Figure 1

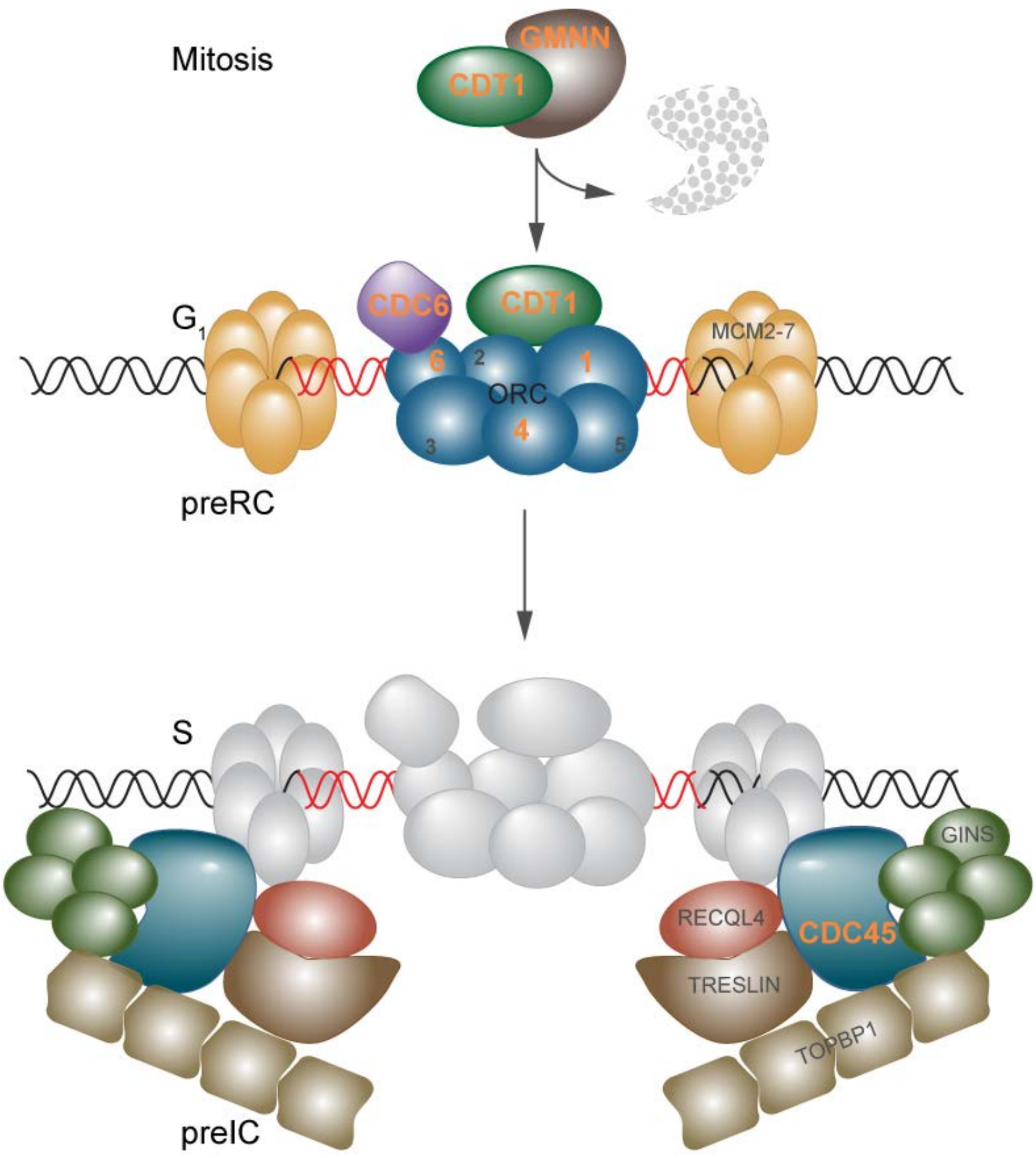

Mitosis
GMNN
CDT1
G1
CDC6
CDT1
6
2
1
ORC
4
3
5
MCM2-7
preRC
S
GINS
RECQL4
CDC45
TRESLIN
TOPBP1
preIC

Figure 2

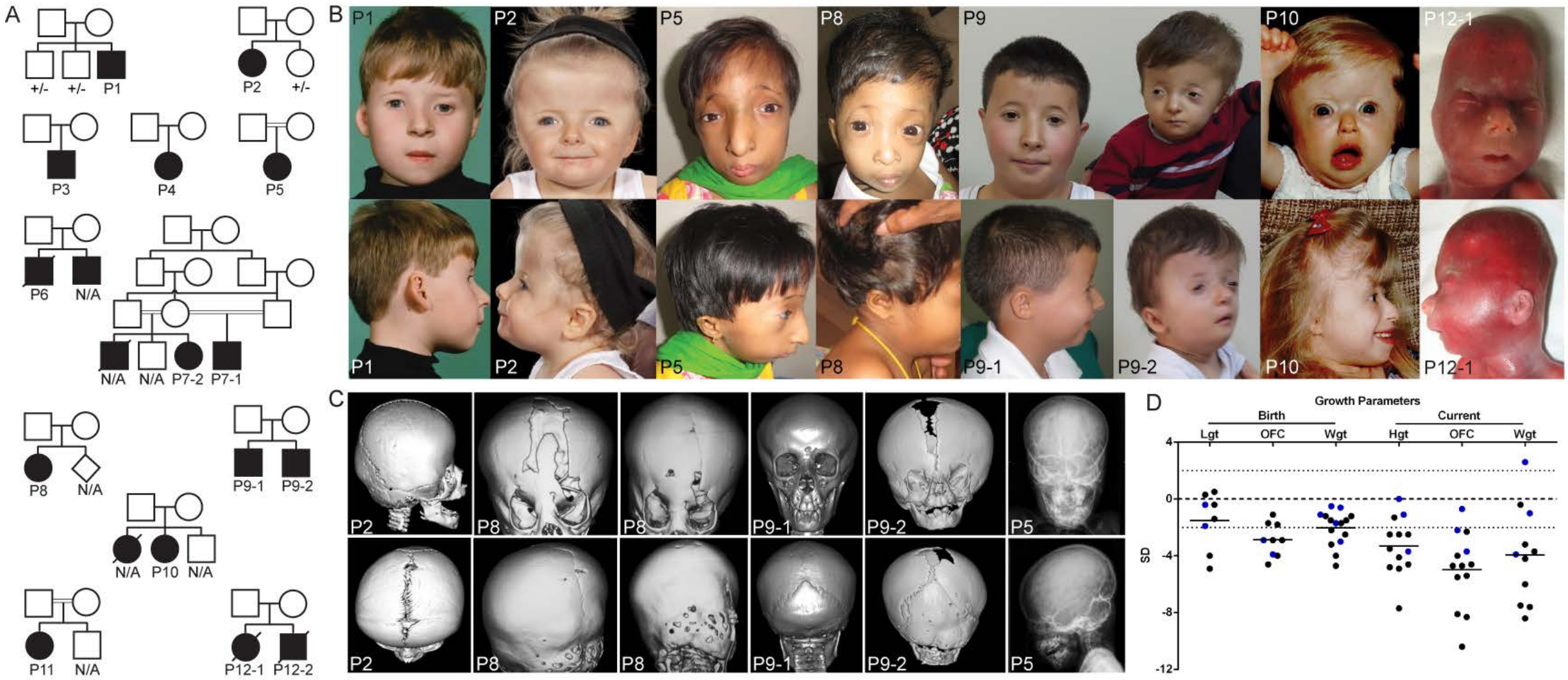
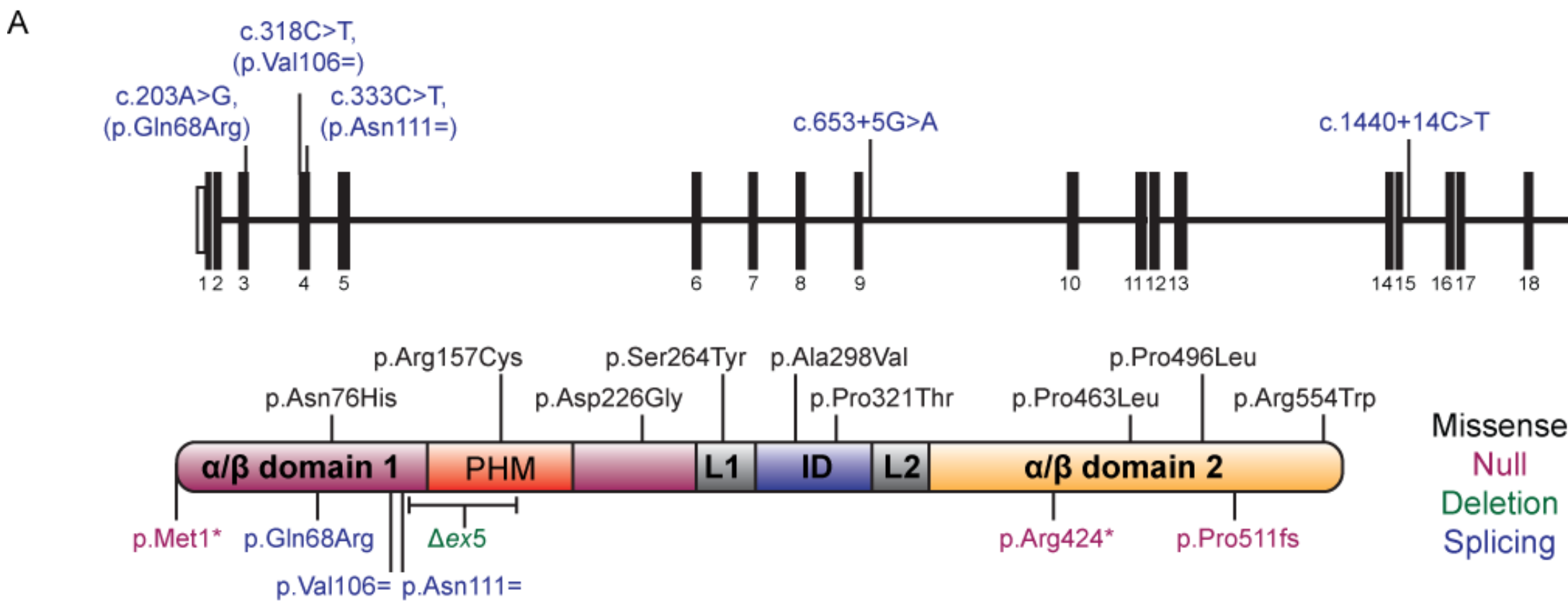

A
+/- +/- P1
P2 +/-
P3
P4
P5
P6 N/A
N/A N/A P7-2 P7-1
P8 N/A
P9-1 P9-2
N/A P10 N/A
P11 N/A
P12-1 P12-2
B
P1
P2
P5
P8
P9
P10
P12-1
P1
P2
P5
P8
P9-1
P9-2
P10
P12-1
C
P2
P8
P8
P9-1
P9-2
P5
P2
P8
P8
P9-1
P9-2
P5
D
Growth Parameters
Birth
Current
Lgt
OFC
Wgt
Hgt
OFC
Wgt
SD
4
0
-4
-8
-12

Figure 3


A
c.318C>T, (p.Val106=)
c.203A>G, (p.Gln68Arg)
c.333C>T, (p.Asn111=)
c.653+5G>A
c.1440+14C>T
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19
p.Arg157Cys
p.Ser264Tyr
p.Ala298Val
p.Pro496Leu
p.Asn76His
p.Asp226Gly
p.Pro321Thr
p.Pro463Leu
p.Arg554Trp
α/β domain 1
PHM
L1
ID
L2
α/β domain 2
p.Met1*
p.Gln68Arg
Δex5
p.Val106=
p.Asn111=
p.Arg424*
p.Pro511fs
Missense
Null
Deletion
Splicing

B

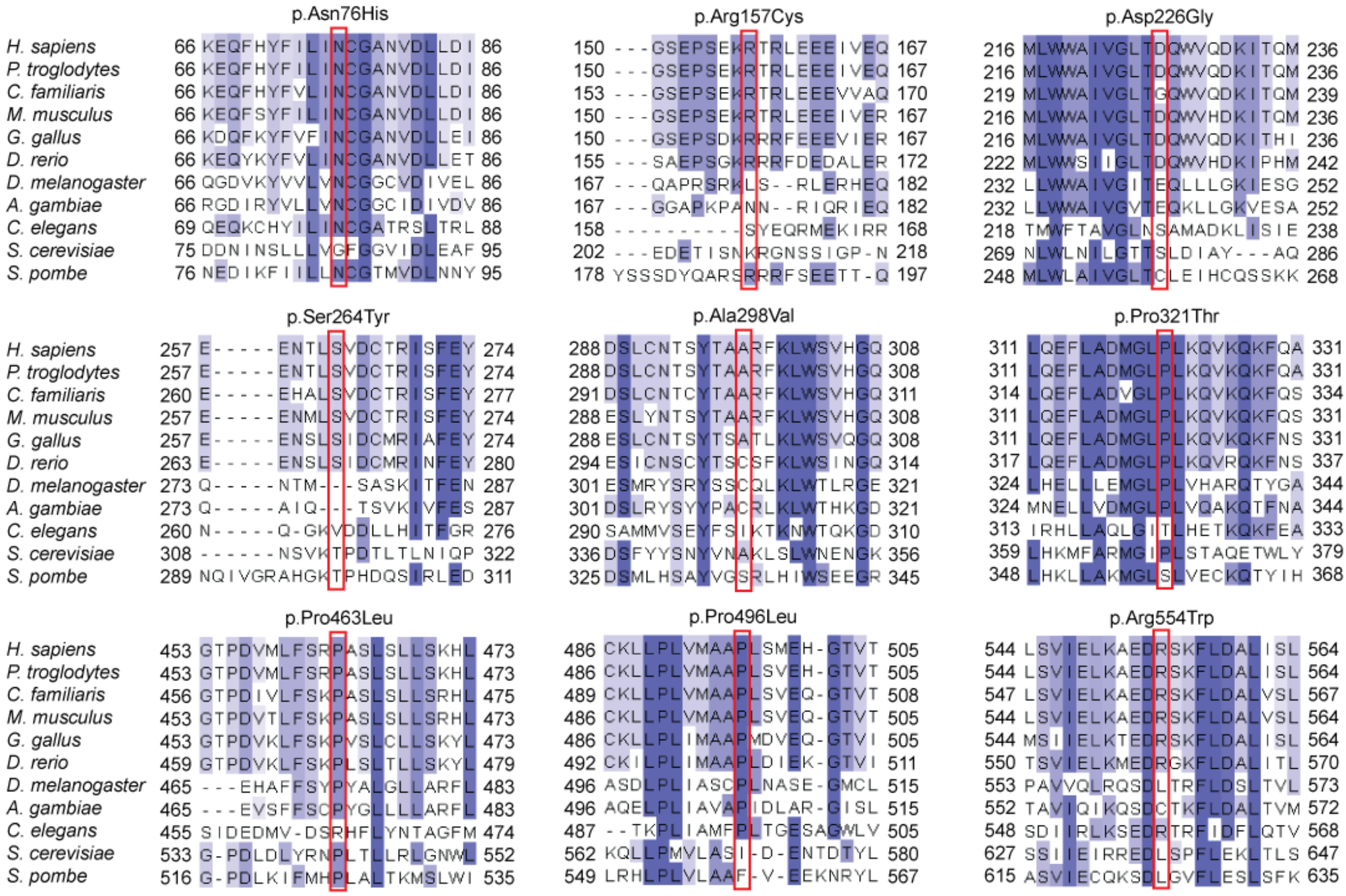

p.Asn76His
p.Arg157Cys
p.Asp226Gly
p.Ser264Tyr
p.Ala298Val
p.Pro321Thr
p.Pro463Leu
p.Pro496Leu
p.Arg554Trp
H. sapiens
P. troglodytes
C. familiaris
M. musculus
G. gallus
D. rerio
D. melanogaster
A. gambiae
C. elegans
S. cerevisiae
S. pombe

Figure 4

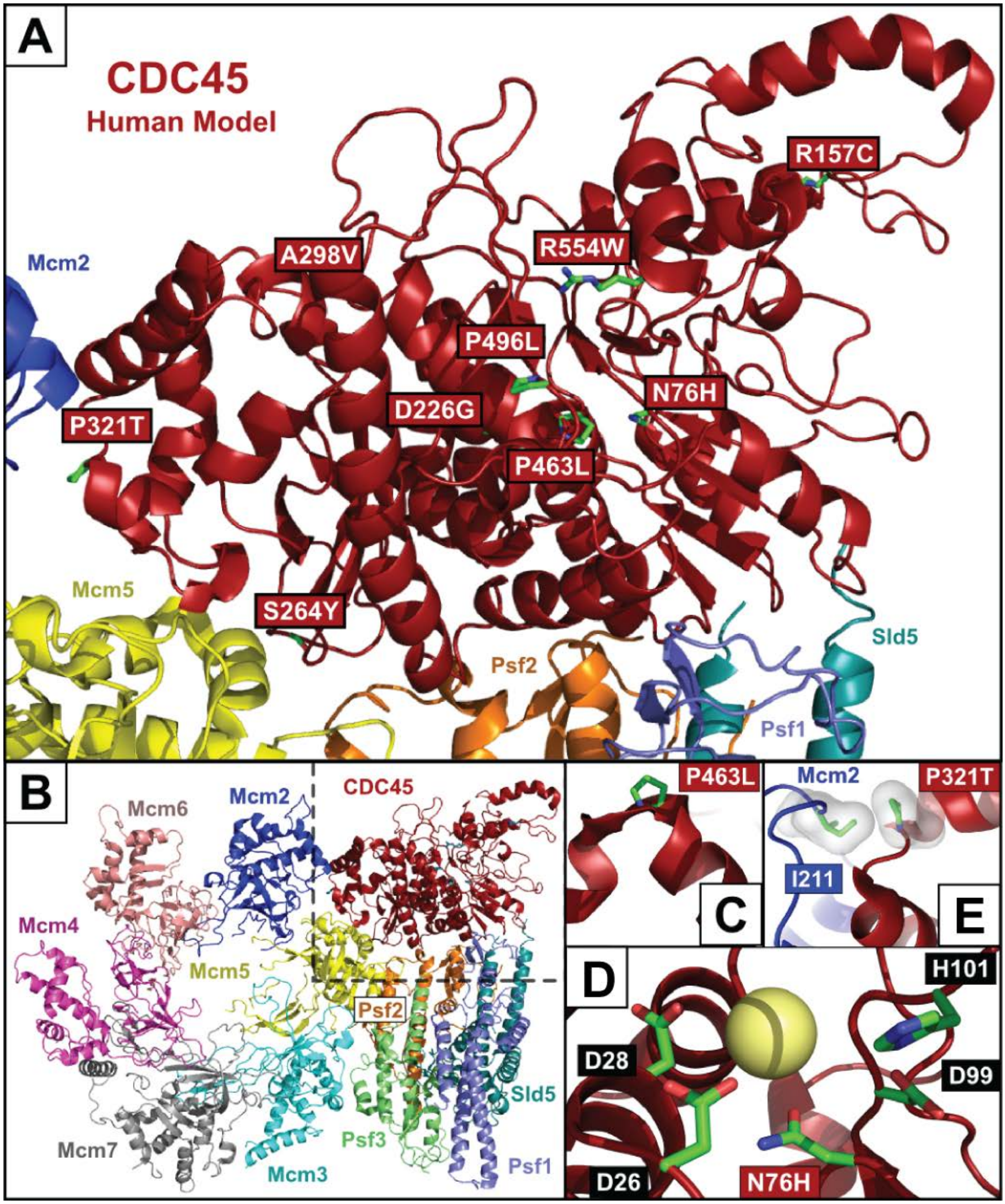

A
CDC45
Human Model
Mcm2
A298V
R554W
R157C
P496L
N76H
D226G
P321T
P463L
Mcm5
S264Y
Psf2
Sld5
Psf1
B
Mcm6
Mcm2
CDC45
Mcm4
Mcm5
Psf2
Psf3
Sld5
Mcm7
Mcm3
Psf1
P463L
C
Mcm2
P321T
I211
E
D
H101
D28
D99
D26
N76H

Figure5

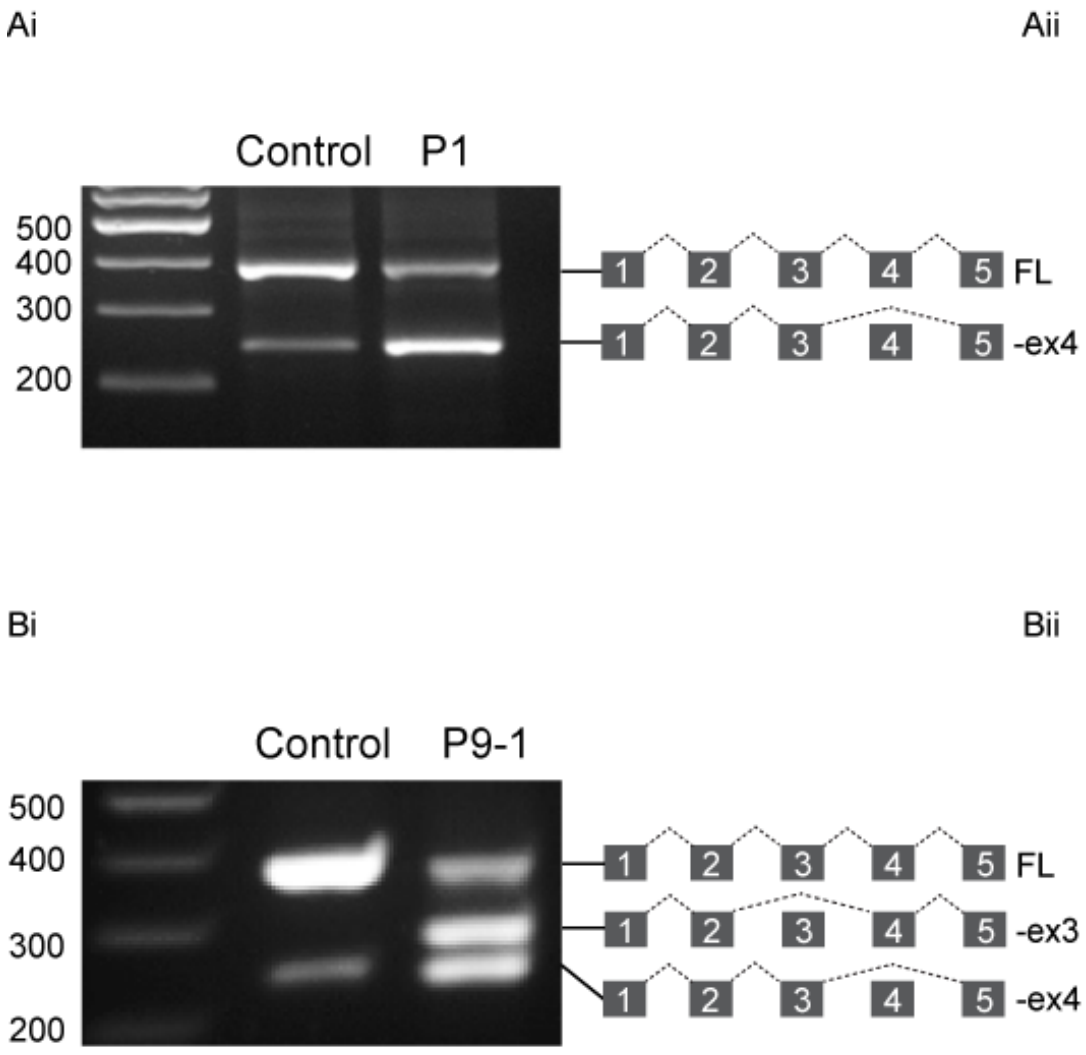
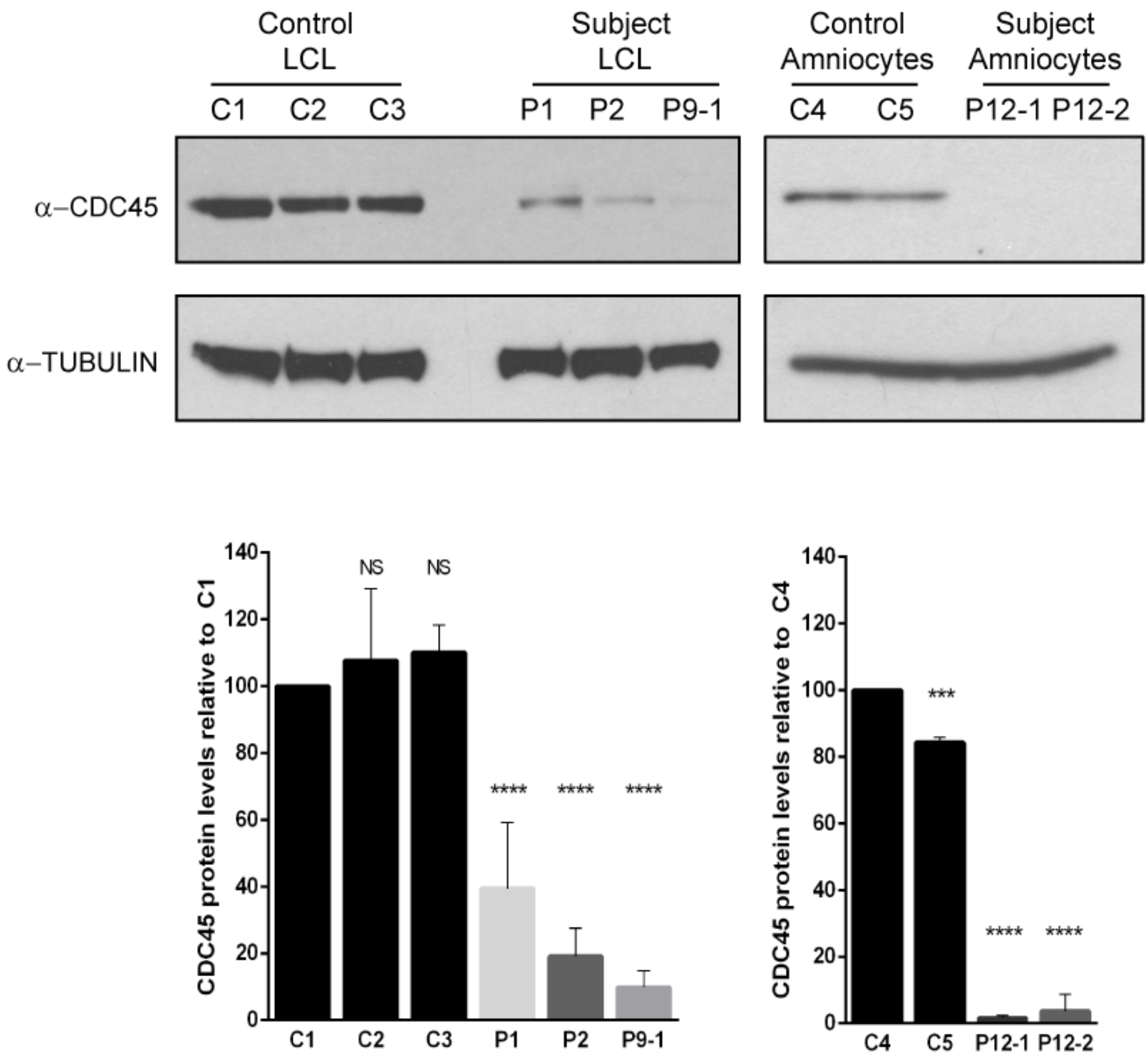

Ai
Control
P1
500
400
300
200
1 2 3 4 5 FL
1 2 3 4 5 -ex4
Aii
Levels relative to exons 1-3
1.5
1.0
0.5
0.0
C1 C2 C3 C4 P2 P1
exons 3-4
C1 C2 C3 C4 P2 P1
exons 5-6
Primer Design
TEST
CONTROL
1 2 3 4 5 6
BASELINE
Bi
Control
P9-1
500
400
300
200
1 2 3 4 5 FL
1 2 3 4 5 -ex3
1 2 3 4 5 -ex4
Bii
Levels relative to GAPDH
p = 0.002
40
30
20
10
0
Control
P9-1
FL
p = 0.005
Control
P9-1
-exon 4
Primer Design
1 2 3 4 5 FL
1 2 3 5 -ex4

Figure 6


Control LCL
Subject LCL
Control Amniocytes
Subject Amniocytes
C1 C2 C3
P1 P2 P9-1
C4 C5
P12-1 P12-2
α–CDC45
α–TUBULIN
CDC45 protein levels relative to C1
NS NS
**** **** ****
C1 C2 C3 P1 P2 P9-1
Cell Line
CDC45 protein levels relative to C4
*** **** ****
C4 C5 P12-1 P12-2
Cell Line