Phe	Tyr	Lys	Ile	Glu
				485					490					495	
Met	Pro	Leu	Val	Asn	Val	Leu	Ala	Arg	Met	Glu	Leu	Asn	Gly	Val	Tyr
		500						505					510		
Val	Asp	Thr	Glu	Phe	Leu	Lys	Lys	Leu	Ser	Glu	Glu	Tyr	Gly	Lys	Lys
	515						520					525			
Leu	Glu	Glu	Leu	Ala	Glu	Glu	Ile	Tyr	Arg	Ile	Ala	Gly	Glu	Pro	Phe
	530					535					540				
Asn	Ile	Asn	Ser	Pro	Lys	Gln	Val	Ser	Arg	Ile	Leu	Phe	Glu	Lys	Leu
545					550					555					560
Gly	Ile	Lys	Pro	Arg	Gly	Lys	Thr	Thr	Lys	Thr	Gly	Asp	Tyr	Ser	Thr
				565					570					575	

23

Arg	Ile	Glu	Val	Leu	Glu	Glu	Leu	Ala	Gly	Glu	His	Glu	Ile	Ile	Pro
			580					585					590		
Leu	Ile	Leu	Glu	Tyr	Arg	Lys	Ile	Gln	Lys	Leu	Lys	Ser	Thr	Tyr	Ile
		595					600					605			
Asp	Ala	Leu	Pro	Lys	Met	Val	Asn	Pro	Lys	Thr	Gly	Arg	Ile	His	Ala
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Ser	Phe	Asn	Gln	Thr	Gly	Thr	Ala	Thr	Gly	Arg	Leu	Ser	Ser	Ser	Asp
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Pro	Asn	Leu	Gln	Asn	Leu	Pro	Thr	Lys	Ser	Glu	Glu	Gly	Lys	Glu	Ile
			645						650					655	
Arg	Lys	Ala	Ile	Val	Pro	Gln	Asp	Pro	Asn	Trp	Trp	Ile	Val	Ser	Ala
			660					665					670		
Asp	Tyr	Ser	Gln	Ile	Glu	Leu	Arg	Ile	Leu	Ala	His	Leu	Ser	Gly	Asp
		675					680					685			
Glu	Asn	Leu	Leu	Arg	Ala	Phe	Glu	Glu	Gly	Ile	Asp	Val	His	Thr	Leu
	690					695					700				
Thr	Ala	Ser	Arg	Ile	Phe	Asn	Val	Lys	Pro	Glu	Glu	Val	Thr	Glu	Glu
	705				710					715					720
Met	Arg	Arg	Ala	Gly	Lys	Met	Val	Asn	Phe	Ser	Ile	Ile	Tyr	Gly	Val
			725						730					735	
Thr	Pro	Tyr	Gly	Leu	Ser	Val	Arg	Leu	Gly	Val	Pro	Val	Lys	Glu	Ala
			740					745					750		
Glu	Lys	Met	Ile	Val	Asn	Tyr	Phe	Val	Leu	Tyr	Pro	Lys	Val	Arg	Asp
		755					760					765			
Tyr	Ile	Gln	Arg	Val	Val	Ser	Glu	Ala	Lys	Glu	Lys	Gly	Tyr	Val	Arg
	770					775					780				
Thr	Leu	Phe	Gly	Arg	Lys	Arg	Asp	Ile	Pro	Gln	Leu	Met	Ala	Arg	Asp
	785				790					795					800
Arg	Asn	Thr	Gln	Ala	Glu	Gly	Glu	Arg	Ile	Ala	Ile	Asn	Thr	Pro	Ile
			805						810					815	
Gln	Gly	Thr	Ala	Ala	Asp	Ile	Ile	Lys	Leu	Ala	Met	Ile	Glu	Ile	Asp
			820					825					830		
Arg	Glu	Leu	Lys	Glu	Arg	Lys	Met	Arg	Ser	Lys	Met	Ile	Ile	Gln	Val
		835					840					845			
His	Asp	Glu	Leu	Val	Phe	Glu	Val	Pro	Asn	Glu	Glu	Lys	Asp	Ala	Leu
	850				855					860					
Val	Glu	Leu	Val	Lys	Asp	Arg	Met	Thr	Asn	Val	Val	Lys	Leu	Ser	Val
	865				870					875					880
Pro	Leu	Glu	Val	Asp	Val	Thr	Ile	Gly	Lys	Thr	Trp	Ser			
			885						890						

<210> 31
 <211> 21
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> synthetic error-prone (mutagenic) PCR
 amplification forward primer

<400> 31
 ctacctcctg gaccctcca a

21

<210> 32
 <211> 25
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> synthetic error-prone (mutagenic) PCR
 amplification reverse primer

<400> 32
 ataaccaact ggtagtggcg tgtaa

25

<210> 33
 <211> 1491

<212> DNA

<213> Artificial Sequence

<220>

<223> synthetic amplicon encoding polymerase domain of Z05
D580G DNA polymerase amplified by error-prone (mutagenic)
PCR between B1pI and BglII restriction sites

<400> 33

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gtggacggag gacgccgccc accgggccct cctcgctgag cggctccagc aaaacctctt 120
ggaacgcctc aagggagagg aaaagctcct ttggctctac caagaggtgg aaaagcccct 180
ctcccgggtc ctggcccaca tggaggccac cgggggtaagg ctggacgtgg cctatctaaa 240
ggccctttcc ctggagcttg cggaggagat tcgcccctc gaggaggagg tcttccgcct 300
ggcggggcac cccttcaacc tgaactcccg tgaccagcta gagcgggtgc tctttgacga 360
gcttaggctt cccgcccttg gcaagacgca aaagacgggg aagcgtcca ccagcgccgc 420
ggtgctggag gccctcaggg agggccaccc catcgtggag aagatcctcc agcaccggga 480
gctcaccaag ctcaagaaca cctacgtaga cccctcccgg ggcctcgtcc acccgaggac 540
gggcccctc cacacccgct tcaaccagac agccacggcc acgggaaggc tctctagctc 600
cgggcccac ctgcagaaca tccccatccg cacccttg ggccagagga tccgccgggc 660
cttcgtggcc gaggcgggat gggcgttggt ggccctggac tatagccaga tagagctccg 720
ggtcctcgcc cacctctccg gggacgagaa cctgatcagg gtcttccagg aggggaagga 780
catccacacc cagaccgcaa gctggatgtt cggcgtctcc ccggaggccg tggaccccct 840
gatgcgccgg gcggccaaga cggtgaactt cggcgtcctc tacggcatgt ccgccatag 900
gctctccag gagcttgcca tcccctacga ggaggcgggt gcctttatag agcgtactt 960
ccaaagcttc ccaaaggtgc gggcctggat agaaaagacc ctggaggagg ggaggaagcg 1020
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gaagagcgct agggaggccg cggagcgcat ggcttcaac atgcccgtcc agggcaccgc 1140
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ccgcatgctc ctccagggtc acgacgagct cctcctggag gcccccaag cgcgggccga 1260
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ggaggtggag gtggggatcg gggaggactg gctttccgcc aagggtgat atcagatctc 1380
cctgattatg cgtcagtcta tgaagaaaaa tcgtatacag atggacgaag agagaatcct 1440
tgtgaattta acagagggtg tagggattac acgccactac cagttgggta t 1491
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<210> 34

<211> 110

<212> DNA

<213> Artificial Sequence

<220>

<223> synthetic wild-type BRAF V600K target
polynucleotide

<400> 34

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gtttgaacag ttgtctggat ccattttgtg gatggtaaga attgaggcta 110
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<210> 35

<211> 110

<212> DNA

<213> Artificial Sequence

<220>

<223> synthetic mutant BRAF V600R target polynucleotide

<400> 35

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gtttgaacag ttgtctggat ccattttgtg gatggtaaga attgaggcta 110
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<210> 36

<211> 921

<212> PRT

<213> Deinococcus radiodurans

<220>

<223> Deinococcus radiodurans DNA polymerase (Dra)

<400> 36

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Ile	Asp	Gly	His 20	Ala	Leu	Ala	Phe	Arg 25	Ser	Tyr	Phe	Ala	Leu 30	Pro	Pro
Leu	Asn	Asn 35	Ser	Lys	Gly	Glu	Met 40	Thr	Asp	Ala	Ile	Val 45	Gly	Phe	Met
Lys	Leu 50	Leu	Leu	Arg	Leu	Ala 55	Arg	Gln	Lys	Ser	Asn 60	Gln	Val	Ile	Val
Val 65	Phe	Asp	Pro	Pro	Val 70	Lys	Thr	Leu	Arg	His 75	Glu	Gln	Tyr	Glu	Gly 80
Tyr	Lys	Ser	Gly	Arg 85	Ala	Gln	Thr	Pro	Glu 90	Asp	Leu	Arg	Gly	Gln 95	Ile
Asn	Arg	Ile	Arg 100	Ala	Leu	Val	Asp	Ala 105	Leu	Gly	Phe	Pro	Arg 110	Leu	Glu
Glu	Pro	Gly 115	Tyr	Glu	Ala	Asp	Asp 120	Val	Ile	Ala	Ser	Leu 125	Thr	Arg	Met
Ala	Glu 130	Gly	Lys	Gly	Tyr	Glu 135	Val	Arg	Ile	Val	Thr 140	Ser	Asp	Arg	Asp
Ala 145	Tyr	Gln	Leu	Leu	Asp 150	Glu	His	Val	Lys	Val 155	Ile	Ala	Asn	Asp	Phe 160
Ser	Leu	Ile	Gly	Pro 165	Ala	Gln	Val	Glu	Glu 170	Lys	Tyr	Gly	Val	Thr 175	Val
Arg	Gln	Trp	Val 180	Asp	Tyr	Arg	Ala	Leu 185	Thr	Gly	Asp	Ala	Ser 190	Asp	Asn
Ile	Pro	Gly 195	Ala	Lys	Gly	Ile	Gly 200	Pro	Lys	Thr	Ala	Ala 205	Lys	Leu	Leu
Gln	Glu 210	Tyr	Gly	Thr	Leu	Glu 215	Lys	Val	Tyr	Glu	Ala 220	Ala	His	Ala	Gly
Thr 225	Leu	Lys	Pro	Asp	Gly 230	Thr	Arg	Lys	Lys	Leu	Leu	Asp	Ser	Glu	Glu 240
Asn	Val	Lys	Phe	Ser 245	His	Asp	Leu	Ser	Cys 250	Met	Val	Thr	Asp	Leu 255	Pro
Leu	Asp	Ile	Glu 260	Phe	Gly	Val	Arg	Arg 265	Leu	Pro	Asp	Asn	Pro 270	Leu	Val
Thr	Glu	Asp 275	Leu	Leu	Thr	Glu	Leu 280	Glu	Leu	His	Ser	Leu 285	Arg	Pro	Met
Ile	Leu 290	Gly	Leu	Asn	Gly	Pro 295	Glu	Gln	Asp	Gly	His 300	Ala	Pro	Asp	Asp
Leu 305	Leu	Glu	Arg	Glu	His 310	Ala	Gln	Thr	Pro	Glu 315	Glu	Asp	Glu	Ala	Ala 320
Ala	Leu	Pro	Ala	Phe 325	Ser	Ala	Pro	Glu	Leu 330	Ala	Glu	Trp	Gln	Thr 335	Pro
Ala	Glu	Gly	Ala 340	Val	Trp	Gly	Tyr	Val 345	Leu	Ser	Arg	Glu	Asp 350	Asp	Leu
Thr	Ala 355	Ala	Leu	Leu	Ala	Ala	Ala 360	Thr	Phe	Glu	Asp	Gly 365	Val	Ala	Arg
Pro	Ala 370	Arg	Val	Ser	Glu	Pro 375	Asp	Glu	Trp	Ala	Gln 380	Ala	Glu	Ala	Pro
Glu 385	Asn	Leu	Phe	Gly	Glu 390	Leu	Leu	Pro	Ser	Asp 395	Lys	Pro	Leu	Thr	Lys 400
Lys	Glu	Gln	Lys	Ala 405	Leu	Glu	Lys	Ala	Gln 410	Lys	Asp	Ala	Glu	Lys 415	Ala
Arg	Ala	Lys	Leu 420	Arg	Glu	Gln	Phe	Pro 425	Ala	Thr	Val	Asp	Glu 430	Ala	Glu
Phe	Val	Gly 435	Gln	Arg	Thr	Val	Thr 440	Ala	Ala	Ala	Ala 445	Lys	Ala	Leu	Ala
Ala	His 450	Leu	Ser	Val	Arg	Gly 455	Thr	Val	Val	Glu	Pro 460	Gly	Asp	Asp	Pro
Leu 465	Leu	Tyr	Ala	Tyr	Leu 470	Leu	Asp	Pro	Ala	Asn 475	Thr	Asn	Met	Pro	Val 480
Val	Ala	Lys	Arg	Tyr 485	Leu	Asp	Arg	Glu	Trp 490	Pro	Ala	Asp	Ala	Pro 495	Thr
Arg	Ala	Ala 500	Ile	Thr	Gly	His	Leu	Val 505	Arg	Glu	Leu	Pro	Pro 510	Leu	Leu
Asp	Asp	Ala 515	Arg	Arg	Lys	Met	Tyr 520	Asp	Glu	Met	Glu	Lys 525	Pro	Leu	Ser
Gly	Val	Leu	Gly	Arg	Met	Glu	Val	Arg	Gly	Val	Gln	Val	Asp	Ser	Asp

530		535		540
Phe 545	Leu Gln Thr Leu	Ile Gln Ala Gly Val	Arg Leu Ala Asp Leu	
Glu 550	Ser Gln Ile His	Tyr Ala Gly Glu Glu	Phe His Ile Arg Ser	
Pro 565	Lys Gln Leu Glu	Thr Val Leu Tyr Asp	Lys Leu Glu Leu Ala Ser	
Ser 580	Lys Lys Thr Lys	Leu Thr Gly Gln Arg	Ser Thr Ala Val Ser Ala	
Leu 595	Glu Pro Leu Arg	Asp Ala His Pro Ile	Ile Pro Leu Val Leu Glu	
Phe 610	Arg Glu Leu Asp	Lys Leu Arg Gly Thr	Tyr Leu Asp Pro Ile Pro	
Asn 625	Leu Val Asn Pro	His Thr Gly Arg Leu	His Thr Thr Phe Ala Gln	
Thr 645	Ala Val Ala Thr	Gly Arg Leu Ser Ser	Leu Asn Pro Asn Leu Gln	
Asn 660	Ile Pro Ile Arg	Ser Glu Leu Gly Arg	Glu Ile Arg Lys Gly Phe	
Ile 675	Ala Glu Asp Gly	Phe Thr Leu Ile Ala	Ala Asp Tyr Ser Gln Ile	
Glu 690	Leu Arg Leu Leu	Ala His Ile Ala Asp	Asp Pro Leu Met Gln Gln	
Ala 705	Phe Val Glu Gly	Ala Asp Ile His Arg	Arg Thr Ala Ala Gln Val	
Leu 725	Gly Leu Asp Glu	Ala Thr Val Asp Ala	Asn Gln Arg Arg Ala Ala	
Lys 740	Thr Val Asn Phe	Gly Val Leu Tyr Gly	Met Ser Ala His Arg Leu	
Ser 755	Asn Asp Leu Gly	Ile Pro Tyr Ala Glu	Ala Ala Thr Phe Ile Glu	
Ile 770	Tyr Phe Ala Thr	Tyr Pro Gly Ile Arg	Arg Tyr Ile Asn His Thr	
Leu 785	Asp Phe Gly Arg	Thr His Gly Tyr Val	Glu Thr Leu Tyr Gly Arg	
Arg 805	Arg Tyr Val Pro	Gly Leu Ser Ser Arg	Asn Arg Val Gln Arg Glu	
Ala 820	Glu Glu Arg Leu	Ala Tyr Asn Met Pro	Ile Gln Gly Thr Ala Ala	
Asp 835	Ile Met Lys Leu	Ala Met Val Gln Leu	Asp Pro Gln Leu Asp Ala	
Ile 850	Gly Ala Arg Met	Leu Leu Gln Val His	Asp Glu Leu Leu Ile Glu	
Ala 865	Pro Leu Asp Lys	Ala Glu Gln Val Ala	Ala Leu Thr Lys Lys Val	
Met 885	Glu Asn Val Val	Gln Leu Lys Val Pro	Leu Ala Val Glu Val Gly	
Thr 900	Gly Pro Asn Trp	Phe Asp Thr Lys		
915		920		

<210> 37

<211> 892

<212> PRT

<213> *Thermosipho africanus*

<220>

<223> *Thermosipho africanus* DNA polymerase (Taf)

<400> 37

Met 1	Gly Lys Met Phe	Leu Phe Asp Gly	Thr Gly Leu Val	Tyr Arg Ala
Phe 20	Tyr Ala Ile Asp	Gln Ser Leu Gln	Thr Ser Ser Gly	Leu His Thr
Asn 35	Ala Val Tyr Gly	Leu Thr Lys Met	Leu Ile Lys Phe	Leu Lys Glu
His 50	Ile Ser Ile Gly	Lys Asp Ala Cys	Val Phe Val Leu	Asp Ser Lys
		55	60	

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Gly 65	Gly	Ser	Lys	Lys	Arg 70	Lys	Asp	Ile	Leu	Glu 75	Thr	Tyr	Lys	Ala	Asn 80
Arg	Pro	Ser	Thr	Pro 85	Asp	Leu	Leu	Leu	Glu 90	Gln	Ile	Pro	Tyr	Val 95	Glu
Glu	Leu	Val	Asp 100	Ala	Leu	Gly	Ile	Lys 105	Val	Leu	Lys	Ile	Glu 110	Gly	Phe
Glu	Ala	Asp 115	Asp	Ile	Ile	Ala	Thr 120	Leu	Ser	Lys	Lys	Phe 125	Glu	Ser	Asp
Phe	Glu 130	Lys	Val	Asn	Ile	Ile 135	Thr	Gly	Asp	Lys	Asp 140	Leu	Leu	Gln	Leu
Val 145	Ser	Asp	Lys	Val	Phe 150	Val	Trp	Arg	Val	Glu 155	Arg	Gly	Ile	Thr	Asp 160
Leu	Val	Leu	Tyr	Asp 165	Arg	Asn	Lys	Val	Ile 170	Glu	Lys	Tyr	Gly	Ile 175	Tyr
Pro	Glu	Gln	Phe 180	Lys	Asp	Tyr	Leu	Ser 185	Leu	Val	Gly	Asp	Gln 190	Ile	Asp
Asn	Ile	Pro 195	Gly	Val	Lys	Gly	Ile 200	Gly	Lys	Lys	Thr	Ala 205	Val	Ser	Leu
Leu	Lys 210	Lys	Tyr	Asn	Ser	Leu 215	Glu	Asn	Val	Leu	Lys 220	Asn	Ile	Asn	Leu
Leu 225	Thr	Glu	Lys	Leu	Arg 230	Arg	Leu	Leu	Glu	Asp 235	Ser	Lys	Glu	Asp	Leu 240
Gln	Lys	Ser	Ile	Glu 245	Leu	Val	Glu	Leu	Ile 250	Tyr	Asp	Val	Pro	Met 255	Asp
Val	Glu	Lys	Asp 260	Glu	Ile	Ile	Tyr	Arg 265	Gly	Tyr	Asn	Pro	Asp 270	Lys	Leu
Leu	Lys	Val 275	Leu	Lys	Lys	Tyr	Glu 280	Phe	Ser	Ser	Ile	Ile 285	Lys	Glu	Leu
Asn	Leu 290	Gln	Glu	Lys	Leu	Glu 295	Lys	Glu	Tyr	Ile	Leu 300	Val	Asp	Asn	Glu
Asp 305	Lys	Leu	Lys	Lys	Leu 310	Ala	Glu	Glu	Ile	Glu 315	Lys	Tyr	Lys	Thr	Phe 320
Ser	Ile	Asp	Thr	Glu 325	Thr	Thr	Ser	Leu	Asp 330	Pro	Phe	Glu	Ala	Lys 335	Leu
Val	Gly	Ile	Ser 340	Ile	Ser	Thr	Met	Glu 345	Gly	Lys	Ala	Tyr	Tyr 350	Ile	Pro
Val	Ser	His 355	Phe	Gly	Ala	Lys	Asn 360	Ile	Ser	Lys	Ser	Leu 365	Ile	Asp	Lys
Phe	Leu 370	Lys	Gln	Ile	Leu	Gln 375	Glu	Lys	Asp	Tyr	Asn 380	Ile	Val	Gly	Gln
Asn 385	Leu	Lys	Phe	Asp	Tyr 390	Glu	Ile	Phe	Lys	Ser 395	Met	Gly	Phe	Ser	Pro 400
Asn	Val	Pro	His	Phe 405	Asp	Thr	Met	Ile	Ala 410	Ala	Tyr	Leu	Leu	Asn 415	Pro
Asp	Glu	Lys	Arg 420	Phe	Asn	Leu	Glu	Glu 425	Leu	Ser	Leu	Lys	Tyr 430	Leu	Gly
Tyr	Lys	Met 435	Ile	Ser	Phe	Asp	Glu 440	Leu	Val	Asn	Glu	Asn 445	Val	Pro	Leu
Phe	Gly 450	Asn	Asp	Phe	Ser	Tyr 455	Val	Pro	Leu	Glu	Arg 460	Ala	Val	Glu	Tyr
Ser 465	Cys	Glu	Asp	Ala	Asp 470	Val	Thr	Tyr	Arg	Ile 475	Phe	Arg	Lys	Leu	Gly 480
Arg	Lys	Ile	Tyr	Glu 485	Asn	Glu	Met	Glu	Lys 490	Leu	Phe	Tyr	Glu	Ile 495	Glu
Met	Pro	Leu	Ile 500	Asp	Val	Leu	Ser	Glu 505	Met	Glu	Leu	Asn	Gly 510	Val	Tyr
Phe	Asp	Glu 515	Glu	Tyr	Leu	Lys	Glu 520	Leu	Ser	Lys	Lys	Tyr 525	Gln	Glu	Lys
Met	Asp 530	Gly	Ile	Lys	Glu	Lys 535	Val	Phe	Glu	Ile	Ala 540	Gly	Glu	Thr	Phe
Asn 545	Leu	Asn	Ser	Ser	Thr 550	Gln	Val	Ala	Tyr	Ile 555	Leu	Phe	Glu	Lys	Leu 560
Asn	Ile	Ala	Pro	Tyr 565	Lys	Lys	Thr	Ala	Thr 570	Gly	Lys	Phe	Ser	Thr 575	Asn
Ala	Glu	Val	Leu 580	Glu	Glu	Leu	Ser	Lys 585	Glu	His	Glu	Ile	Ala 590	Lys	Leu
Leu	Leu	Glu 595	Tyr	Arg	Lys	Tyr	Gln 600	Lys	Leu	Lys	Ser	Thr 605	Tyr	Ile	Asp

28

Ser	Ile	Pro	Leu	Ser	Ile	Asn	Arg	Lys	Thr	Asn	Arg	Val	His	Thr	Thr
610						615				620					
Phe	His	Gln	Thr	Gly	Thr	Ser	Thr	Gly	Arg	Leu	Ser	Ser	Ser	Asn	Pro
625					630					635					640
Asn	Leu	Gln	Asn	Leu	Pro	Thr	Arg	Ser	Glu	Glu	Gly	Lys	Glu	Ile	Arg
				645					650					655	
Lys	Ala	Val	Arg	Pro	Gln	Arg	Gln	Asp	Trp	Trp	Ile	Leu	Gly	Ala	Asp
			660					665					670		
Tyr	Ser	Gln	Ile	Glu	Leu	Arg	Val	Leu	Ala	His	Val	Ser	Lys	Asp	Glu
		675					680					685			
Asn	Leu	Leu	Lys	Ala	Phe	Lys	Glu	Asp	Leu	Asp	Ile	His	Thr	Ile	Thr
690						695					700				
Ala	Ala	Lys	Ile	Phe	Gly	Val	Ser	Glu	Met	Phe	Val	Ser	Glu	Gln	Met
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Pro	Tyr	Gly	Leu	Ser	Lys	Arg	Ile	Gly	Leu	Ser	Val	Ser	Glu	Thr	Lys
			740					745					750		
Lys	Ile	Ile	Asp	Asn	Tyr	Phe	Arg	Tyr	Tyr	Lys	Gly	Val	Phe	Glu	Tyr
		755					760					765			
Leu	Lys	Arg	Met	Lys	Asp	Glu	Ala	Arg	Lys	Lys	Gly	Tyr	Val	Thr	Thr
770						775					780				
Leu	Phe	Gly	Arg	Arg	Arg	Tyr	Ile	Pro	Gln	Leu	Arg	Ser	Lys	Asn	Gly
785					790					795					800
Asn	Arg	Val	Gln	Glu	Gly	Glu	Arg	Ile	Ala	Val	Asn	Thr	Pro	Ile	Gln
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Gly	Thr	Ala	Ala	Asp	Ile	Ile	Lys	Ile	Ala	Met	Ile	Asn	Ile	His	Asn
			820					825				830			
Arg	Leu	Lys	Lys	Glu	Asn	Leu	Arg	Ser	Lys	Met	Ile	Leu	Gln	Val	His
		835					840					845			
Asp	Glu	Leu	Val	Phe	Glu	Val	Pro	Asp	Asn	Glu	Leu	Glu	Ile	Val	Lys
		850				855					860				
Asp	Leu	Val	Arg	Asp	Glu	Met	Glu	Asn	Ala	Val	Lys	Leu	Asp	Val	Pro
865					870					875					880
Leu	Lys	Val	Asp	Val	Tyr	Tyr	Gly	Lys	Glu	Trp	Glu				
				885					890						

<210> 38
 <211> 893
 <212> PRT
 <213> Thermotoga maritima

<220>
 <223> Thermotoga maritima DNA polymerase (Tma)

<400> 38

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Tyr	Tyr	Ala	Leu	Asp	Arg	Ser	Leu	Ser	Thr	Ser	Thr	Gly	Ile	Pro	Thr
			20					25					30		
Asn	Ala	Thr	Tyr	Gly	Val	Ala	Arg	Met	Leu	Val	Arg	Phe	Ile	Lys	Asp
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His	Ile	Ile	Val	Gly	Lys	Asp	Tyr	Val	Ala	Val	Ala	Phe	Asp	Lys	Lys
	50					55					60				
Ala	Ala	Thr	Phe	Arg	His	Lys	Leu	Leu	Glu	Thr	Tyr	Lys	Ala	Gln	Arg
65					70					75					80
Pro	Lys	Thr	Pro	Asp	Leu	Leu	Ile	Gln	Gln	Leu	Pro	Tyr	Ile	Lys	Lys
				85					90					95	
Leu	Val	Glu	Ala	Leu	Gly	Met	Lys	Val	Leu	Glu	Val	Glu	Gly	Tyr	Glu
			100					105					110		
Ala	Asp	Asp	Ile	Ile	Ala	Thr	Leu	Ala	Val	Lys	Gly	Leu	Pro	Leu	Phe
		115					120					125			
Asp	Glu	Ile	Phe	Ile	Val	Thr	Gly	Asp	Lys	Asp	Met	Leu	Gln	Leu	Val
	130					135					140				
Asn	Glu	Lys	Ile	Lys	Val	Trp	Arg	Ile	Val	Lys	Gly	Ile	Ser	Asp	Leu
145					150					155					160
Glu	Leu	Tyr	Asp	Ala	Gln	Lys	Val	Lys	Glu	Lys	Tyr	Gly	Val	Glu	Pro

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Gln	Gln	Ile	Pro	165	Leu	Leu	Ala	Leu	170	Gly	Asp	Glu	Ile	175	Asp	Asn
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Glu	Lys	Tyr	Lys	195	Asp	Leu	Glu	200	Ile	Leu	Asn	His	Val	205	Arg	Glu
Pro	Gln	Lys	Val	210	Arg	Lys	Ala	215	Leu	Leu	Arg	Asp	Arg	220	Glu	Asn
225	Leu	Ser	Lys	230	Leu	Ala	Ile	235	Leu	Glu	Thr	Asn	Val	240	Pro	Ile
Asn	Trp	Glu	Glu	245	Leu	Arg	Tyr	250	Gln	Gly	Tyr	Asp	Arg	255	Glu	Lys
Pro	Leu	Leu	Lys	260	Glu	Leu	Glu	265	Phe	Ala	Ser	Ile	Met	270	Lys	Glu
Leu	Tyr	Glu	Glu	275	Ser	Glu	Pro	280	Val	Gly	Tyr	Arg	Ile	285	Val	Lys
Val	305	Glu	Phe	310	Glu	Lys	Ile	315	Leu	Arg	Glu	Ser	Pro	320	Ser	Phe
Ala	Ile	Asp	Leu	325	Glu	Thr	Ser	330	Leu	Asp	Pro	Phe	Asp	335	Cys	Asp
Val	Gly	Ile	Ser	340	Val	Ser	Phe	345	Lys	Pro	Lys	Glu	Ala	350	Tyr	Ile
Leu	His	His	Arg	355	Asn	Ala	Gln	360	Asn	Leu	Asp	Glu	Lys	365	Glu	Val
Lys	Leu	Lys	Glu	370	Ile	Leu	Glu	375	Asp	Pro	Gly	Ala	Lys	380	Ile	Val
Asn	Leu	Lys	Phe	385	Asp	Tyr	Lys	390	Val	Leu	Met	Val	Lys	395	Gly	Val
Val	Pro	Pro	Tyr	405	Phe	Asp	Thr	410	Met	Ile	Ala	Ala	Tyr	415	Leu	Leu
Asn	Glu	Lys	Lys	420	Phe	Asn	Leu	425	Asp	Leu	Ala	Leu	Lys	430	Phe	Leu
Tyr	Lys	Met	Thr	435	Ser	Tyr	Gln	440	Glu	Leu	Met	Ser	Phe	445	Ser	Phe
Phe	Gly	Phe	Ser	450	Phe	Ala	Asp	455	Val	Pro	Val	Glu	Lys	460	Ala	Ala
Ser	Cys	Glu	Asp	465	Ala	Asp	Ile	470	Thr	Tyr	Arg	Leu	Tyr	475	Lys	Thr
Leu	Lys	Leu	His	485	Glu	Ala	Asp	490	Leu	Glu	Asn	Val	Phe	495	Tyr	Lys
Met	Pro	Leu	Val	500	Asn	Val	Leu	505	Ala	Arg	Met	Glu	Leu	510	Asn	Gly
Val	Asp	Thr	Glu	515	Phe	Leu	Lys	520	Lys	Leu	Ser	Glu	Glu	525	Tyr	Gly
Leu	Glu	Glu	Leu	530	Ala	Glu	Glu	535	Ile	Tyr	Arg	Ile	Ala	540	Gly	Glu
Asn	Ile	Asn	Ser	545	Pro	Lys	Gln	550	Val	Ser	Arg	Ile	Leu	555	Phe	Glu
Gly	Ile	Lys	Pro	565	Arg	Gly	Lys	570	Thr	Thr	Lys	Thr	Gly	575	Asp	Tyr
Arg	Ile	Glu	Val	580	Leu	Glu	Glu	585	Ala	Gly	Glu	His	Glu	590	Ile	Ile
Leu	Ile	Leu	Glu	595	Tyr	Arg	Lys	600	Ile	Gln	Lys	Leu	Lys	605	Ser	Thr
Asp	Ala	Leu	Pro	610	Lys	Met	Val	615	Asn	Pro	Lys	Thr	Gly	620	Arg	Ile
Ser	Phe	Asn	Gln	625	Thr	Gly	Thr	630	Ala	Thr	Gly	Arg	Leu	635	Ser	Ser
Pro	Asn	Leu	Gln	645	Asn	Leu	Pro	650	Thr	Lys	Ser	Glu	Glu	655	Gly	Lys
Arg	Lys	Ala	Ile	660	Val	Pro	Gln	665	Asp	Pro	Asn	Trp	Trp	670	Ile	Val
Asp	Tyr	Ser	Gln	675	Ile	Glu	Leu	680	Arg	Ile	Leu	Ala	His	685	Leu	Ser
Glu	Asn	Leu	Leu	690	Arg	Ala	Phe	695	Glu	Glu	Gly	Ile	Asp	700	Val	His
Thr	Ala	Ser	Arg		Ile	Phe	Asn	Val	Lys	Pro	Glu	Glu	Val		Thr	Glu

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				725					730					735			
Thr	Pro	Tyr	Gly	Leu	Ser	Val	Arg	Leu	Gly	Val	Pro	Val	Lys	Glu	Ala		
			740					745					750				
Glu	Lys	Met	Ile	Val	Asn	Tyr	Phe	Val	Leu	Tyr	Pro	Lys	Val	Arg	Asp		
		755					760					765					
Tyr	Ile	Gln	Arg	Val	Val	Ser	Glu	Ala	Lys	Glu	Lys	Gly	Tyr	Val	Arg		
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Thr	Leu	Phe	Gly	Arg	Lys	Arg	Asp	Ile	Pro	Gln	Leu	Met	Ala	Arg	Asp		
	785				790					795					800		
Arg	Asn	Thr	Gln	Ala	Glu	Gly	Glu	Arg	Ile	Ala	Ile	Asn	Thr	Pro	Ile		
			805						810					815			
Gln	Gly	Thr	Ala	Ala	Asp	Ile	Ile	Lys	Leu	Ala	Met	Ile	Glu	Ile	Asp		
			820					825					830				
Arg	Glu	Leu	Lys	Glu	Arg	Lys	Met	Arg	Ser	Lys	Met	Ile	Ile	Gln	Val		
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His	Asp	Glu	Leu	Val	Phe	Glu	Val	Pro	Asn	Glu	Glu	Lys	Asp	Ala	Leu		
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Val	Glu	Leu	Val	Lys	Asp	Arg	Met	Thr	Asn	Val	Val	Lys	Leu	Ser	Val		
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			20					25					30				
Asn	Ala	Val	Tyr	Gly	Val	Ala	Arg	Met	Leu	Val	Lys	Phe	Ile	Lys	Glu		
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His	Ile	Ile	Pro	Glu	Lys	Asp	Tyr	Ala	Ala	Val	Ala	Phe	Asp	Lys	Lys		
	50					55					60						
Ala	Ala	Thr	Phe	Arg	His	Lys	Leu	Leu	Val	Ser	Asp	Lys	Ala	Gln	Arg		
	65				70					75				80			
Pro	Lys	Thr	Pro	Ala	Leu	Leu	Val	Gln	Gln	Leu	Pro	Tyr	Ile	Lys	Arg		
				85				90						95			
Leu	Ile	Glu	Ala	Leu	Gly	Phe	Lys	Val	Leu	Glu	Leu	Glu	Gly	Tyr	Glu		
		100						105					110				
Ala	Asp	Asp	Ile	Ile	Ala	Thr	Leu	Ala	Val	Arg	Ala	Ala	Arg	Phe	Leu		
		115					120					125					
Met	Arg	Phe	Ser	Leu	Ile	Thr	Gly	Asp	Lys	Asp	Met	Leu	Gln	Leu	Val		
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Asn	Glu	Lys	Ile	Lys	Val	Trp	Arg	Ile	Val	Lys	Gly	Ile	Ser	Asp	Leu		
	145				150					155					160		
Glu	Leu	Tyr	Asp	Ser	Lys	Lys	Val	Lys	Glu	Arg	Tyr	Gly	Val	Glu	Pro		
			165						170					175			
His	Gln	Ile	Pro	Asp	Leu	Leu	Ala	Leu	Thr	Gly	Asp	Asp	Ile	Asp	Asn		
			180					185					190				
Ile	Pro	Gly	Val	Thr	Gly	Ile	Gly	Glu	Lys	Thr	Ala	Val	Gln	Leu	Leu		
		195					200					205					
Gly	Lys	Tyr	Arg	Asn	Leu	Glu	Tyr	Ile	Leu	Glu	His	Ala	Arg	Glu	Leu		
	210					215					220						
Pro	Gln	Arg	Val	Arg	Lys	Ala	Leu	Leu	Arg	Asp	Arg	Glu	Val	Ala	Ile		
	225				230					235					240		
Leu	Ser	Lys	Lys	Leu	Ala	Thr	Leu	Val	Thr	Asn	Ala	Pro	Val	Glu	Val		
				245					250					255			
Asp	Trp	Glu	Glu	Met	Lys	Tyr	Arg	Gly	Tyr	Asp	Lys	Arg	Lys	Leu	Leu		
			260					265					270				

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Pro	Ile	Leu	Lys	Glu	Leu	Glu	Phe	Ala	Ser	Ile	Met	Lys	Glu	Leu	Gln
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Leu	Tyr	Glu	Glu	Ala	Glu	Pro	Thr	Gly	Tyr	Glu	Ile	Val	Lys	Asp	His
	290					295					300				
Lys	Thr	Phe	Glu	Asp	Leu	Ile	Glu	Lys	Leu	Lys	Glu	Val	Pro	Ser	Phe
305					310					315					320
Ala	Leu	Asp	Leu	Glu	Thr	Ser	Ser	Leu	Asp	Pro	Phe	Asn	Cys	Glu	Ile
				325					330					335	
Val	Gly	Ile	Ser	Val	Ser	Phe	Lys	Pro	Lys	Thr	Ala	Tyr	Tyr	Ile	Pro
			340					345					350		
Leu	His	His	Arg	Asn	Ala	His	Asn	Leu	Asp	Glu	Thr	Leu	Val	Leu	Ser
		355					360					365			
Lys	Leu	Lys	Glu	Ile	Leu	Glu	Asp	Pro	Ser	Ser	Lys	Ile	Val	Gly	Gln
	370					375					380				
Asn	Leu	Lys	Tyr	Asp	Tyr	Lys	Val	Leu	Met	Val	Lys	Gly	Ile	Ser	Pro
385					390					395					400
Val	Tyr	Pro	His	Phe	Asp	Thr	Met	Ile	Ala	Ala	Tyr	Leu	Leu	Glu	Pro
				405					410					415	
Asn	Glu	Lys	Lys	Phe	Asn	Leu	Glu	Asp	Leu	Ser	Leu	Lys	Phe	Leu	Gly
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Tyr	Lys	Met	Thr	Ser	Tyr	Gln	Glu	Leu	Met	Ser	Phe	Ser	Ser	Pro	Leu
		435					440					445			
Phe	Gly	Phe	Ser	Phe	Ala	Asp	Val	Pro	Val	Asp	Lys	Ala	Ala	Glu	Tyr
	450					455					460				
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465					470					475					480
Met	Lys	Leu	His	Glu	Ala	Glu	Leu	Glu	Asn	Val	Phe	Tyr	Arg	Ile	Glu
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			500					505					510		
Val	Asp	Thr	Glu	Phe	Leu	Lys	Lys	Leu	Ser	Glu	Glu	Tyr	Gly	Lys	Lys
		515					520					525			
Leu	Glu	Glu	Leu	Ala	Glu	Lys	Ile	Tyr	Gln	Ile	Ala	Gly	Glu	Pro	Phe
	530					535					540				
Asn	Ile	Asn	Ser	Pro	Lys	Gln	Val	Ser	Asn	Ile	Leu	Phe	Glu	Lys	Leu
545					550					555					560
Gly	Ile	Lys	Pro	Arg	Gly	Lys	Thr	Thr	Lys	Thr	Gly	Asp	Tyr	Ser	Thr
				565					570					575	
Arg	Ile	Glu	Val	Leu	Glu	Glu	Ile	Ala	Asn	Glu	His	Glu	Ile	Val	Pro
			580					585					590		
Leu	Ile	Leu	Glu	Phe	Arg	Lys	Ile	Leu	Lys	Leu	Lys	Ser	Thr	Tyr	Ile
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Ser	Phe	His	Gln	Thr	Gly	Thr	Ala	Thr	Gly	Arg	Leu	Ser	Ser	Ser	Asp
625					630					635					640
Pro	Asn	Leu	Gln	Asn	Leu	Pro	Thr	Lys	Ser	Glu	Glu	Gly	Lys	Glu	Ile
				645					650					655	
Arg	Lys	Ala	Ile	Val	Pro	Gln	Asp	Pro	Asp	Trp	Trp	Ile	Val	Ser	Ala
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Asp	Tyr	Ser	Gln	Ile	Glu	Leu	Arg	Ile	Leu	Ala	His	Leu	Ser	Gly	Asp
		675					680					685			
Glu	Asn	Leu	Val	Lys	Ala	Phe	Glu	Glu	Gly	Ile	Asp	Val	His	Thr	Leu
	690					695				700					
Thr	Ala	Ser	Arg	Ile	Tyr	Asn	Val	Lys	Pro	Glu	Glu	Val	Asn	Glu	Glu
705					710					715					720
Met	Arg	Arg	Val	Gly	Lys	Met	Val	Asn	Phe	Ser	Ile	Ile	Tyr	Gly	Val
				725					730					735	
Thr	Pro	Tyr	Gly	Leu	Ser	Val	Arg	Leu	Gly	Ile	Pro	Val	Lys	Glu	Ala
			740					745					750		
Glu	Lys	Met	Ile	Ile	Ser	Tyr	Phe	Thr	Leu	Tyr	Pro	Lys	Val	Arg	Ser
		755					760					765			
Tyr	Ile	Gln	Gln	Val	Val	Ala	Glu	Ala	Lys	Glu	Lys	Gly	Tyr	Val	Arg
	770					775					780				
Thr	Leu	Phe	Gly	Arg	Lys	Arg	Asp	Ile	Pro	Gln	Leu	Met	Ala	Arg	Asp
785					790					795					800
Lys	Asn	Thr	Gln	Ser	Glu	Gly	Glu	Arg	Ile	Ala	Ile	Asn	Thr	Pro	Ile
				805					810					815	

Gln	Gly	Thr	Ala	Ala	Asp	Ile	Ile	Lys	Leu	Ala	Met	Ile	Asp	Ile	Asp
			820					825					830		
Glu	Glu	Leu	Arg	Lys	Arg	Asn	Met	Lys	Ser	Arg	Met	Ile	Ile	Gln	Val
		835					840					845			
His	Asp	Glu	Leu	Val	Phe	Glu	Val	Pro	Asp	Glu	Glu	Lys	Glu	Glu	Leu
	850					855					860				
Val	Asp	Leu	Val	Lys	Asn	Lys	Met	Thr	Asn	Val	Val	Lys	Leu	Ser	Val
865					870					875					880
Pro	Leu	Glu	Val	Asp	Ile	Ser	Ile	Gly	Lys	Ser	Trp	Ser			
				885					890						

Ile 385	Glu 370	Leu	Arg	Gly	Val 390	Val 375	Phe	Asp	Leu	Leu 395	Leu 380	Ala	Ala	Tyr	Leu 400
Leu	Asp	Pro	Ala	Gln 405	Ala	Ala	Gly	Asp	Val 410	Ala	Ala	Val	Ala	Lys 415	Met
His	Gln	Tyr	Glu 420	Ala	Val	Arg	Ser	Asp 425	Glu	Ala	Val	Tyr	Gly 430	Lys	Gly
Ala	Lys	Arg	Thr	Val	Pro	Asp	Glu 440	Pro	Thr	Leu	Ala	Glu 445	His	Leu	Ala
Arg	Lys 450	Ala	Ala	Ala	Ile	Trp 455	Ala	Leu	Glu	Glu	Pro 460	Leu	Met	Asp	Glu
Leu 465	Arg	Arg	Asn	Glu	Gln 470	Asp	Arg	Leu	Leu	Thr 475	Glu	Leu	Glu	Gln	Pro 480
Leu	Ala	Gly	Ile	Leu 485	Ala	Asn	Met	Glu	Phe 490	Thr	Gly	Val	Lys	Val 495	Asp
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Ala	Val	Glu 515	Arg	Arg	Ile	Tyr	Glu 520	Leu	Ala	Gly	Gln	Glu 525	Phe	Asn	Ile
Asn	Ser 530	Pro	Lys	Gln	Leu	Gly 535	Thr	Val	Leu	Phe	Asp 540	Lys	Leu	Gln	Leu
Pro 545	Val	Leu	Lys	Lys	Thr 550	Lys	Thr	Gly	Tyr	Ser 555	Thr	Ser	Ala	Asp	Val 560
Leu	Glu	Lys	Leu	Ala 565	Pro	His	His	Glu	Ile 570	Val	Glu	His	Ile	Leu 575	His
Tyr	Arg	Gln	Leu 580	Gly	Lys	Leu	Gln	Ser 585	Thr	Tyr	Ile	Glu	Gly 590	Leu	Leu
Lys	Val	Val 595	His	Pro	Val	Thr	Gly 600	Lys	Val	His	Thr	Met 605	Phe	Asn	Gln
Ala	Leu 610	Thr	Gln	Thr	Gly	Arg 615	Leu	Ser	Ser	Val	Glu 620	Pro	Asn	Leu	Gln
Asn 625	Ile	Pro	Ile	Arg	Leu 630	Glu	Glu	Gly	Arg	Lys 635	Ile	Arg	Gln	Ala	Phe 640
Val	Pro	Ser	Glu	Pro 645	Asp	Trp	Leu	Ile	Phe 650	Ala	Ala	Asp	Tyr	Ser 655	Gln
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Glu	Ala	Phe 675	Arg	Arg	Gly	Leu	Asp 680	Ile	His	Thr	Lys	Thr 685	Ala	Met	Asp
Ile	Phe 690	His	Val	Ser	Glu	Glu 695	Asp	Val	Thr	Ala	Asn 700	Met	Arg	Arg	Gln
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Leu	Ala	Gln	Asn	Leu 725	Asn	Ile	Thr	Arg	Lys 730	Glu	Ala	Ala	Glu	Phe 735	Ile
Glu	Arg	Tyr	Phe 740	Ala	Ser	Phe	Pro	Gly 745	Val	Lys	Gln	Tyr	Met 750	Asp	Asn
Ile	Val	Gln 755	Glu	Ala	Lys	Gln	Lys 760	Gly	Tyr	Val	Thr	Thr 765	Leu	Leu	His
Arg	Arg 770	Arg	Tyr	Leu	Pro	Asp 775	Ile	Thr	Ser	Arg	Asn 780	Phe	Asn	Val	Arg
Ser 785	Phe	Ala	Glu	Arg	Thr 790	Ala	Met	Asn	Thr	Pro 795	Ile	Gln	Gly	Ser	Ala 800
Ala	Asp	Ile	Ile	Lys 805	Lys	Ala	Met	Ile	Asp 810	Leu	Ser	Val	Arg	Leu 815	Arg
Glu	Glu	Arg	Leu 820	Gln	Ala	Arg	Leu	Leu 825	Leu	Gln	Val	His	Asp 830	Glu	Leu
Ile	Leu	Glu 835	Ala	Pro	Lys	Glu	Glu 840	Ile	Glu	Arg	Leu	Cys 845	Arg	Leu	Val
Pro	Glu 850	Val	Met	Glu	Gln	Ala 855	Val	Ala	Leu	Arg	Val 860	Pro	Leu	Lys	Val
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Phe	Arg	His	Glu	Ala	Phe	Gln	Glu	Tyr	Lys	Gly	Gly	Arg	Gln	Gln	Thr
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Ile	Ile	Gly	Thr	Leu	Ala	Ala	Arg	Ala	Glu	Gln	Glu	Gly	Phe	Glu	Val
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Lys	Val	Ile	Ser	Gly	Asp	Arg	Asp	Leu	Thr	Gln	Leu	Ala	Ser	Pro	His
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				165					170					175	
Val	Asp	Leu	Lys	Gly	Leu	Met	Gly	Asp	Lys	Ser	Asp	Asn	Ile	Pro	Gly
			180					185					190		
Val	Pro	Gly	Ile	Gly	Glu	Lys	Thr	Ala	Val	Lys	Leu	Leu	Arg	Gln	Phe
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Gly	Thr	Val	Glu	Asn	Val	Leu	Ala	Ser	Ile	Asp	Glu	Ile	Lys	Gly	Glu
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Lys	Leu	Lys	Glu	Thr	Leu	Arg	Gln	His	Arg	Glu	Met	Ala	Leu	Leu	Ser
225					230					235				240	
Lys	Lys	Leu	Ala	Ala	Ile	Arg	Arg	Asp	Ala	Pro	Val	Glu	Leu	Ser	Leu
				245					250					255	
Asp	Asp	Ile	Ala	Tyr	Gln	Gly	Glu	Asp	Arg	Glu	Lys	Val	Val	Ala	Leu
			260					265					270		
Phe	Lys	Glu	Leu	Gly	Phe	Gln	Ser	Phe	Leu	Glu	Lys	Met	Glu	Ser	Pro
		275					280					285			
Ser	Ser	Glu	Glu	Glu	Lys	Pro	Leu	Ala	Lys	Met	Ala	Phe	Thr	Leu	Ala
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Asp	Arg	Val	Thr	Glu	Glu	Met	Leu	Ala	Asp	Lys	Ala	Ala	Leu	Val	Val
305					310					315				320	
Glu	Val	Val	Glu	Glu	Asn	Tyr	His	Asp	Ala	Pro	Ile	Val	Gly	Ile	Ala
				325					330					335	
Val	Val	Asn	Glu	His	Gly	Arg	Phe	Phe	Leu	Arg	Pro	Glu	Thr	Ala	Leu
			340					345					350		
Ala	Asp	Pro	Gln	Phe	Val	Ala	Trp	Leu	Gly	Asp	Glu	Thr	Lys	Lys	Lys
		355					360					365			
Ser	Met	Phe	Asp	Ser	Lys	Arg	Ala	Ala	Val	Ala	Leu	Lys	Trp	Lys	Gly
	370					375					380				
Ile	Glu	Leu	Cys	Gly	Val	Ser	Phe	Asp	Leu	Leu	Ala	Ala	Ala	Tyr	Leu
385					390					395					400
Leu	Asp	Pro	Ala	Gln	Gly	Val	Asp	Asp	Val	Ala	Ala	Ala	Ala	Lys	Met
				405					410					415	
Lys	Gln	Tyr	Glu	Ala	Val	Arg	Pro	Asp	Glu	Ala	Val	Tyr	Gly	Lys	Gly
			420					425					430		
Ala	Lys	Arg	Ala	Val	Pro	Asp	Glu	Pro	Val	Leu	Ala	Glu	His	Leu	Val
		435					440					445			
Arg	Lys	Ala	Ala	Ala	Ile	Trp	Ala	Leu	Glu	Arg	Pro	Phe	Leu	Asp	Glu
	450					455					460				
Leu	Arg	Arg	Asn	Glu	Gln	Asp	Arg	Leu	Leu	Val	Glu	Leu	Glu	Gln	Pro
465					470					475					480
Leu	Ser	Ser	Ile	Leu	Ala	Glu	Met	Glu	Phe	Ala	Gly	Val	Lys	Val	Asp
				485					490					495	

35

Thr	Lys	Arg	Leu	Glu	Gln	Met	Gly	Glu	Glu	Leu	Ala	Glu	Gln	Leu	Arg
			500					505					510		
Thr	Val	Glu	Gln	Arg	Ile	Tyr	Glu	Leu	Ala	Gly	Gln	Glu	Phe	Asn	Ile
		515					520					525			
Asn	Ser	Pro	Lys	Gln	Leu	Gly	Val	Ile	Leu	Phe	Glu	Lys	Leu	Gln	Leu
	530					535					540				
Pro	Val	Leu	Lys	Lys	Ser	Lys	Thr	Gly	Tyr	Ser	Thr	Ser	Ala	Asp	Val
	545				550					555					560
Leu	Glu	Lys	Leu	Ala	Pro	Tyr	His	Glu	Ile	Val	Glu	Asn	Ile	Leu	Gln
				565					570					575	
His	Tyr	Arg	Gln	Leu	Gly	Lys	Leu	Gln	Ser	Thr	Tyr	Ile	Glu	Gly	Leu
			580					585					590		
Leu	Lys	Val	Val	Arg	Pro	Asp	Thr	Lys	Lys	Val	His	Thr	Ile	Phe	Asn
		595					600					605			
Gln	Ala	Leu	Thr	Gln	Thr	Gly	Arg	Leu	Ser	Ser	Thr	Glu	Pro	Asn	Leu
	610					615					620				
Gln	Asn	Ile	Pro	Ile	Arg	Leu	Glu	Glu	Gly	Arg	Lys	Ile	Arg	Gln	Ala
	625				630					635					640
Phe	Val	Pro	Ser	Glu	Ser	Asp	Trp	Leu	Ile	Phe	Ala	Ala	Asp	Tyr	Ser
				645					650					655	
Gln	Ile	Glu	Leu	Arg	Val	Leu	Ala	His	Ile	Ala	Glu	Asp	Asp	Asn	Leu
			660					665					670		
Met	Glu	Ala	Phe	Arg	Arg	Asp	Leu	Asp	Ile	His	Thr	Lys	Thr	Ala	Met
		675					680					685			
Asp	Ile	Phe	Gln	Val	Ser	Glu	Asp	Glu	Val	Thr	Pro	Asn	Met	Arg	Arg
	690					695					700				
Gln	Ala	Lys	Ala	Val	Asn	Phe	Gly	Ile	Val	Tyr	Gly	Ile	Ser	Asp	Tyr
	705				710					715					720
Gly	Leu	Ala	Gln	Asn	Leu	Asn	Ile	Ser	Arg	Lys	Glu	Ala	Ala	Glu	Phe
				725					730					735	
Ile	Glu	Arg	Tyr	Phe	Glu	Ser	Phe	Pro	Gly	Val	Lys	Arg	Tyr	Met	Glu
			740					745					750		
Asn	Ile	Val	Gln	Glu	Ala	Lys	Gln	Lys	Gly	Tyr	Val	Thr	Thr	Leu	Leu
		755					760					765			
His	Arg	Arg	Arg	Tyr	Leu	Pro	Asp	Ile	Thr	Ser	Arg	Asn	Phe	Asn	Val
	770					775					780				
Arg	Ser	Phe	Ala	Glu	Arg	Met	Ala	Met	Asn	Thr	Pro	Ile	Gln	Gly	Ser
	785				790					795					800
Ala	Ala	Asp	Ile	Ile	Lys	Lys	Ala	Met	Ile	Asp	Leu	Asn	Ala	Arg	Leu
				805					810					815	
Lys	Glu	Glu	Arg	Leu	Gln	Ala	Arg	Leu	Leu	Leu	Gln	Val	His	Asp	Glu
			820					825					830		
Leu	Ile	Leu	Glu	Ala	Pro	Lys	Glu	Glu	Met	Glu	Arg	Leu	Cys	Arg	Leu
		835					840					845			
Val	Pro	Glu	Val	Met	Glu	Gln	Ala	Val	Thr	Leu	Arg	Val	Pro	Leu	Lys
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Val	Asp	Tyr	His	Tyr	Gly	Ser	Thr	Trp	Tyr	Asp	Ala	Lys			
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