

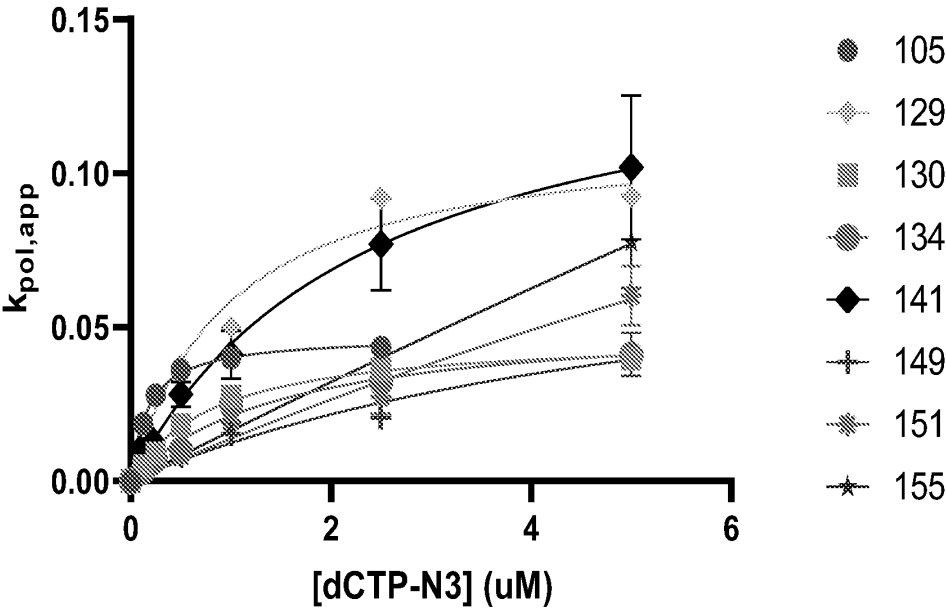


FIG. 1

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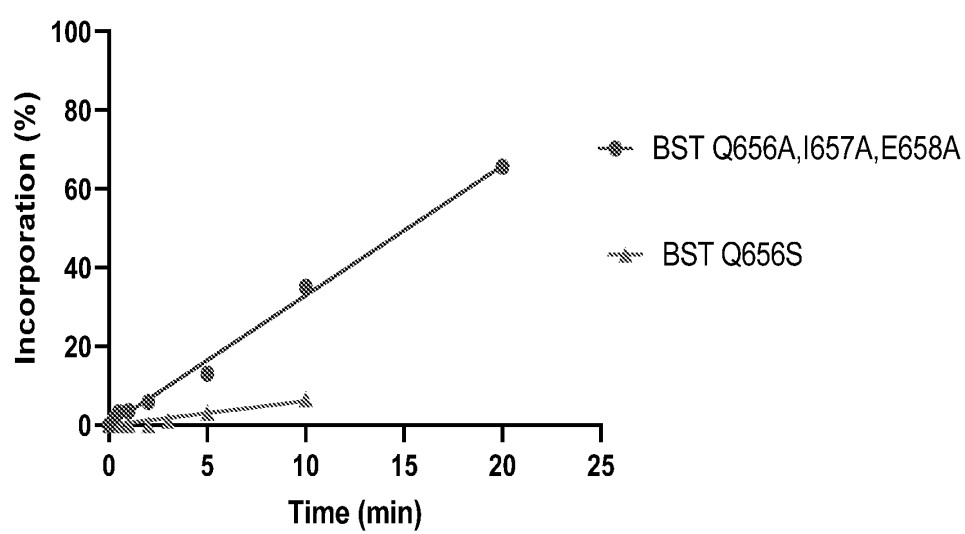


FIG. 2

Table 1:

SEQ ID NO:	Mutation(s) relative to SEQ ID NO:1	Incorp'n
1	Wild Type	0
2	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_M142L	++
3	L416A_Y417S_P418S	+
4	Y502I	0
5	L416T_Y417G_P418A	0
6	L416S_Y417A_P418G_I529H_A493S_S443N	+
7	L416S_Y417A_P418G_I529H_A493S_Q492A_L496S	+
8	L416S_Y417A_P418G_I529H_A493S_L496N	+
9	Y417G_P418G_Y502V	+
10	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_I63T	++
11	S415A	+
12	L416G_Y417T_P418S_I529H	+
13	S415A_P418G	0
14	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_D305N_E328Q	+
15	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_E434R	+
16	Y417A_P418G	+
17	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_I343V	++
18	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_M501I_N705D	++
19	L416G_Y417G	+
20	L416S_Y417A_P418G_I529H_A493S_R515L_S577I	+
21	L416V_Y417G_P418A	+

FIG. 3A

Table 1 (continued):

SEQ ID NO:	Mutation(s) relative to SEQ ID NO:1	Incorp'n
22	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_M501V	++
23	A493V_K495A_N499A	0
24	L416A_P418S	+
25	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_R509H_D560G	++
26	L416A_Y417G_P418S_I529H	+
27	L416S_Y417A_P418G_I529H_A493S	+
28	Y417G_P418G	0
29	L416S_Y417A_P418G_I529H_K473A_L496A	0
30	L416T_Y417G_P418A_I529H	+
31	L416S_Y417A_P418G_I529H_A493S_R515L_L611S	+
32	L416S_Y417A_P418G_I529H_Q492R	+
33	Y417A_P418A	0
34	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_M41L	++
35	S415V_L416S	0
36	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_G96S	++
37	L416A_Y417G_P418G_I529H	+
38	L416S_Y417A_P418G_I529H_A493S_R697G	+
39	L416A_Y417A_P418A	+
40	Y417V_P418G_Y502G	+
41	L416S_Y417A_P418G	+
42	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_D636G	++

FIG. 3B

Table 1 (continued):

SEQ ID NO:	Mutation(s) relative to SEQ ID NO:1	Incorp'n
43	L416V_P418G	0
44	S415G_Y417S	0
45	L416G_Y417A	+
46	A493V_K495G_N499A	0
47	L416S_Y417A_P418G_I529H_A493S_R515L_N567D_C104S	+
48	L416I_Y417A_P418G_I529F	+
49	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_I272V	+
50	L416V_Y417A_P418S	+
51	L416S_Y417A_P418G_I529H_Q492R_P335Q	+
52	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_Y448H_F507S_Y502F_V564I_M565V_E578N	++
53	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_R483H_K574R	++
54	L416S_Y417A_P418G_I529H_A493S_L496C	+
55	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_M501I	++
56	S415G_P418A	0
57	S415G_Y417V	0
58	L416V_Y417A_P418S_I529H	+
59	Y417G_P418C	+
60	Y502A	0
61	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_R467C_E581G_T618A	++
62	L416S_Y417A_P418G_I529H_A493S_Q492C_L496R	+
63	L416S_Y417A_P418G_I529H_A493S_L496H	+

FIG. 3C

Table 1 (continued):

SEQ ID NO:	Mutation(s) relative to SEQ ID NO:1	Incorp'n
64	L416S_Y417A_P418G_I529H_A493S_R515P	+
65	L416F_Y417A_P418A_A493S_I529H_R515L_N567D_E516G	++
66	L416A_Y417A_P418S_I529H	+
67	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_S520G	++
68	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_T344I	++
69	H405P_A493V_K495G_N499A	0
70	L416V_Y417G_P418G_I529H	+
71	L416S_Y417A_P418G_I529H_A493S_R515L_N567D_C514S	+
72	I529H	+
73	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_M41L	++
74	Y417A_P418S	0
75	L416V_P418S	0
76	Y10F_E14K_H48R_D75N_C104V_A115V_C130V_L416F_Y417A_P418G_R515L_I529H_N567D_E680D_N705D_T522S	+
77	Y417S_P418V_Y502R	0
78	S415V_P418V	0
79	L416S_Y417A_P418G_I529H_R608K_A493S	+
80	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_M501I_V789A	++
81	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_I63V_E77G_Q87H	++
82	R414S	0
83	A493V_K495Q_N499G	0
84	A493V_K495V_N499A	0

FIG. 3D

Table 1 (continued):

SEQ ID NO:	Mutation(s) relative to SEQ ID NO:1	Incorp'n
85	L416F_Y417A_P418G_A493S_I529H_R515L_N567D	++
86	L416S_Y417A_P418G_A493S_I529H_K610E	+
87	A493V_K495S_N499V	0
88	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_E14G_I68V	++
89	L416M_Y417A_P418G_A493S_I529H_R515L_N567D	+
90	S415G_L416V	0
91	L416S_Y417A_P418G_I529H_A493S_R515L_N567D_E179R	+
92	L416S_Y417A_P418G_I529H_A493S_Q492G	+
93	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_I343V	++
94	Y417G_P418V	0
95	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_N480I_T618A	++
96	Y417G_P418A	0
97	L416S_Y417A_P418G_I529H_R608K	+
98	S415V_Y417S	+
99	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_P45S_K58R	++
100	L416S_Y417A_P418G_I529H_A493S_R515L_N567D_C269S	+
101	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_A498G	++
102	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_D573N	++

FIG. 3E

Table 1 (continued):

SEQ ID NO:	Mutation(s) relative to SEQ ID NO:1	Incorp'n
103	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_M501I_N705D	++
104	I529G	0
105	L416S_Y417A_P418G_I529H_A493S_Q492T_L496S	+
106	Y417G_P418S	+
107	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_E205K_K225E	++
108	S415G_L416S	0
109	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_M501I_G763S	+
110	L416L_Y417Y_P418P_I529H	0
111	Y417S_P418A	+
112	Y502Q	0
113	L416S_Y417A_P418G_I529H_V489I_Q492R	0
114	C104V_C130V_C269V_L416F_Y417A_P418G_A493S_R515L_I529H_N567D_M768*	+
115	L416V_Y417V_P418A	+
116	Y417G_P418A_Y502N	+
117	E14K_H48R_D75N_C104V_A115V_C130V_D141A_E143A_C269V_F369I_N385S_L416S_Y417A_P418G_A493S_M501I_R515L_I529H_N567D_N705D	++
118	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_S500G	++
119	L416S_Y417A_P418G_I529H_A493S_Q492R	0
120	A493V_K495S_N499G	0
121	L416S_Y417A_P418G_I529H_K473A	+
122	L416V_Y417T_P418I	0

FIG. 3F

Table 1 (continued):

SEQ ID NO:	Mutation(s) relative to SEQ ID NO:1	Incorp'n
123	L416S_Y417A_P418G_I529H_A493S_R515L_N567D_C450S	+
124	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_A115V	+
125	S415V_P418S	0
126	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_V239I_R256H	++
127	S415A_L416S	0
128	L416I_Y417A_P418A_I529L	+
129	Y10F_E14K_H48R_D75N_C104V_A115V_C130V_D141A_E143A_L416F_Y417A_P418G_R515L_I529H_N567D_E680D_N705D	++
130	L416A_Y417A_P418A_I529H	+
131	L416S_Y417A_P418G_I529H_K473A_Q492R	+
132	L416S_Y417A_P418G_I529H_A493S_G355S_S440N_R515L	+
133	L416V_Y417A_P418A	+
134	A493V_K495V_N499G	0
135	L416S_Y417A_P418G_I529H_A493S_L496R	+
136	L416S_Y417A_P418G_I529H_A493S_R515L_N567D_E730R	+
137	L416S_Y417A_P418G_I529H_A493S_E760G	+
138	L416V_Y417A_P418G_I529T	+
139	L416I_Y417A_P418A	+
140	L416S_Y417G_P418G_I529H	+
141	Y417V_P418A	0
142	S415A_Y417G	+
143	L416V_Y417T_P418S_I529H	+
144	S415G_P418G	0

FIG. 3G

Table 1 (continued):

SEQ ID NO:	Mutation(s) relative to SEQ ID NO:1	Incorp'n
145	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_D9N	++
146	A493V_K495G_N499S	0
147	L416S_Y417A_P418G_I529H_A493S_L496I	+
148	S415V_Y417A	0
149	L416S_P418G	+
150	L416S	+
151	L416S_Y417A_P418G_I529H_A493S_L496Y	+
152	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_E116G	++
153	S415G_L416A	0
154	L416V_Y417A_P418G_I529S	+
155	Y502S	0
156	Y417S_P418S	+
157	S415V_Y417A_A493V_K495G_N499S	0

FIG. 3H

Table 2:

SEQ ID NO:	Mutation(s) relative to SEQ ID NO:1	Incorp'n
158	L416A_P418A	+
159	A493V_K495S_N499G_F507S	0
160	L416S_Y417A_P418G_I529H_A493S_R515Y	+
161	L416S_Y417A_P418G_I529H_A493S_R515L_N567D_E308R	+
162	L416S_Y417A_P418G_I529H_A493S_L496S	+
163	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_A568V	+
164	L416S_Y417A_P418G_I529H_A493S_R515L	+
165	R468G	0
166	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_H48R	+
167	S415G	0
168	L416S_Y417A_P418G_I529H_A493S_Q492G_L496I	+
169	L416S_Y417T_P418G_I529H_A493S_R515L_N567D	+
170	Y417T_P418K	0
171	L416S_Y417A_P418G_I529H_D622T	+
172	L416S_Y417A_P418G_I529H_A493S_L496G	+
173	L416V_Y417G_P418G	+
174	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_M84L	++
175	L416V_Y417G_P418A_I529H	+
176	Y417S_P418G_Y502S	0
177	L416T_Y417A_P418A	+
178	L416I_Y417S_P418S	+

FIG. 4A

Table 2 (continued):

SEQ ID NO:	Mutation(s) relative to SEQ ID NO:1	Incorp'n
179	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_D191G	+
180	L416S_Y417A_P418G_I529H_A493S_R515L_N567D_E291R	+
181	L416S_Y417A_P418G_I529H_Q673I	+
182	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_Q54L_P126S	++
183	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_G474D	++
184	L416S_Y417A_P418G_I529H_A493S_L494V_L496N	+
185	I529S	0
186	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_F539Y	++
187	A493V_K495G_N499V	0
188	L416S_Y417A_P418G_I529H_A493S_R515L_N567D_E434R	+
189	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_K762R_G763V_L764W_G765A_K766S_Q767K_M768*	++
190	L416G_P418A	0
191	L416I_Y417A_P418S	+
192	L416S_Y417A_P418G_I529H_A493S_S443N_Q492F	+
193	L416A	+
194	L416S_Y417A_P418G_A493S_I529H_K58M	+
195	L416S_Y417A_P418G_I529H_L496A	+
196	L416S_Y417A_P418G_I529H_V489I	+

FIG. 4B

Table 2 (continued):

SEQ ID NO:	Mutation(s) relative to SEQ ID NO:1	Incorp'n
197	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_M501I_N705D	++
198	L416A_Y417A_P418I	0
199	L416S_Y417A_P418G_I529H_A493S_D653G_A669D_S717G_I750V	+
200	L416V_Y417G_P418S_I529H	+
201	L416S_Y417A_P418G_I529H_A493S_R515F	+
202	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_K51R	++
203	A493V_K495G_N499G_M501I	0
204	Y502P	0
205	L416S_Y417A_P418G_I529H_A493S_V651M	+
206	Y417V_P418S	0
207	L416Y_Y417A_P418G_A493S_I529H_R515L_N567D	++
208	Y10F_E14K_H48R_D75N_C104V_A115V_C130V_L416Y_Y417A_P418P_R515L_I529H_N567D_E680D_N705D_T522S	++
209	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_M501I_M41L	+
210	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_R509H_S520N_M583K	0
211	L416G_P418G	0
212	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_M501I	++
213	L416S_Y417A_P418G_I529H_A493S_D381Y	+
214	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_D75N	+
215	L416S_Y417A_P418G_I529H_V489I_A493S	+
216	Y417V_P418V_Y502S	0

FIG. 4C

Table 2 (continued):

SEQ ID NO:	Mutation(s) relative to SEQ ID NO:1	Incorp'n
217	R468H	0
218	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_E116G	++
219	L416A_Y417A_P418V	0
220	L416S_Y417A_P418G_I529H_A493S_R515L_N567D_E27R	+
221	L416S_Y417A_P418G_I529H_A493S_L496A	+
222	L416S_Y417A_P418G_I529H_A493S_Q492L_L496M	0
223	A493V_K495S_N499G	0
224	L416S_Y417A_P418G_I529H_A493S_R515L_N567D_C130S	+
225	L416S_Y417A_P418G_I529H_A493S_R515L_N567D	+
226	Y417V_P418A_Y502R	0
227	L416S_Y417A_P418G_I529F	+
228	L416S_Y417A_P418G_I529H_R515L	+
229	R468V	0
230	L416S_Y417A_P418G_I529H_A493S_D622T	+
231	S415A_Y417A	+
232	A493V_K495V_N499S	0
233	L416I_Y417A_P418S_I529H	+
234	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_E308R	++
235	L416F_Y417A_P418G_A493S_M501I_R515L_I529H_N567D_N657D_E700K_N705S	+
236	L416S_Y417A_P418G_I529H_A493S_R515L_N567D_C517S	+

FIG. 4D

Table 2 (continued):

SEQ ID NO:	Mutation(s) relative to SEQ ID NO:1	Incorp'n
237	H405P_A493V_K495V_N499A	0
238	L416I_Y417G_P418A_I529L	+
239	L416S_Y417A_P418G_I529H_A493S_R515L_N567D_E102R	+
240	L416S_Y417A_P418T_I529H	+
241	Y502G	0
242	L416V_Y417V_P418G	+
243	R468A	0
244	L416A_Y417A_P418G	+
245	S415G_P418S	0
246	L416S_Y417A_P418G_I529H_Q492R_Q673I	+
247	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_I11F_K105R	++
248	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_K61E	+
249	Y417A_P418S_Y502R	+
250	L416I_Y417A_P418G	+
251	Y10F_E14K_H48R_D75N_C104V_A115V_C130V_L416F_Y417A_P418P_R515L_I529H_N567D_E680D_N705D_T522S	++
252	L416F_Y417A_P418P_A493S_I529H_R515L_N567D_F507S	++
253	L416S_Y417A_P418G_I529H_A493S_R515L_N567D_E310R	+
254	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_E14K	+
255	A493V_K495G_N499G	0

FIG. 4E

Table 3:

SEQ ID NO:	Mutation(s) relative to SEQ ID NO:1	Incorp'n
288	L416A_P418G	+
289	L416S_Y417A_P418G_A493S_I529H_E569G	+
290	L416S_Y417A_P418G_I529H_A493S_R515L_N567D_C130R	+
291	L416S_Y417A_P418G_I529H_A493S_R515L_S717G	+
292	L416S_Y417G	+
293	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_K58M	++
294	L416F_Y417A_P418A_A493S_I529H_R515L_N567D_S500G	++
295	A493V_K495Q_N499G_F507S	0
296	G403A_H405S_D406H	0
297	L416S_Y417A_P418G_I529H	+
298	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_M501I_S717N_S746C	+
299	A493V_K495A_N499G	0
300	Y502H	0
301	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_N132S	++
302	L416A_Y417S_P418A	+
303	L416I_Y417I_P418V	0
304	S415V_L416V	0
305	Y417S_P418G	+
306	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_A568V	+
307	L416V	+
308	L416S_P418V	0
309	S415V_P418G	0

FIG. 5A

Table 3 (continued):

SEQ ID NO:	Mutation(s) relative to SEQ ID NO:1	Incorp'n
310	H48R_D75N_A115V_L416F_Y417A_P418G_A493S_M501I_R515L_I529H_N567D_N705D	+
311	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_M501I_E434R	++
312	Y502F	0
313	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_D488N_G474S	++
314	L416A_Y417G_P418A	+
315	L416S_Y417A_P418G_I529H_A493S_R723H	+
316	S415G_P418V	0
317	A493V_K495S_N499S	0
318	Y502V	0
319	E14K_H48R_D75N_C104V_K105R_A115V_D129N_C130V_D141A_E143A_C269V_F369I_N385S_L416F_Y417A_P418G_A493S_M501I_R515L_I529H_N567D_N705D	+
320	L416S_Y417A_P418G_I529H_R608K_Q492R	0
321	L416S_Y417A_P418G_I529H_R515L_Q492R	+
322	L416S_Y417A_P418G_I529H_A493S_R515L_N567D_E758R	+
323	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_Q767*	+
324	L416S_Y417A_P418G_I529H_R515L_Q673I	+
325	R468K	0
326	L416S_Y417A_P418G_I529H_L496A_V489I	+
327	L416S_Y417A_P418G_I529H_L496A_A493S_Q492R	+

FIG. 5B

Table 3 (continued):

SEQ ID NO:	Mutation(s) relative to SEQ ID NO:1	Incorp'n
328	L416S_Y417A_P418G_I529H_V489I_R515L	+
329	L416A_Y417A_P418S	+
330	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_V465M	++
331	L416S_Y417G_P418A	+
332	A493V_K495Q_N499A	0
333	E14K_H48R_D75N_C104V_A115V_D129N_C130V_D141A_E143A_C269V_F369I_N385S_L416F_Y417A_P418G_A493S_M501I_R515L_I529H_N567D_N705D	+
334	S415V	0
335	L416F_Y417A_P418G_I529H_A493S_R515L_N567D_E434R	+
336	L416S_Y417A_P418G_I529H_A493S_R515W	+
337	L416S_Y417G_P418V_I529H	+
338	L416S_Y417G_P418V	0
339	S415G_L416G	0
340	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_L50P	++
341	Y417G_P418A_Y502G	0
342	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_M501I_T675A_K682I_N705D	+
343	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_E73K	++
344	L416S_Y417G_P418G	0
345	L416I_Y417S_P418G_I529H	+
346	L416A_Y417G_P418A_I529H	+
347	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_V107I	++

FIG. 5C

Table 3 (continued):

SEQ ID NO:	Mutation(s) relative to SEQ ID NO:1	Incorp'n
348	L416A_Y417A_P418A_I529L	+
349	L416S_Y417A_P418G_I529H_A493S_E370D	+
350	L416S_Y417A_P418G_I529H_R608K_L496A	0
351	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_R170H	++
352	L416S_Y417A_P418G_I529H_A493S_S717G	+
353	L416V_Y417A_P418A_I529H	+
354	L416A_Y417A_P418G_I529H_A493S_R515L_N567D	+
355	Y10F_E14K_H48R_D75N_C104V_A115V_C130V_L416F_Y417G_P418P_R515L_I529H_N567D_E680D_N705D_T522S	++
356	R468S	0
357	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_K538R	++
358	A493V_K495S_N499A_Y502T	0
359	A493V_K495Q_N499V	0
360	L416T_Y417A_P418G_I529H	+
361	L416A_Y417S	+
362	L416V_Y417A_P418G_I529H	+
363	L416S_Y417A_P418G_I529H_A493S_L496S_D439S	+
364	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_E14K_H48R_D75N_A115V_M501I	+
365	L416V_Y417A_P418G	+
366	D141A_E143A_L416F_Y417A_P418G_A493S_R515L_I529H_N567D	+
367	I529A	0
368	L416I_Y417S_P418G	+
369	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_A115V	+

FIG. 5D

Table 3 (continued):

SEQ ID NO:	Mutation(s) relative to SEQ ID NO:1	Incorp'n
370	L416A_Y417S_P418G	+
371	L416S_Y417A_P418G_I529H_A493S_Q492G_L496A	+
372	L416I_Y417G_P418A	+
373	L416A_Y417I_P418T	0
374	L416S_Y417A	+
375	L416T_Y417A_P418A_I529H	+
385	Y417V_P418V	0
386	L416S_Y417A_P418G_I529H_K473A_R515L	0
387	Y417A_P418V	0
388	L416G_Y417G_P418G	0
389	I529V	0
390	L416S_Y417A_P418G_I529H_L496A_A493S_V489I	+
394	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_E14K_H48R_D75N_A115V_M501I_N705D	++
395	L416S_Y417A_P418G_I529H_L496A_R515L	0
396	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_L124Q_F37S_E14G	++
397	L416F_Y417A_P418G_A493S_I529H_R515L_N567D_D560E	++

FIG. 5E

Table 4:

Candidatus Altiarchaeales archaeon DNA Polymerase	9 ^o N Polymerase	Vent DNA Polymerase	Deep Vent DNA Polymerase	Geobacillus stearothermoph ilus DNA Polymerase I	Pfu Polymerase	Pyrococcus abyssi Polymerase
Y10	Y7	Y7	Y7	G10	Y7	Y7
E14	N11	D11	D11	R16	E11	D11
H48	D45	S46	D49	E49	S46	D49
K58	T55	K61	K61	D59	K61	K61
D75	Q72	G77 ins R78	G77 ins R78	G76 ins R77	G77 ins K78	G77 ins R78
V91	V93	V93	V93	---	V93	V93
C104	V106	V106	V106	A97	V106	V106
A115	A117	A117	A117	Y108	A117	A117
C130	D132	D132	D132	Q123	E150	N132
C269	I264	V266	I264	S240	I264	I264
R296	Y291	G293	Y291	G277	Y291	Y291
D305	E300	E302	E300	A286	E300	E300
E328	E321	E323	E321	L318	E321	E321
P335	P328	P330	P328	E325	P328	P328
G355	S348	S350	S348	G342	S348	S348
R359	L352	L354	L352	R343	L352	L352
E370	K363	A365	E363	E349	E363	E363
D381	E374	E376	E374	A359	E374	E374
G403	G395	G398	G396	G384	G396	G396
H405	W397	W400	W398	E386	W398	W398
D406	D398	E401	E399	L387	E399	E399
R414	R406	R409	R407	L394	R407	R407
S415	S407	S410	S408	L395	S408	S408
L416	L408	L411	L409	L396	L409	L409
Y417	Y409	Y412	Y410	A397	Y410	Y410
P418	P410	P413	P411	A398	P411	P411
D439	Y431	Y434	Y432	E420	Y432	Y432
S440	D432	D435	D433	A421	D433	D433
S443	P435	P438	P436	S424	P436	P436
C450	C442	C445	C443	K431	C443	C443

FIG. 6A

Table 4 (continued):

Candidatus Altiarchaeales archaeon DNA Polymerase	9°N Polymerase	Vent DNA Polymerase	Deep Vent DNA Polymerase	Geobacillus stearothermoph ilus DNA Polymerase I	Pfu Polymerase	Pyrococcus abyssi Polymerase
R468	R460	R463	R461	K450	R461	R461
K473	R465	K468	R466	W455	T466	K466
V489	Y481	Y484	Y482	K476	Y482	Y482
Q492	R484	R487	R485	Q479	K485	R485
A493	A485	A488	A486	P480	A486	A486
L494	I486	I489	I487	L481	I487	I487
K495	K487	K490	K488	A482	K488	K488
L496	I488	L491	I489	A483	L489	I489
N499	N491	N494	N492	A486	N492	N492
M501	F493	I496	I494	M488	F494	Y494
Y502	Y494	Y1035	Y1032	E489	Y495	Y495
F507	Y499	Y1040	Y1037	V493	Y500	Y500
C514	C506	S1047	C1044	G504	C507	C507
R515	K507	K1048	K1045	S505	K508	K508
C517	C509	C1050	C1047	L507	C510	C510
I529	I521	I1062	I1059	N527	I522	I522
N567	K559	K1490	K1097	N573	K560	K559
A568	A560	A1491	A1098	I574	A561	A560
E569	K561	K1492	L1099	L575	L562	L561
S577	P569	S1500	A1107	S585	S570	S569
R608	E600	E1531	E1138	E632	E601	E600
K610	K602	R1533	K1140	R634	K603	K602
L611	I603	I1534	I1141	K635	V604	I603
D622	D614	D1545	D1152	D647	D615	D614
V651	V643	V1574	V1181	I689	V644	V643
D653	E645	D1576	E1183	H691	E646	E645
A669	V661	V1592	V1199	A707	A662	V661
Q673	Q665	Q1596	Q1203	G711	Q666	Q665

FIG. 6B

Table 4 (continued):

Candidatus Altiarchaeales archaeon DNA Polymerase	9°N Polymerase	Vent DNA Polymerase	Deep Vent DNA Polymerase	Geobacillus stearothermoph ilus DNA Polymerase I	Pfu Polymerase	Pyrococcus abyssi Polymerase
E680	D672	D1604	E1210	D718	E673	E672
R697	R689	R1620	R1227	P744	K690	K689
S717	R709	K1640	P1247	Y772	P710	P709
R723	I715	I1646	I1253	S799	I716	I715
I750	I744	I1675	I1282	V828	I745	I744
E760	D754	D1685	D1292	E840	D755	D754
N705	T697	T1628	M1235	N752	M698	M697
K762	R756	R1687	R1294	E842	R757	K756
G763	G764	Q1689	G1302	R843	G765	Q758
L764	L765	S1690	L1303	L844	L766	K759
G765	G766	S1691	T1304	C845	T767	T760
K766	A767	K1692	A1305	E846	S768	K761
Q767	W768	Q1693	W1306	P861	W769	Q762
M768	L4769	T1694	L1307	L862	L770	V763

FIG. 6C

FIG. 7A

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Candid__WT	VIRNIKTGKIPLKDLAINTQITRGMAEYKTEGPHIVAACKAMKRGLEFKQGNIVTYVVTK
90N	VTEKLSKYEVPPEKLVIEHQITRDLRDYKATGPHVAVAKRLAARGVKIRPGTVISYIVLK
	* :... ::* :.*,*: *****: ;**; ***:..... **::: . *,:::*,* *
Candid__WT	KGKSISDKARVIDFVEEGD--YDPDYINNQLPSVLRILEALGYSEDELK-----GL
90N	GSGRIGDRAIPADEFDPTKHYDAEYYIENQVLP AVERILKAFGYRKEDLRYQKTKQVGL
	. *,*,* * ,: . **:***:*****;* ***,*;** :::*. **
Candid__WT	GKQMKLGGF--
90N	GAWLKVKGKK
	* .,*: *

FIG. 7B

FIG. 8A

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Candid_WT	-----
Vent	RLKKYKQLYEKLAGSVKYNGNKREYLVMFNEIKDFISYFPQKELEEWKIGTLNGFRTNCI
Candid_WT	-----
Vent	LKVEDDFGKLLGYVYVSEGYAGAQNKTGGISYSVKLYNEDPNVLES MNVAEKFFGKVRV
Candid_WT	-----
Vent	DRNCVSI SKKMAYLV MKCLCGALAENKRIPSVILTSPEPV RWSFLEAYFTGDGDHPSKR
Candid_WT	-----
Vent	FRLSTKSELLANQLVFLLSNLGSISSVKIGFD SGVYRVYINEDLQFPQTSREKNTYYSNLI
Candid_WT	-----
Vent	PKEILRDVFGKEFQKNMTFKKFELVDSGKLNREKAKLLEFFINGDIVLDRVKSVEKDY
Candid_WT	-----YGYFGFPRARWYCRECAESITALGRKYILHTI
Vent	EGYVYDLSVEDNENFLVGFGLLYAHNSYGYMGYPKARWYSKECAESVTAWGRHYIEMTI ***:*.*.***.***.***:*.***:*.***
Candid_WT	-DIVPKFGFDVIYGD-----
Vent	REIEEKFGFKVLYADSVSGESEIIIRQNGKIRFVKIKDLFSKVDYSIGEKEYCILEGVEA :* ****.:.*.*
Candid_WT	-----TDSVY-----
Vent	LTLD DDGKLVWKPVYPYVMRHRANKRMFRIWLTNSWYIDVTEDHSLIGYLN TSKTKTAKKI *: * *
Candid_WT	-----LIKPN-----
Vent	GERLKEVKPFELGKAVKSLICPNAPLKDENTKTSEIAVKFWELVGLIVGDGNWGGDSRWA ** **
Candid_WT	-----
Vent	EYYLGLSTGKDABEIKQKLEPLKTYGVISNYYPKNEKGDFNILAKSLVKFMKRHFKDEK
Candid_WT	-----
Vent	GRRKIPEFMYELPVTYIEAFLRGLFSADGTVTIRKGVPEIRLTNIDADFLREVRKLLWIV
Candid_WT	-----ITDRER-----
Vent	GISNSIFAETTPNRYNGVSTGTYSKHLRIKNKWRFAERIGFLIERKQKRLLEHLKSARVK : :*:.
Candid_WT	-----
Vent	RNTIDFGFDLVHVKKVEEIPYEGYVDIEVEETHRFFANNILVHNTDGFYATIPGEKPEL

FIG. 8B

Candid_WT	VMKNAEHFLDKINSELPEAMELEFEGFYPRGIFITKKRYALIDERGKLIVKGLETKRPDW
Vent	IKKKAKEFLNYINSKLPGLLELEYEGFYLRGGFFVTKKRYAVIDEGRITTRGLEVRVDW : *:* : ** : ***:** :***:*** ***:*****:*** *: : .****. ***
Candid_WT	ANIAKDTQEKVLDALLKDKNPEKAASIVKDVIRNIKTGKIPLKDLAINTQITRGMAEYKT
Vent	SEIAKETQAKVLEAILKEGSVEKAVEVVRDVEKIAKYRVPLEKLVIIHEQITRDLKDYKA :;***:** ***:*.**: . ****.,*,** : * . .:*.:.*: :****.: ;**:
Candid_WT	EGPHIVAANKAMKRGLEFKQGNIIVTYVVTTKKGKSISDKARVIDFE--EGDYDPDYINN
Vent	IGPHVAIAKRLAARGIKVKPGTIISYIVLKGSGKISDRVILITEYDPRKHXYDFDYIEN ***:. **. **:.* *.*:;* * . .***. : : : .*****:*
Candid_WT	QVLPSVLRILEALGYSEDELK-GLGKQMKGGF---
Vent	QVLPAVLRILEAFGYRKEDLRYQSSKQTGLDAWLKR *****:*****:* :*: ** *

FIG. 8C

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Candid_WT M K K T L L D A D Y I T R E E K A V V R L F Y K T E E G R E I Q E V A D F R P Y M Y V L P E E - - - - H D L K K L - -
Deep - - - M I L D A D Y I T E D G K P I I R I F K K E N G E F K V E Y D R N F R P Y I Y A L L K D D S Q I D E V R K I T A
: * * * * * : * . : : * * : : : : * * * : * . * : : : : * :

Candid_WT Q R E I K E L K N I T N V E I K R M I E G D R E V E V L K V M V N Q P R D V P N L R G L I K E L E G C K E V R E A H I P
Deep E R H G K I V R I I D A E K V R K K F L G - R P I E V W R L Y F E H P Q D V P A I R D K I R E H S A V I D I F E Y D I P
: * * : . * : . . : * * : * : : . : * . * * : * . * . * . : : * * *

Candid_WT F A E R Y L I D S G L I P M Q D C E N F D L R I A A F D M E V Y N P R G E P K A E R D P I I I S Y A D N R G L R R V W
Deep F A K R Y L I D K G L I P M E G D E - - E L K L L A F D I E T L Y H E G E E F A - K G P I I M I S Y A D E E E - A K V I
* : * * * * . * * * * : . * : * * : * . * * * . * * * . * * * : * * * : * * *

Candid_WT T Y K T V E N L N D Y M E V L K D E R E I I R R F I D T I R E R E I D I I V T Y N G D N F D F P Y L K E R A E K H R I
Deep T W K K I D - - - L P Y V E V S S E R E M I K R F L K V I R E K D P V I I T Y N G D S F D L P Y L V K R A E K L G I
* : * . : : * * : * * : . * * : * * : . * * : : * * : * * * : * * : * * * : * * * : * * *

Candid_WT P V S L G V D G S P L R L E R R G M N L G A R V T G R P H I D M Y P V C R Q I F N L S R Y T L E D V Y L E I T G R E K K
Deep K L P L G R D G S E P K M Q R L G D M T A V E I K G R I H F D L Y H V I R R T I N L P T Y T L E A V Y E A I F G K P K E
: . * * * * : . : * * : . . : . * * : * : * * * . : * * . * * * * * * * . * :

Candid_WT D I R V G E M A G I W D N P E K E K F K E L I E Y A M S D A E S T L E I A I T L L P L H Y E I S R I T R E L I Y Q S S R
Deep K V Y A H E I A E A W E T - - G K G L E R V A K Y S M E D A K V T Y E L G R E F F P M E A Q L S R L V G Q P L W D V S R
: . : * * * : . : : : * * : * * : * * . : * : : * * : : * * : : : * *

Candid_WT A G S G Q R V E S L L I K K A F E K S I L V P N R P S D R V V N E R Q R K T Y I G A Y V V E P K R G I H D N I L L F D F
Deep S S T G N L V E W Y L L R K A Y E R N E L A P N K P D E R E Y E R R L R E S Y A G G Y V K E P K G L W E G L V S L D F
: . : * : * * : . * * : . . * . * * : * : * : * * : * * : * * : * * : * * : * * : * * :

Candid_WT R S L Y P S I I I S H N I D P S T I D C E C C P E D S Y R S P T G H Y F C K K K R G L I P E T L N E L V Q R R I E V K K
Deep R S L Y P S I I I T H N V S P D T L N R E G C R E Y D V A P E V G H K F C K D F P G F I P S L L K R L L D E R Q E I K R
* * * * * : * : . * : : * * * . . . * * * * . * : * * . * : * : * * : *

Candid_WT G L K N E K N P E R R R F L D V K Q Q A L K L L A N S M - - - - -
Deep K M K A S K D P I E K K M L D Y R Q R A I K I L A N S I L P E E W V P L I K N G K V K I F R I G D F V D G L M K A N Q G
: * . * : * : . : * * . * . : * * * :

Candid_WT - - - - -
Deep K V K K T G D T E V L E V A G I H A F S F D R K S K K A R V M A V K A V I R H R Y S G N V Y R I V L N S G R K I T I T E

Candid_WT - - - - -
Deep G H S L F V Y R N G D L V E A T G E D V K I G D L L A V P R S V N L P E K R E R L N I V E L L N L S P E E T E D I I L

Candid_WT - - - - -
Deep T I P V K G R K N F F K G M L R T L R W I F G E E K R V R T A S R Y L R H L E N L G Y I R L R K I G Y D I I D K E G L E

FIG. 9A

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Candid_WT	-----
Deep	KYRTLYEKLVDVVRNGNKR EYLVEFNVRDVISLMP EELKEWRIGTRNGFRMGTFVDI
Candid_WT	-----
Deep	DEDFAKLLGYYVSEGSARKWKNQTGGWSYTVRLYNENDEVLDDMEHLAKKFFGKVKRGKN
Candid_WT	-----
Deep	YVEIPKKMAYIIFESLCGTLAENKRVPEVIFTSSKGVRWAFLEGYFIGDGDVHFPSKRVRL
Candid_WT	-----
Deep	STKSELLVNGLVLLLSLGVSAIKLGYDSGVYRVYVNEELKFTEYRKKKNVYHSHIVPKD
Candid_WT	-----
Deep	ILKETFGKV FQKNISYKKFREL VENGKLDREKAKRIEWLLNGDIVLDRVVEIKREYYDGY
Candid_WT	-----YGYFGFP RARWYCRECAESITALGK KYI-LHTIDI
Deep	VYDLSVDE DENFLAGFGFLYAHNSY YGYGYAKARWYCKECAESVTAWGREYIEFVRKEL ***:*.:.*****.*****:** **:* : ::
Candid_WT	VPKFGFDVIYGD TDSVYLKPNITDRE RVMKNAEHFLDKINSELPEAMELEFEGFYPRGI
Deep	EEKFGFKVLYI DTDGLYATIPG-AKPEE IKKKALEFVDYINAKLPGLLELEYEGFYVRGF ****.*:* **.*:* * . :. * : *:* *:* **:* ** :***:**** **:
Candid_WT	FITKKRYALID ERGKLIVKGLETKR RDWANIADTQEKVLDALLKDKNPEKAASIVKDVI
Deep	FVTRKKRYAL IDEEGKIITRGLEIVRR DWSEIAKETQAKVLEAILKHGNVEEAVKIVKEVT *:***.***** **:*.*** ****:***:** **:*:** * *:*.***:*
Candid_WT	RNIKTGKIPLKDLAINTQITRGMAEYKTEGPHIVA AKKAMKRGLEFKQGNIVTVVTKKG
Deep	EKLSKYEIPPEK LVIYEQITRPLHEYKAIGPHVAVAKRLAARGVKVRPGMVIGYIVLRGD :.. :** :.*.* **** : ***: ***:..** . **:.. * : : *:* . .
Candid_WT	KSISDKARVIDFVE--EGDYDPDYYINNQVLPSVLRILEALGYSEDELK-----GLGK
Deep	GPISKRAILAE EFDLRKKHYDAEYYIENQVLP AVLRILEAFGYRKEDLRWQKTKQTGLTA .*..* : : .: : .**:*:**:*****:*****:** :*: . **
Candid_WT	QMKLGGF
Deep	WLNKKK .:::

FIG. 9B

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Candid WT	MKKTLLDADYITREEKAVVRL-FYKTEEGREIQEVADFRPYMYVLPEEHDLLKKLQREIK
Geobacillus	MKKKLVLIDGNSVAYRAFFALPLLHNDKGIHTNAVYGFMMMLNKILAEQPTHLLVAFD ***.*: * : .*. * : :.* : * . * : : * : .:* :.
Candid WT	ELKNITNVEIKRMIEGDREVEVLKVMVNQPRDVPNLRGLIKELEGCKEVREAHIPFAERY
Geobacillus	AGKTTFRHETFQEQYKGGRRQ-----QTPPELSEQFPLLRELLKAYRIPAYELDHYEAD * . . * . :*. *: : * :.: *.** . : : . *
Candid WT	LIDSGLIIPMQDCENFDLRIAADFMEVYNPRGEPKAERDPIIIISYADNRGLRRVWYTKTV
Geobacillus	DIIGTLAARAEQEGFEVKIIS-----GDRDLTQLAS-----RHVTV * . * . : *.**.: * : :.*** : * : : **
Candid WT	ENLNLDYMEVLKDEREIIIRRFIDTIREREIDIIVTYNGDNFDFPYLKERAEKHRIPV--S
Geobacillus	DITKKGITDIEPYTPETVREKYGLTPEQIVDLKGLMGDKSDNIPGVPGIGEXTAVKLLKQ : : . : : * : * . * . :*: : . . . :*: : .** : : .
Candid WT	LGVDGSPLRL--ERRGMNLGARVTGRPHIDMYPVCRQIFNLSR-----YTLEDVYLEITG
Geobacillus	FGTVENVLASIDEVKGEKLEKLN--RQHRDLALLSKQLASICRDAPVELSLDDIVYEQD :*. . * * * . * : * : * * : :.*** : .** :*: : * .
Candid WT	REK-----KDIRVGEMAGIWDNP--EKEKFKELEYAMSD-----AESTLEIAITLLP
Geobacillus	REKVIALFKELGFQSFLEKMAAPAAEGEKPLEEMFAIVDVITEEMLADKAALVVEVMEE *** *: . . : * * * * :*: : * :*: : . . :
Candid WT	LHYEISRITRELIYQSSRAGSGQRVESLLIKKAFKESILVPNRPSDRVVNERQKRKYIGA
Geobacillus	NYHDAPIVGIALVNEHGR-----FFMRP---ETALADSQFLAWLADETKKSMFDA : : . : * : : . * : : . : : * . . . :*: :*: :. *
Candid WT	--YVVEPK-RGIHDNILLFDFRSLYPSIIISHNIDPSTID--CECCPEDSYRSPGTGHYFC
Geobacillus	KRAVVALKWKGIELRGVAFDL--LLAAYLLNPAQDAGDIAAVAKMKQYEA VRSD EAVY GK * * * . * * . : **: * : :. * . * . : : * * . *
Candid WT	KKKRGLIPE-TLNELVQRRIEVKKGLKNE-----KNPERRRFLDVKQQALKLLANSMYGY
Geobacillus	GVRKSLPDEQTLAEHLVRKAAAIWALEQPFMDLLENNEQDQLLTKEQPLAAILAEM-EF **.* * * * : * . . .*: : * * . . : * . * : . * :
Candid WT	FGF-----PRRWYCRECAESITAL-----GRKYILHTIDIVPKFGFD----VIYGDT
Geobacillus	TGVNVDTKRLEQMGSELAEQLRAIEQRIYELAGQEFNINSPKQLGVILFEKLQLPVLKKT * . . * . * **.: *: * : :. : : : : : : * : : *
Candid WT	DSVYLIKPNITDR-----ERVMMKNAEHF--LDKINSELPEAM-----ELEFEGFYPRGI
Geobacillus	KTGYSTSADVLEKLAPHHEIVENILHYRQLGKLQSTYIEGLLKVVPRPDTGKVHTMFNQAL . : * . : : . : : * * : *.**:* * . : : . : : . :
Candid WT	FITKK-----RYALIDERGKLIVKGLETKRRDWANIAKD-----TQEK
Geobacillus	TQTGRLSSAEPNLQNIPIRLEEGRKIRQAFVPSEPDWLI FAADYSQIELRVLAHIADDDN * . . . : * * . * : : . . ** : * * : : :

FIG. 10A

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```
Candid_WT      VLDALLKDKN-PEKAASIVKDVIRNIKTGKIPLKDLAINTQITRGMAEY-----KT
Geobacillus    LIEAFQRDLDIHTKTAMDIFHVSEEEVTANMRRQAKAVNFGIVYGISDYGLAQNINITRK
                :::*:. * :   ** :  * :  *:: :  ** * . *::* ..

Candid_WT      EGP HIVA AKKAMKRGLEFKQGNIVT-----YVVT--KKGKSISD-----
Geobacillus    EAAEFIERYFASFPGVKQYMENIVQEAQKG YVTLLHRRRYLPDITSRNFNVR SFAERT
                *.. ::  *  *::  ***  **,*  :. . :.*

Candid_WT      -----KARVIDFVEEGDYDPDYINNQVLPS---VLRILEA---LGYSEDELKGLGK-----
Geobacillus    AMNTPIQGSAAADI IKKAMIDL AARLKEEQ LQARLLLQVHDELILEAPKEEIERLC ELVPE
                :. . *:::. *  ::: * :  :*. :  *  .::*: * :

Candid_WT      -----QMKLGGF-----
Geobacillus    VMEQAVTLRVPLKVDYHYGPTWYDAK
                :*:. .
```

FIG. 10B

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Candid_WT Pfu	MKKTLLDADYITREEKAVVRLFYKTEEGREIQEVADFRPYMY--VLPEEHDLLKKLQREIK ---MILDVDYITEEGKPVIRLFKKENGKFKIEHDRTFRPYIYALLRDDSKIIEVKKITG : ** . ***** * * . : * * * * * : : * : : * * * * * : * * : : : : : .
Candid_WT Pfu	E----LKNITNVE- IKRMIEGDREVEVLKVMVNQPRDVPNLRGLIKELEGCKEVREAHIP ERHGKIVRIVDVEKVEKKFLG-KPITVWKLYLEHPQDVPTIREKVVREHFAVVDI FEYDIP * : . * . : * * : : * . : * * : : * . * * * . : * : * . : * * *
Candid_WT Pfu	FAERYLIDSGLIPMQDCENFDLRIAAFDMEVYNPRGEPKAERDPIIIISYADNRGLRRVW FAKRYLIDKGLIPMEGEE--ELKILAFDIETLYHEGE--EFGKGPIIMISYADENE-AKVI * : * * * * * . * * * * * : * * * * * : * * : * * * * * : * * * * * : *
Candid_WT Pfu	TYKTVENLNDYMEVLKDEREIIIRRFIDTIREREIDIIIVTYNGDNFDFPYLKEPRAEKHRI TWK----NIDL PYVEVVSSEPEMIKRLRIIREKDPDIIVTYNGDSFDFPYLAKRAEKLGI * : * * * : * * : * * : * * : * * : * * : * * : * * : * * : * * : * * : *
Candid_WT Pfu	PVSLGVDGSPRLRLERRGMNLGARVTGRPHIDMYPVCRQIFNLSRYTLEDVYLEITGREKK KLTIGRDGSEPKMQRIGDMTAVEVKGRIHFDLYHVITRTINLPTYTLEAVYEAIFGKPKKE : : * * * * . : : * * * . . * . * * * : * * * * . : * * . * * * * * * * . : *
Candid_WT Pfu	DIRVGEMAGIWDNPEKEKFKELIEYAMSDAESTLEIAITLLPLHYEISRITRELIYQSSR KVYADEIAKAWES--GENLERVAKYSMEDAKATYELGKEFLPMEIQLSRLVGGQPLWDVSR : . : * * * * : . : * * * : : * * : * * : * * : * * : * * : * * : * * *
Candid_WT Pfu	AGSGQRVESLLIKKAPEKSILVFNRPSPDRVVNERQKTYIGAYVVEPKRGIHDNILLFDF SSTGNLVEWFLLRKAYERNEVAPNKPSEEEYQRRRLRESYTGGFVKEPEKGLWENIVYLDLF : : * : * * : * : * * * : . : * * : * * : * * : * * : * * : * * : * * *
Candid_WT Pfu	RSLYPSIIISHNIDPSTIDCECCPEDSYRSPTGHYFCKKKRGLIPETLNELVQRRIEVKK RALYPSIIITHNVSPDTLNLEGCNKYDIAPQVGHKFKCDIPGFIPSLGLHLLERQRIKT * : * * * * * : * * : * * : * * : * * : * * : * * : * * : * * : * * *
Candid_WT Pfu	GLKNEKNPERRRFLDVKQQAALKLLANSMYGYFGFPRARWYCRECAESITALGRKYI--LHT KMKETQDPIEKILLDYRQKAIKLLANSFYGYGYAKARWYCKECAESVTAWGRKYIELVW : * : : * * . : * * . * : * * * * * : * * : * * : * * : * * : * * : * *
Candid_WT Pfu	IDIVPKFGFDVIYGDTSVYLIKPNITDRERVMKNAEHFLDKINSELPEAMELEFEGFYF KELEEKFGFKVLYIDTDGLYATIPG-GESEI KKKALEFVKYINSKLPGLLELEYEGFYK : : * * * * : * * * * : * * : * * : * * : * * : * * : * * : * * : * * *
Candid_WT Pfu	RGIFITKKRYALIDERGKLI VKGLETKRRDWANIAKDTQEKVLDALLKDKNPEKAASIVK RGFFVTKKRYAVIDEKGKLVITRGLIVRRDWSEIAKETQARVLETILKHGDVEEAVRIVK * : * : * * * * * * * * * * * * * * * * * * : * * : * * : * * : * * *

FIG. 11A

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Candid_WT	DVIRNIKTGKIPLKDLAINTQITRGMAEYKTEGPHIVAACKAMKRGLEFKQGNIVTYVVT
Pfu	EVIQKLANYEIPPEKLAIYEQITRPLHEYKAIGPHVAVAKKLAAGVKIKPGMVIGYIVL
	;**::: . : ** : ,*** ***** ; ***; ***:..*** .*:::* * :; *;* *
Candid_WT	KKGKSISDKARVIDEVE--EGDYDPDYYINNQVLPVLRILEALGYSEDELK-----G
Pfu	RGDGPISNRAILAEEDPKKKHYDAEYYIENQVLPVLRILEGFGYRKEDLRYQKTRQVG
	. . .***.* : : : : .**::***;*****;*****;*** :::*. *
Candid_WT	LGKQMKLGGF
Pfu	LTSWLNKKS
	* .:::

FIG. 11B

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Candid_WT	MKKTLLDADYITREEKAVVRLFYKTEEGREIQEVADFRPYMYVLPPE-----HDLKKLQR
Pyroc_abyssi	---MIIDADYITEDGKPIIRIFKKEKGEFKVEYDRTERFYIYALLKDDSAIDEVKKITA :***** :*:::* * : : : : *****:* : : : : :
Candid_WT	EIK-ELKNITNVE-IKRMIEGDREVEVLKVMVNQPRDVPNLRGLIKELEGCKEVR EAHIP
Pyroc_abyssi	ERHGKIVRITEVEKVQKKFLG-RPIEVWKLYLEHPQDVPAPREKIREHPAVVDIFEYDIP * : : : .*:.* : : : * * ;* * : : :*.*** :* *.* . : : * **
Candid_WT	FAERYLIDSGLIPMQDCENFDLRIAAFDMEVYNPRGEPKAERDPIIIISYADNRGLRRVW
Pyroc_abyssi	FAKRYLIDKGLTPMEGNE--ELTFLAVDIETLYHEGE--EFGKGPIIMISYADEEG-AKVI **;*****.* **;. * : * : *.**.* ** : ..***;*****: * ,*
Candid_WT	TYKTVENLNLDYMEVLKDEREIIIRRFIDTIREREIDIIIVTYNGDNFDFPYLKERA EKHRI
Pyroc_abyssi	TWKSID----LPYVEVVSSEPEMIKRLVKVIREKDPVITTYNGDNFDFPYLLKRAEKLGI *::*: : * *;***.***:*.*::,***. : *::*****;**** *
Candid_WT	PVSLGVDGSPLRLERRGMNLGARVTGRPHIDMYPVCRQIFNLSRYTLEDVYLEITGREKK
Pyroc_abyssi	KLPLGRDNSEPKMQRMGDSLAVEIKGRIHFDLFPVIRRTINLPTYTLEAVYEAIFGKSKE :.** *.* :*: * *. . :.* *;*:** *. :*. **** * * * *,*:
Candid_WT	DIRVGEMAGIWDNPEKEKFKELIEYAMSDAESTLEIAITLLPLHYEISRITRELIYQSSR
Pyroc_abyssi	KVYAHEIAEAWET--GKGLERVAKYSMEDAKVTFELGKEFFPMEAQLARLVGQPVWDVSR .: . *:* *:. : : : *:*.*: *:. : : : : : : : : : *
Candid_WT	AGSGQRVESLLIKKAFEKSILVFNRPSPDRVVNERQRKTYIGAYVVEPKRGIHDNILLDFD
Pyroc_abyssi	SSTGNLVEWFLLRKAYERNELAPNKPDEREYERRLRESYEGGYVKEPEKGLWEGIVSLDF :.*: * * :*:.***:. *.*.*:* : * *:* * *.* ** :*:. : : : : *
Candid_WT	RSLYPSIIISHNIDPSTIDCECCPEDSYRSPTGHYFCKKKRGLIPETLNELVQRRIEVKK
Pyroc_abyssi	RSLYPSIIITHNVSPDTLNRENCKEYDVAPQVGRFCKDFPGFIPSLGNLLEERQRIKK *****;*:*.*: : * * * . . .** ***. *;*. *. : : : * :*:*
Candid_WT	GLKNEKNPERRRFLDVKQQAALKLLANSMYGYFGFPRARWYCRECAESITALGRKYILHTI
Pyroc_abyssi	RMKESKDFVEKKLLDYRQRAIKILANSYYGYGYAKARWYCKECAESVTAWGRQYIDLVR :*:.*: * ..*: * .*:*:**** **:*:..*****.*****;* **;* *
Candid_WT	DIVPKFGFDVIYGDTSVYLIKPNITDRERVMKNAEHFLDKINSELPEAMELEFEGFYPR
Pyroc_abyssi	RELESRGFKVLYIDTDGLYATIPG-AKHEEIKKALKFVEYINSKLPGLLELEYEGFYAR : . **.*:* ****;* * . . . * : : : * : : : ****;* :****;***.*
Candid_WT	GIFITKKRYALIDERGKLIVKGLETKRRDWANIAKDTQEKVLDALLKDKNPEKAASIVKD
Pyroc_abyssi	GFFVTKKRYALIDEEGKIVTRGLEIVRRDWSEIAKETQAKVLEAILKHGNVDEAVKIVKE *;*.*.*.***** **;..** * : : : * : : : * : : : * : : : * : : : *

FIG. 12A

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Candid_WT	VIRNIKTGKIPLKDLAINTQITRGMAEYKTEGPHIVAACKAMKRGLEPKQGNIVTYVVTK
Pyroc_abyssi	VTEKLSKYEIPPEKLVIEQITRPLSEYKAIGPHVAVAKRLAAKGVKVPGMVIGYIVLR
	* :... : ** : . * * * * : : * * * : * * : * : : . * * : : * : * .
Candid_WT	KGKSISDKARVIDFVE--EGDYDPDYINNQVLPVLRILEALGYSEDELK-GLGKQMKL
Pyroc_abyssi	GDGPISKRAIAIEEFDPKKHKYDAEYYIENQVLPAPERILRAFGYRKEDLKYQKTKQVGL
	. . * * . . * . * : . : : . * * . : * * : * * * * : * * * * * * * : * * : * * : *
Candid_WT	GGF---
Pyroc_abyssi	GAWLKE
	* . :

FIG. 12B

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```
Candid_WT      MKKTLLDADYITREEKAVVRLF--YKTEEGREIQEVADFRPYMYVL-PEEHDLKKLQRE
RB69            -----MKEFYLTVEQIGDSIFERYIDSNGRERTREVEYKPSLFAHCPESQATKYF---
                  ::      *:      :* *      ,;***      .:. * :.  **.:  * :

Candid_WT      IKELKNITNVEIKRMIEGDREVEVLKVMVNQPRDVNLRGLIKELEGCKEVREAHIPFAE
RB69            -----DIYGKPCTR-----KLFANMRDASQWIKRMEDIGLEALGMDDFKLAYLSDTY
                  :* .      .*      :. :      * : .. : .. :      * * .:. * :. :

Candid_WT      RYLIDSGLIPMQDCENFDLRIAADFMEVYNPRG--EPKAERDFIIIIISYADN-----
RB69            NYEI-----KYDHTKIRVANFDIEVTS PDGFPEPSQAKHPIDAITHYDSIDDRFYVF
                  ,* *      . :. :;*:* **;* ,* *      **.      . ** * : : * ,

Candid_WT      -----RGLRRVWYKTVENL-----NLDYMEVLKDEREIIIRRFIDTIRER
RB69            DLLNSPYGNVEEWSIEIAAKLQEQGGDEVPSEIIDKIIYMP-FDNEKELLMEYLNFWQQK
                  *      *: : . :*      : : **      :. :*. : : : : :. :.

Candid_WT      EIDIIVTYNGDNFDFPYLKERAE-----KHRIPVSLGVDGSPRLRERRGM
RB69            TPVILTGWNVESFDIPYVYVNRKINIFGESTAKRLSPHRKTRVKVIENMYGSREIITLFGI
                  * :. :* :. **:* : : * :      * * : * . : ** : * :

Candid_WT      NLGARVTGRPHIDMYPVCRQIFNLSRYTLEDVYLEITGREKKDIRVGEMAGIWDNP----
RB69            SV-----LDYIDLYKKF-SFTNQPSYSLDYI-----SEFELNVGKLK--YDGPISKL
                  . :      : **:*      . : * . * : : :      . : :. :. :. : * ,*

Candid_WT      EKEKFKELEIYAMSDAESTLEIAI--TLLPLHYEI--SRITRELIYQSSRAGSGQRVES
RB69            RESNHQRYISYNIIDVYRVLIQIDAKRQFINLSLDMGYAKIQISVFSPIKT----WDA
                  :. :. : * ,* : * , . : *      : : * : : : . : * : :. :. : :

Candid_WT      LLIKKAFEKSI LVPNRPSDRVVNERQRKTYIGAYVVEPKRGIHDNILLDFRSLYPSIII
RB69            IIFNSLKEQNKVIPQGRSHPV-----QPYPGAFVKEPIPNRYKYVMSFDLTSLYPSIIR
                  : : :. : * :. : : : * *      : ,* **:* * * . :. : : ** : *****

Candid_WT      SHNIDPSTI-----DCECCPEDSYR-SPTGHYFCKKKRGLIPETLNLVQR
RB69            QVNISPETIAGTFKVAPLHDYINAVAERP SDVYSCSPNGMMYYKDRDGVVPTEITKVFNQ
                  . ** ,* ,**      * ,* *      **,* : * ,. * : : * : : :. :.

Candid_WT      RIE-----VKKGLKN-----EKNPERRRFLDVK-----
RB69            RKEHKGMYLAAQRNGEIIKEALHNP NLSVDEPLDVYRFDSD EIKEIKKLSAKSLNEM
                  * *      : * ,. : * :      : : * . . * ,*

Candid_WT      -----QQALKLLANS MYGYFGFPRARWYCRECAESITALGRKYILHTIDIV
RB69            LFRAQRTEVAGMTAQINRKLINSLYGALGNVWFRYYDLRNATAITTFGQMALQWIERKV
                  *      *** **:* : * . * : *      * : * : : * . : .      *

Candid_WT      PKF----GFD---VIYGD TDSVYLIKPNITDR--ERVMKNAEHFLDKINSELPEAMEL
RB69            NEYLNEVCGTEGEAFVLYGPTDSIYVSADKIIDKVGESKFRDTNHWVDFLDKFAREPMEP
                  : :      * :      * : ***** : :      : * * . * : : : : : * :.      * **
```

FIG 13A

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Candid_WT	EFE-GFYPR-----GIFITKKRYAL--IDERG----
RB69	AIDRGFREMCEYMNNKQHLMFMDREALAGPPLGSKGIGGFWTGKKRYALNVWDMEGTRYA
	:: ** *:: ***** * *
Candid_WT	--KLIVKGLETKRRDWANIAKDTQEKVLDALLKDKNPEKAASIVKDVIRNIKTGKIPLKD
RB69	EPKLKIMGLETQKSSTPKAVQKALKECIRRLQEGEES-----LQEYFKEFEKEFRQLNY
	** : ****;. . .: .: : : : *:: : . ::: :. .: *
Candid_WT	LAIN-T-QITRGMAEYKTEG-----PHIVAACKAMKRGLEFKQ---GNIVTYVVTK
RB69	ISIASVSSANNIAKYDVGGFPKPCPFHIRGILTYNRAIKGNIDAPQVVEGEKVYVLPRL
	::* : . :.:.*:*,. * *:: :.:* *:: * *:: * : .
Candid_WT	KGKSISDKA-----RVIDFVEEGDYDPDYINNQVL--PSVLRIEALGYSED-ELKG
RB69	EGNPFQDKCIAWPSGTEITDLIKD----DVLHWMDYTVLLEKTFIKPLEGFTSAAKLDYEK
	:*:.*.**. : *::: * :::: ** :.:. **. : . : :
Candid_WT	LGKQMKLGGF
RB69	KASLFDMFDF
	. . :. : *

FIG. 13B

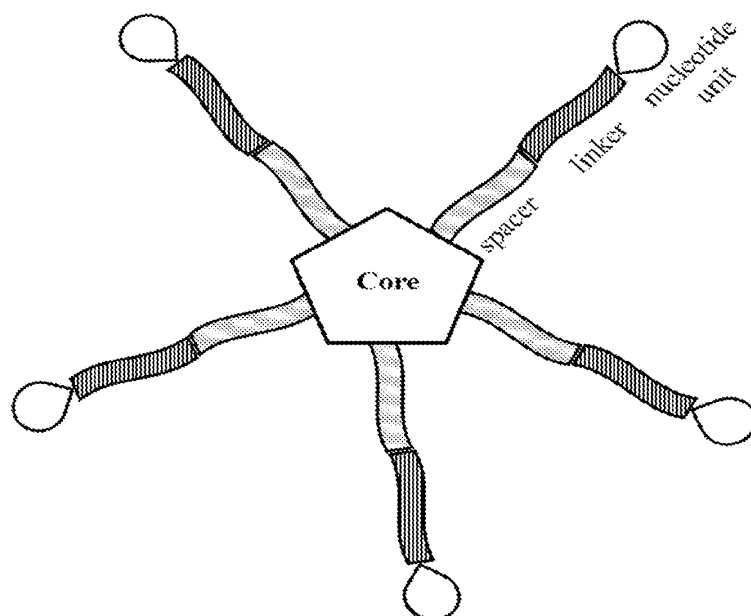


FIG. 14A

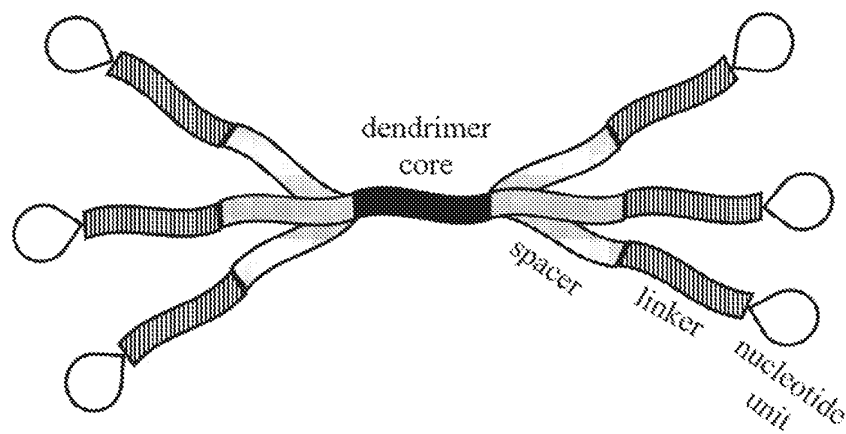


FIG. 14B

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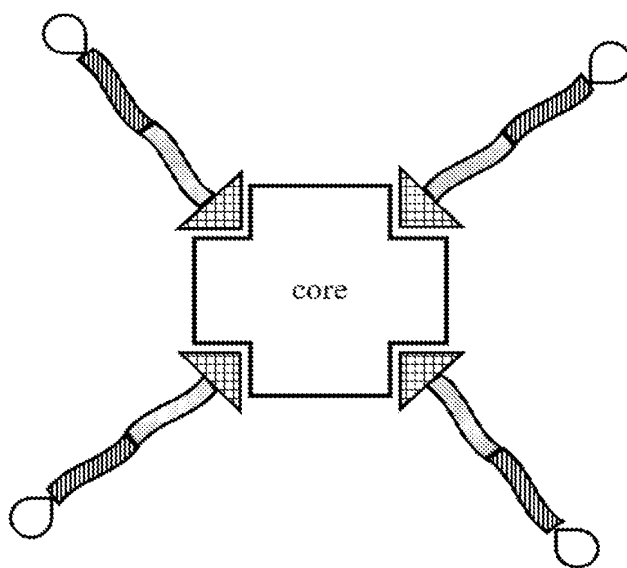


FIG. 15A

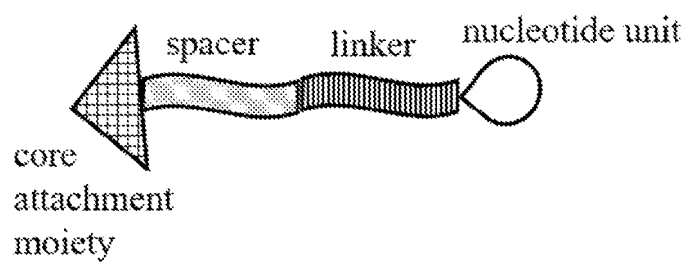
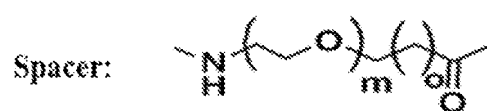


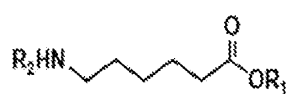
FIG. 15B

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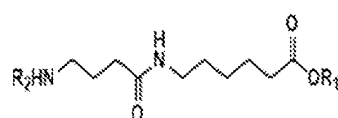


Linkers:

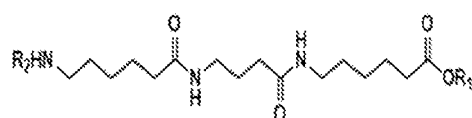
11 atom Linker:



16 atom Linker:



23 atom Linker:



N3 Linker:

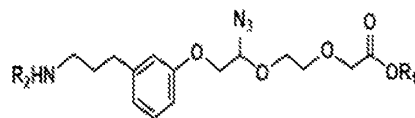


FIG. 16A

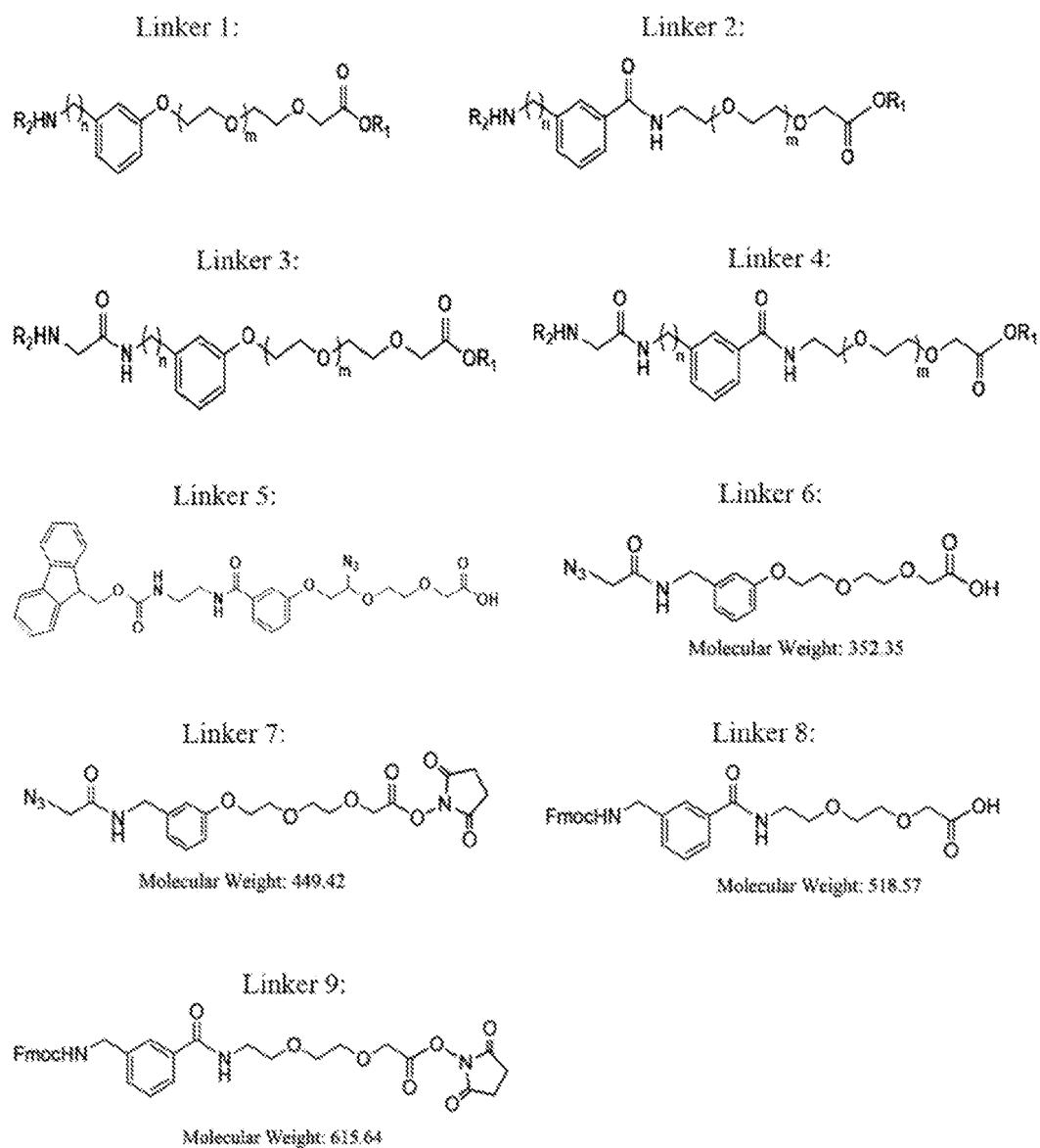
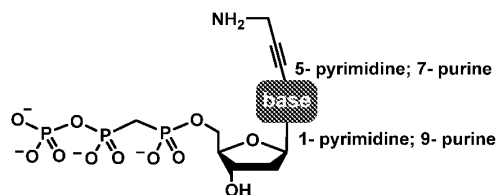
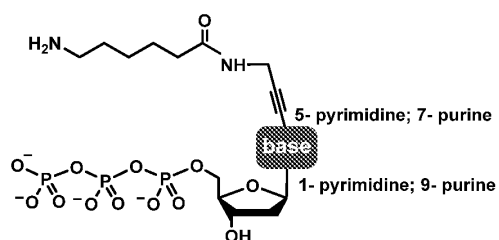
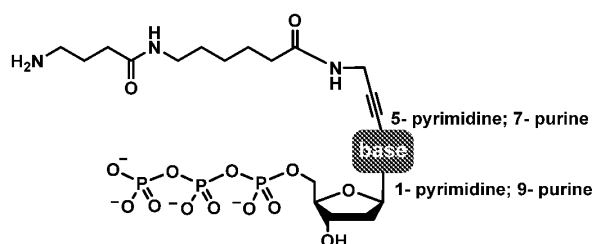
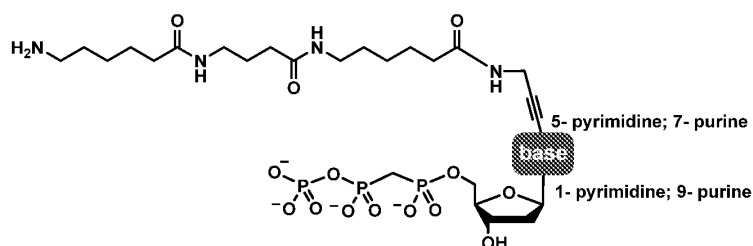
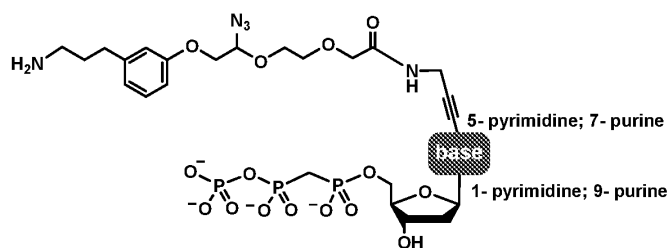
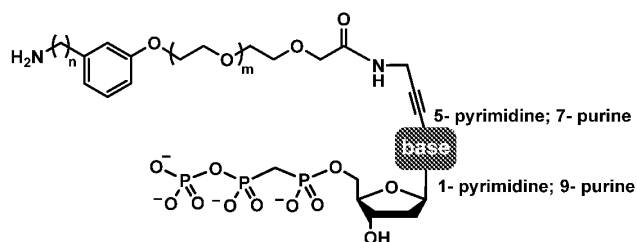
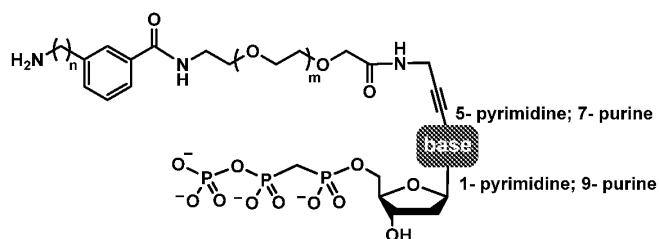
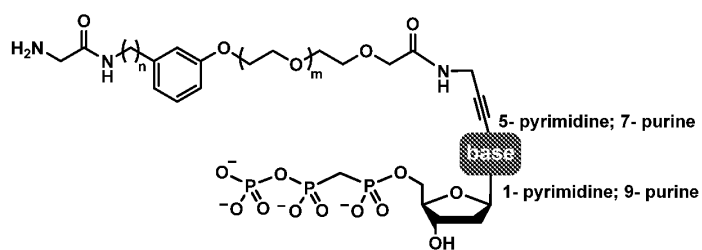
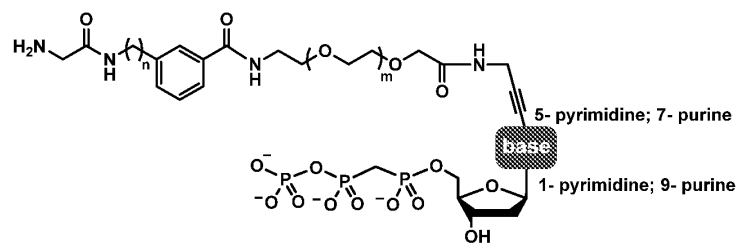
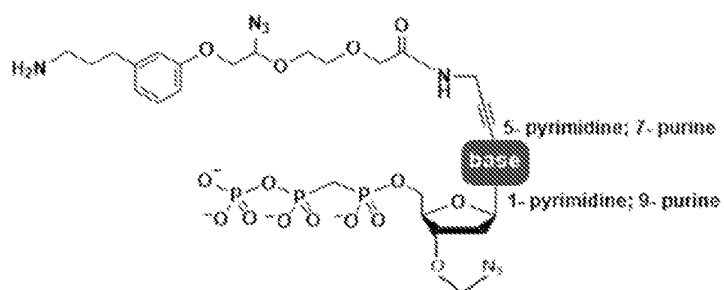


FIG. 16B

dNTP-PA-NH₂:**dNTP-PA-11 Atom Linker-NH₂:****dNTP-PA-16 Atom Linker-NH₂:****dNTP-PA-23 Atom Linker-NH₂:****FIG. 17A**

dNTP-PA-N3 Linker-NH₂:**dNTP-PA-Linker 1-NH₂:****dNTP-PA-Linker 2-NH₂:****dNTP-PA-Linker 3-NH₂:****FIG. 17B**

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dNTP-PA-Linker 4-NH₂:**dNTP-PA-N3 Linker-NH₂:****FIG. 17C**

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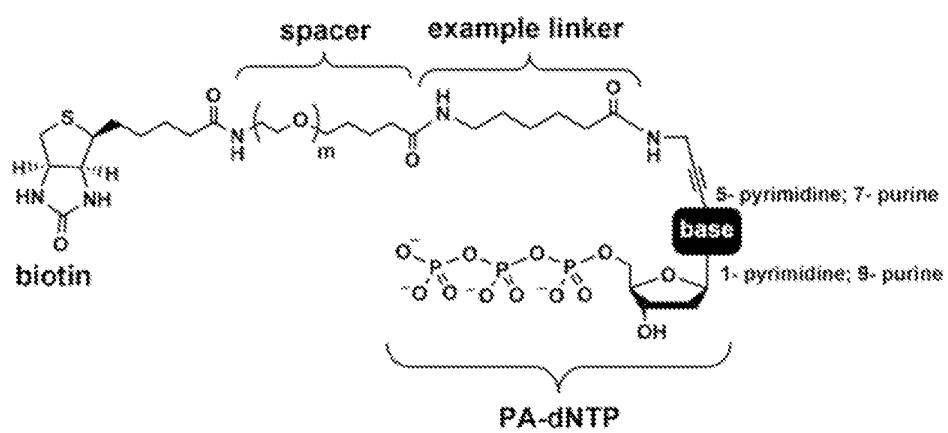


FIG. 18

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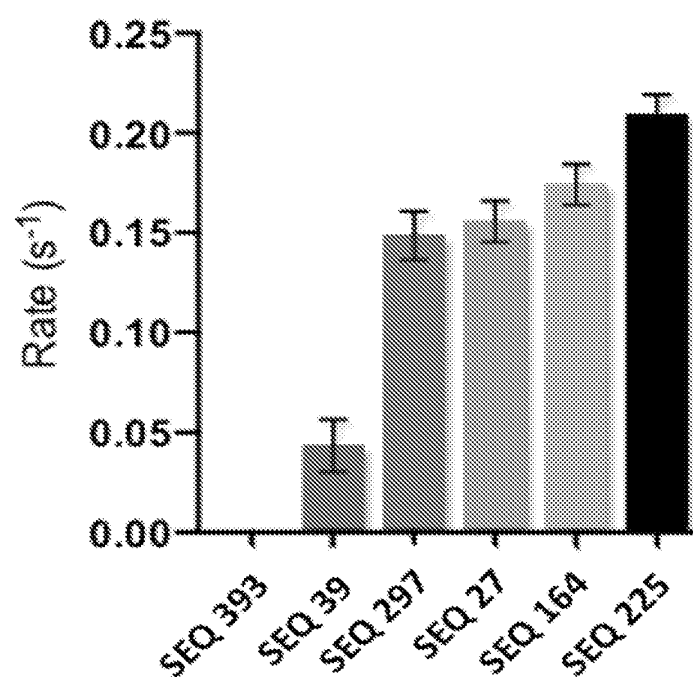


FIG. 19

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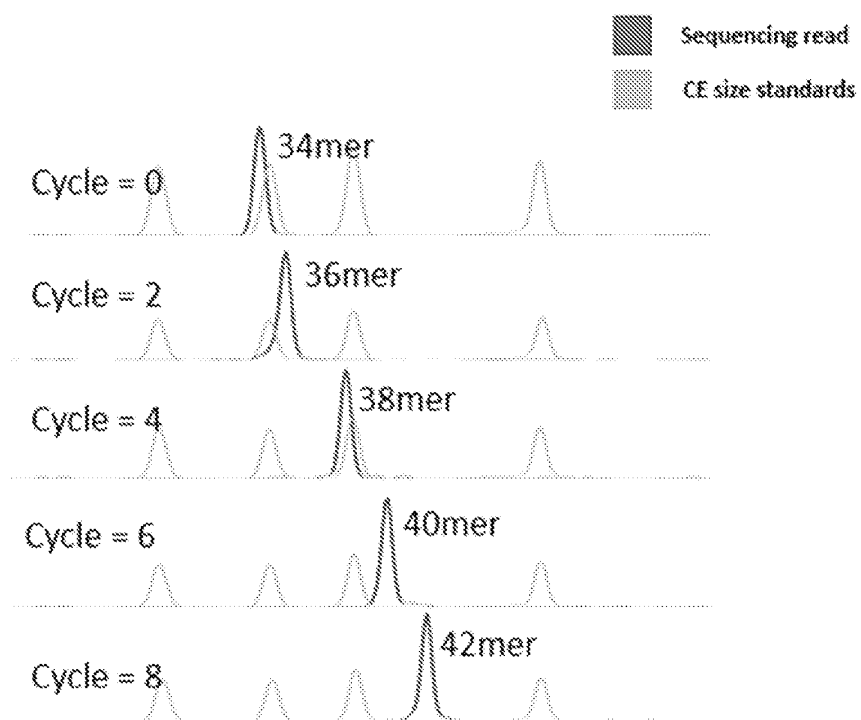


FIG. 20