LIST OF FIGURES

Figure 1	Multistep Carcinogenesis model
Figure 2	Structure of P-glycoprotein (PGP) consisting of 12 transmembrane domains and 2 ATP binding sites.
Figure 3	Drug efflux in tumour cells due to overexpression of P-glycoprotein
Figure 4	Little overlap of the three environmental gene datasets from Gene Venn tool indicate that all three datasets should be taken together for analysis.
Figure 5	Overlap of the environment susceptible and breast cancer genes from cosmic. 68 genes were found to be common.
Figure 6 (a)	Protein RMSD Native structure up to 2500 ps
Figure 6 (b)	Protein RMSD of mutant R538S structure up to 2500 ps
Figure 7(a)	Protein RMSD native structure from 2500 to 7500 ps
Figure 7 (b)	Protein RMSD of mutant R538S structure from 2500ps up to 7500 ps
Figure 8(a)	RMSF of native structure up to 7500 ps
Figure 8(b)	RMSF of mutant structure R538S up to 7500 ps

Figure 9(a)	RMSD of native structure up to 5000ps
Figure 9(b)	RMSD of variant structure M701R up to 5000ps
Figure 10(a)	RMSF of native structure up to 5000 ps
Figure 10(b)	RMSF of variant structure M701R up to 5000ps

LIST OF TABLES

TABLE 1	Role of polymorphisms in carcinogen metabolizing enzymes and other important genes
TABLE 2	Pubmatrix search showing understudied and novel susceptible genes in relation to breast cancer as can be seen from number of studies carried out for them
TABLE 3	nsSNPs in P-gp and prediction of their functional impact and disease association by PolyPhen 2.0 and PHD-SNP respectively.
TABLE 4	nsSNPs in P-gp and prediction of their structural impact by MUTPRED

LIST OF ABBREVIATIONS

ABCB1 ATP-Binding Cassette, Sub-Family B (MDR/TAP), Member 1

P-gp P-glycoprotein

COSMIC Collection of somatic mutations in cancer

MDS Molecular dynamics simulation

ATP Adenosine tri phosphate

nsSNP Nonsynonymous single nucleotide polymorphism

TMD Transmembrane domain

NMD Nucleotide binding domain

CTD Comparative toxicological database

ABC ATP binding cassette

EGP Environmental Genome Project
GEI Gene environment interaction

MDR Multi drug resistance

GBM Glioblastoma

BBB Blood brain barrier

NIH National institute of health

PSIC Position-specific independent counts

SVM Support vector machine AAS Amino acid substitution

SIFT Sorting intolerant from tolerant HGMD Hugo gene mutation database

SPC Simple point charge

RMSD Root mean square deviation RMSF Root mean square fluctuation