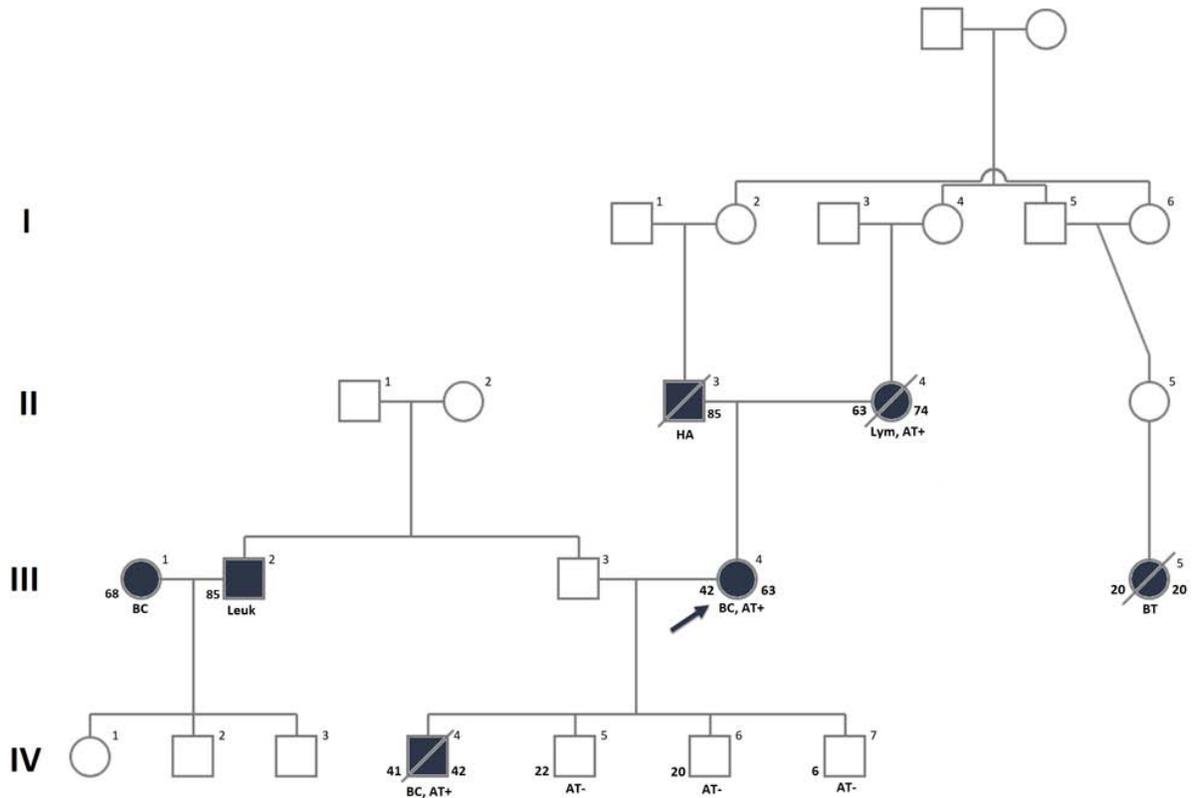
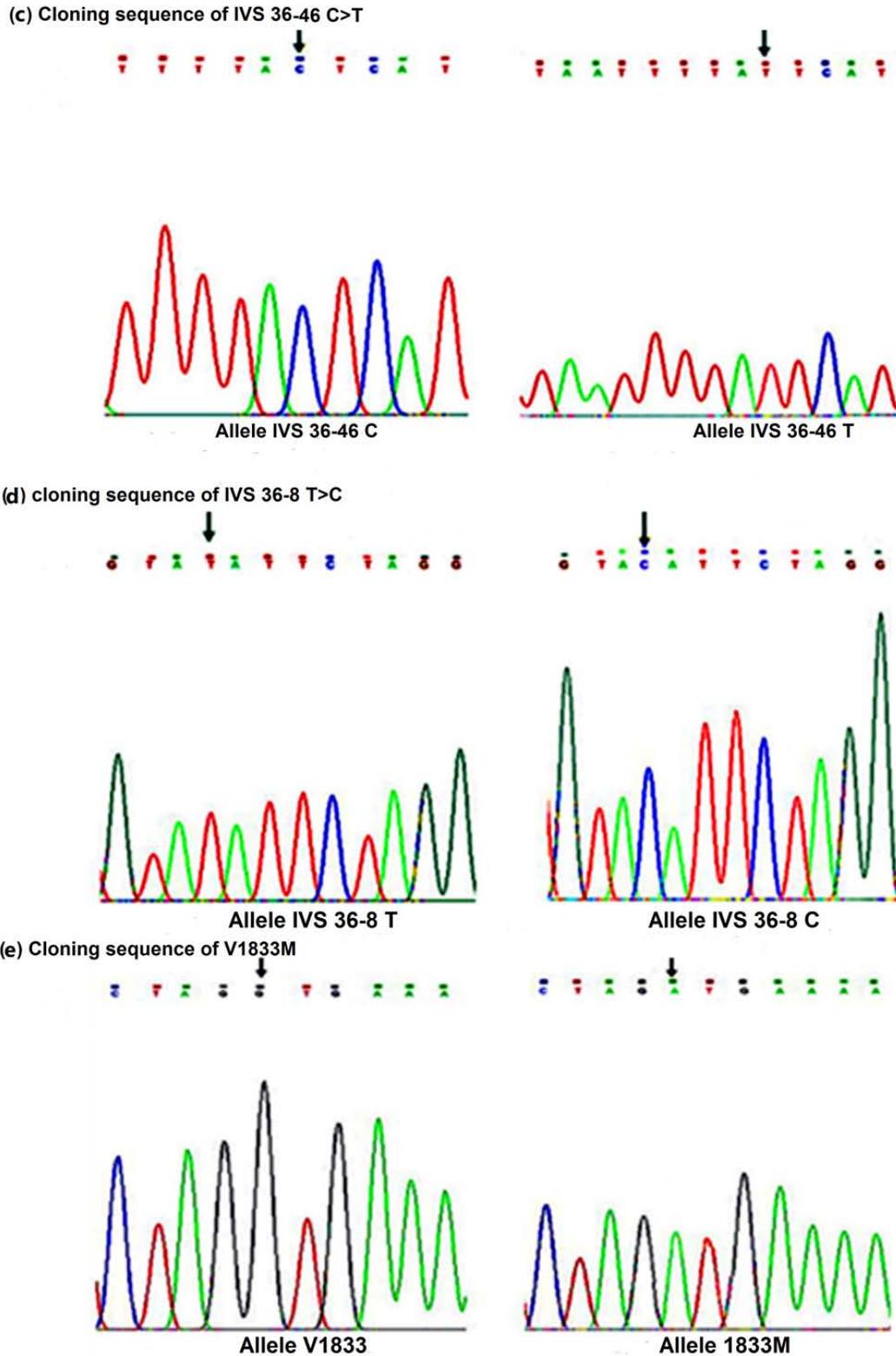


SUPPLEMENTARY FIGURE

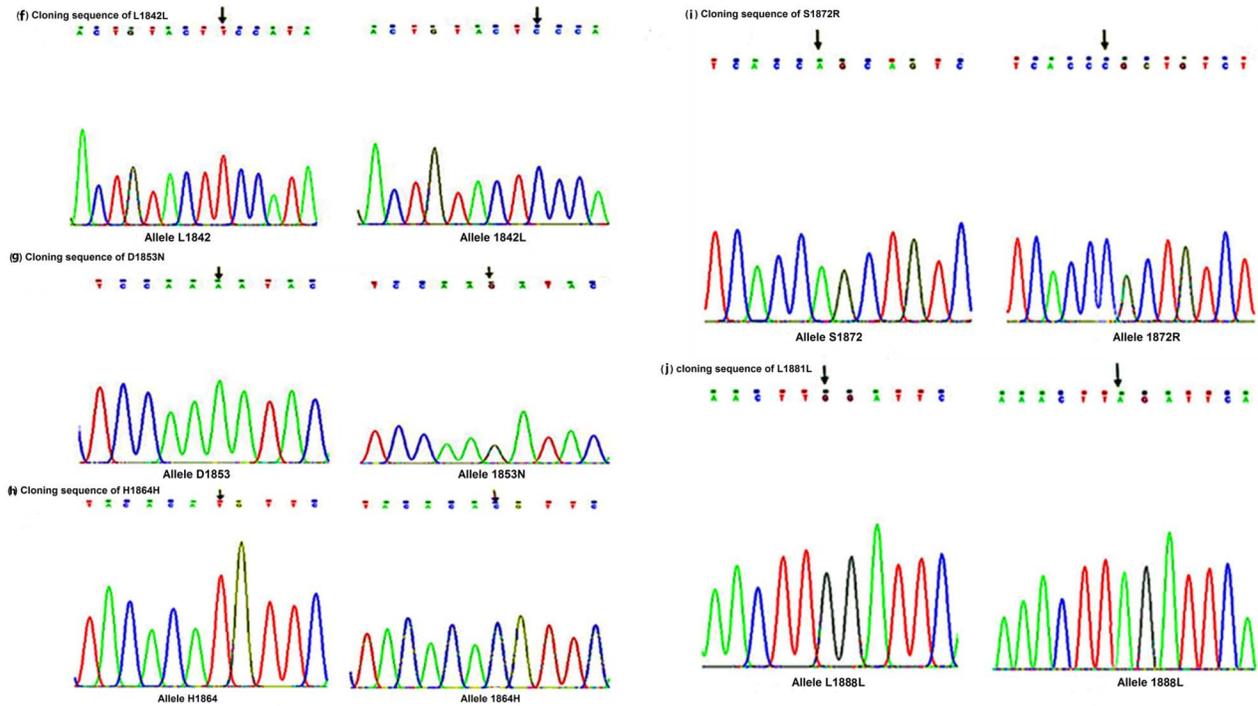


S. Figure 1. The pedigree of a proband affected with IDC-BC. Right-side numbers of each individual presents systematic reference number of individuals through each generation. Left/bottom-side numbers of each individual current age of onset (years) and right/bottom-side number presents deceased age (years) in the pedigree. Right/bottom-side number of proband presents her current age. AT+ represent “positive D1853N” and AT- represent “negative D1853N”. The carcinoma-type of each person is indicated in the bottom of subjects: BC = Breast Carcinoma; Lym = Lymphoma; BT = Brain Tumor; Leuk = Leukemia; HA = Heart Attack.



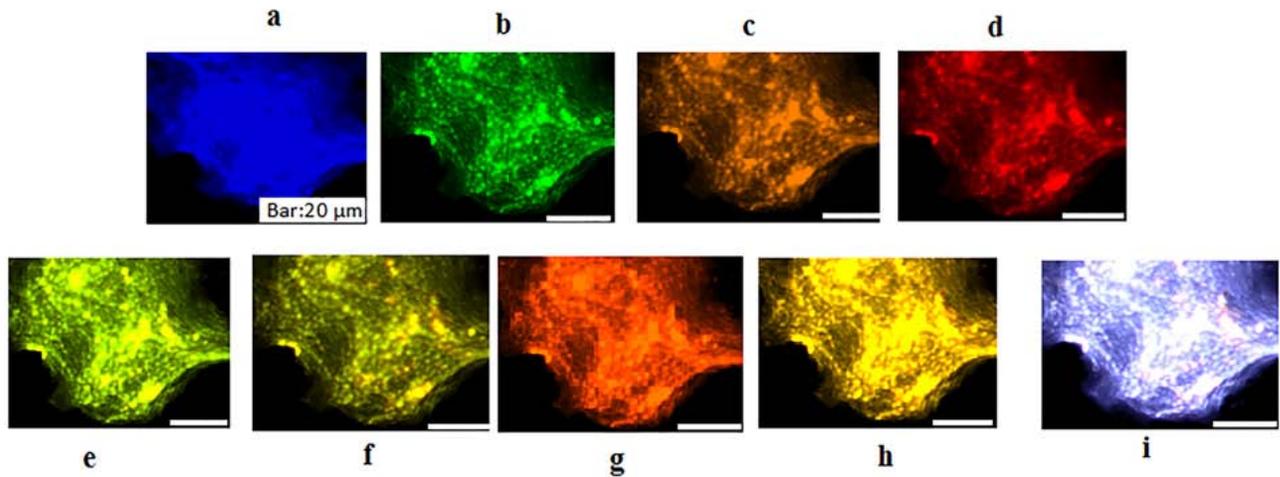
S. Figure 2. The alterations found in Exon 37 and surrounding region of ATM (cont.). Sequencing of clones containing target region of ATM at genomics and tumor levels in a patient affected with primary BC.

(c) Cloning sequence: IVS 36-46 C>T (left, Allele C; right, Allele T); (d) Cloning sequence: IVS 36-8 T>C (left, Allele T; right, Allele C); (e) Cloning sequence: L1842L (left, V1833; right, M1832). "Sequencing of clones containing target region of ATM at genomics and tumor levels in a patient affected with primary BC".



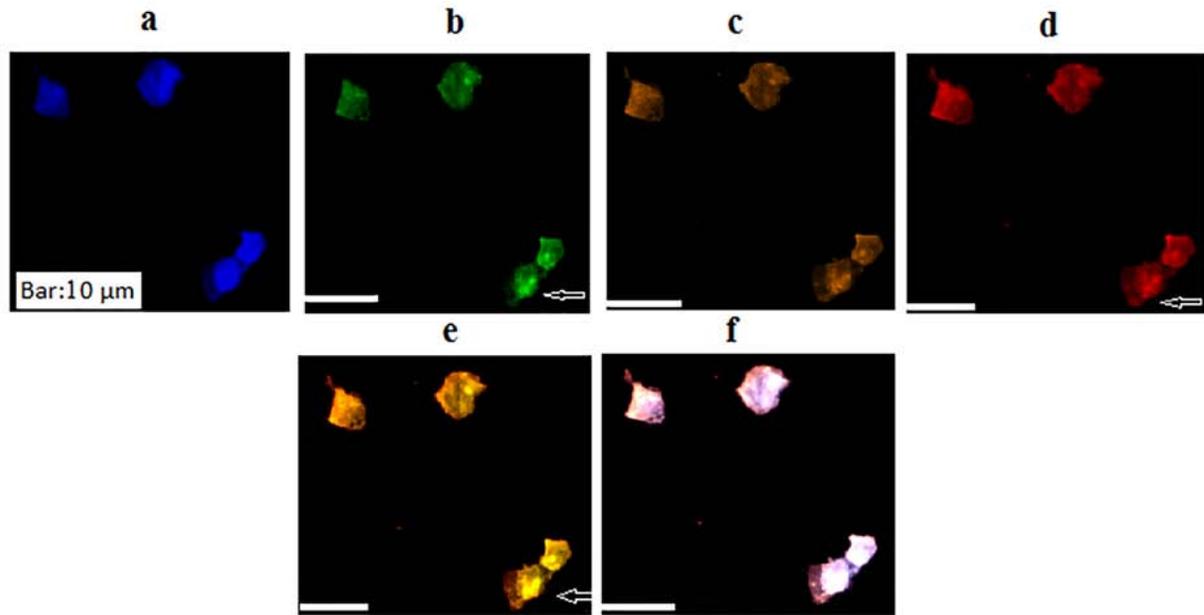
S. Figure 3. The alterations found in Exon 37 and surrounding region of ATM (cont.: S Figure 2).

(f) Cloning sequence: L1842L (left, L1842; right, L1842); (g) Cloning sequence: left shows normal allele (D1853), right shows mutant allele (D1853N alteration); (h) Cloning sequence: left shows normal allele, right shows mutant allele (H1864H); (i) Cloning sequence: left shows normal allele, right shows mutant allele (S1872R); (j) Cloning sequence: left shows normal allele, right shows mutant allele (L1888L).



S. Figure 4. Protein expression status of Ki-67, Cyclin D1, and P53 in the tumor of a patient with Breast carcinoma.

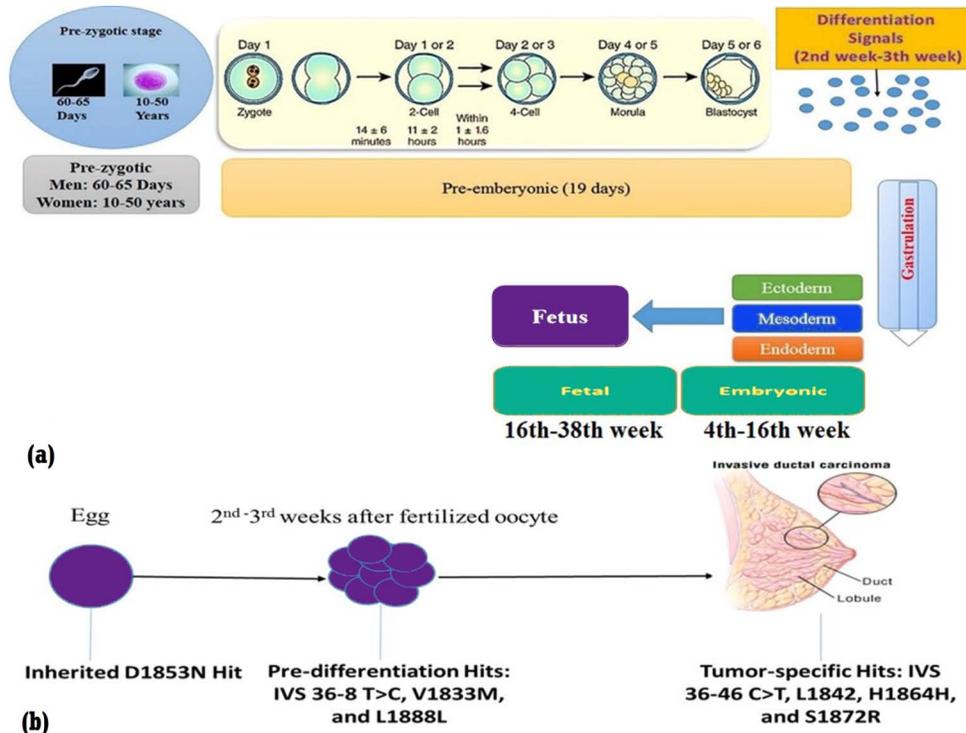
a) Breast tumor cells with dapi; b) The same cells conjugated with FITC, reflecting the expression of Ki-67; c) The same cells conjugated with Rpe, reflecting the expression of Cyclin D1; d), The same cells presenting the expression of P53 and conjugated with Pe-cy5; e) The co-expression of Ki-67/Cyclin D1; f) The co-expression of cyclin Ki-67/ P53; g) The co-expression of Cyclin D1/P53; h) The co-expression of Ki-67/Cyclin D1/P53; i) The merged of dapi/ Ki-67/Cyclin D1/P53. Remarkable heterogeneity is observable.



S. Figure 5. Status of protein expression of Cyclin E, ATM and CDC25A in buccal in a patient affected with breast carcinoma after 21 years after surgery.

Arrows show the high expression and co-expression of of Cyclin E and CDC25A in limited buccal cells 21 years after surgery.

a) Buccal cells with dapi; **b)** The same cells conjugated with FITC, reflecting the expression of Cyclin E; **c)** The same cells conjugated with Rpe, reflecting the expression of ATM; **d)** The same cells presenting expression of CDC25A and conjugated with Pe-cy5; **e)** The co-expression of Cyclin E/ATM/CDC25A; **f)** The merged image of dapi/Cyclin E/ATM/CDC25A.



S. Figure 6. Development of human embryo from zygote to birth. The alterations including IVS 36-8 T>C, V1833M and L1888L that were observed both in blood and tumor tissues are as the result of events occurred in pre-differentiation stage between 2nd and 3rd weeks of gestation. further evolution has occurred at tumor level which are found as tumor-specific hits including IVS 36-46 C>T, L1842, H1864H, and S1872R, characterized as the 5th, 6th, 7th and 8th hits, respectively.