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Structural Comparisons of the Kinases Involved in Cancer Disease Development

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Abstract: *More than 575,000 people die of cancer, and more than 1.5 million people are diagnosed with cancer per year in the US.Cancer is considered to be one of the leading causes of morbidity and mortality worldwide.The financial costs of cancer in the US per year are an estimated $263.8 billion in medical costs and lost productivity.African Americans are more likely to die of cancer than people of any other race or ethnicity.It is believed that cancer risk can be reduced by avoiding tobacco, limiting alcohol intake, limiting UV ray exposure from the sun and tanning beds and maintaining a healthy diet, level of fitness and seeking regular medical care.Screening can locate cervical cancer, colorectal cancer and breast cancer at an early, treatable stage.According to the World Health Organization (WHO), the numbers of new cancer cases is expected to rise by about 70% over the next 20 years.The most common sites of cancer among men are lung, prostate, colon, rectum, stomach and liver.The most common sites of cancer among women are breast, colon, rectum, lung, cervix and stomach.*

Keywords: *Cancer disease,genes, kinases ,strural comparison swiss pdb viewer.*

I. Introduction

A large number of genes with diverse normal functions are involved in human cancer. More than 500 genes have been identified as strongly implicated in the process of transforming normal cells to cancer cells. The expression of these genes in normal cells contributes to normal growth, survival and function, whereas dysregulated expression, including overexpression, loss of expression or expression of a defect protein, in cancer cells contributes to ungoverned tumor growth. Altered gene expression can be caused by coarse structural and numerical chromosomal rearrangements, specific gene amplifications, silencing of transcription through methylation and mutations, e.g. point mutations with single base substitutions and small inserts or deletions, that lead to loss or gain of function of the corresponding protein.

II. Methodology

protein structures can be downloaded from PDB ,these are grouped in to different families ,to compare the RMSD of the proteins from different families using Swiss Pdb viewer ,the 3D structures with good resolution can be taken for the comparison two proteins from each family will be selected for comparisons , the comparison will be from point of view like C Aplha carbons backbone ,sidechain atoms ,and all the atoms this will elaborate the difference among same family ,it will help in selecting a Lead compound for docking study i.e.drug target valdation

Genes and Proteins Altered in Cancer

Currently, more than 1% of all human genes are implicated via mutation in cancer. Of these, approximately 90% have somatic mutations in cancer, 20% bear germline mutations that predispose to cancer and 10% show both somatic and germline mutations. A list of genes strongly implicated in cancer (n=528) has been defined through the cancer Gene Census, catalogue of somatic mutations in cancer (COSMIC).

Table 1. List of different genetic alterations in 528 genes that are implicated

Genetic alteration	**Number of genes**
Somatic Mutations	489
Translocations	333
Missense Mutations	177
Frameshift Mutations	118
Nonsense Mutations	109
Germline Mutations	80
Splicing Mutations	73
Large Deletions	38
Other Mutations	31
Amplifications	16
Total number of mutated genes	528

Table 2

Name of the protein family	**Pdb Id**		**RMSD C Aplpha A°**	**RMSD Backbone Atoms A°**	**RMSD Side chain Atoms A°**	**All Atoms A°**
AGC Ser/Thr protein kinase family	ADRBK1 ADRBK2	ADRBK1 Beta-adrenergic receptor kinase 1 3CIK	59 atoms 1.71	240 atoms 1.72	240 atoms 1.72	240 Atoms 1.72
		RAC-alpha serine/threonine-protein kinase 1UNP				
CAMK Ser/Thr protein kinase family	BRSK2 CHEK2	4FG8 CAMK1 Calcium/calmodulin-dependent protein kinase type 1	90 atoms 1.49	888 atoms 0.87	888 atoms 0.87	888 atoms 0.87
		CAMK1D Calcium/calmodulin-dependent protein kinase type 1D 2JC6				
CK1 Ser/Thr protein kinase family	CSNK1E CSNK1G1	CSNK1E Casein kinase I isoform epsilon 4HNI	156 atoms 1.71	640 atoms 1.70	640 atoms 1.70	640 atoms 1.70
		CSNK1G1 Casein kinase I isoform gamma-1 2CMW	229 atoms 1.17	920 atoms 1.22	920 atoms 1.22	920 atoms 1.22
CMGC Ser/Thr protein kinase family	CDK1 CDK2	CDK1 Cyclin-dependent kinase 1 4Y72	210 atoms 1.08	840 atoms 1.16	840 atoms 1.16	840 atoms 1.16
		CDK12 Cyclin-dependent kinase 12 4NST				
NEK Ser/Thr protein kinase family	NEK1 NEK2	NEK1 Serine/threonine-protein kinase Nek1 4B9D	154 atoms 1.75	632 atoms 1.72	632 atoms 1.72	632 atoms 1.72
		NEK2 Serine/threonine-protein kinase Nek2 2W5A				
STE Ser/Thr protein kinase family	MAP3K14 MAP2K2	MAP2K2 Dual specificity mitogen-activated protein kinase kinase 2 1S9I	210 atoms 1.08	840 atoms 1.16	840 atoms 1.16	840 atoms 1.16
		MAP2K4 Dual specificity mitogen-activated protein kinase kinase 4 3ALO				
TKL Ser/Thr protein kinase family	ACVR1 BMPR1B	ACVR1 Activin receptor type-1 3MTF	256 atoms 0.98	1024 atoms 1.02	1024 atoms 1.02	1024 atoms 1.02
		ACVR2A Activin receptor type-2A 2QLU				
Tyr protein kinase family	ABL1 ABL2	ABL1 Tyrosine-protein kinase ABL1 1AB2	118 atoms 1.52	496 atoms 1.59	496 atoms 1.59	496 atoms 1.59

III. Result and Discussion

1. AGC Ser/Thr protein kinase family has RMSD of the selected structures 1.72 **A°**
2. CAMK Ser/Thr protein kinase family has RMSD of the selected structures 0.87 **A°**
3. CK1 Ser/Thr protein kinase family has RMSD of the selected structures 1.70 **A°**
4. CMGC Ser/Thr protein kinase famil has RMSD of the selected structures 1.16 **A°**
5. NEK Ser/Thr protein kinase family has RMSD of the selected structures 1.72 **A°**
6. STE Ser/Thr protein kinase family has RMSD of the selected structures 1.16 **A°**
7. TKL Ser/Thr protein kinase family has RMSD of the selected structures 1.02 **A°**
8. Tyr protein kinase family has RMSD of the selected structures 1.59 **A°**

The swiss PDB viewer has been used for the structural of the selected proteins this analytical result will help in identifying the drug targets ,it will also helpful in insilico annotation of the protein ,table 1 shows the number of genes involved in cancer disease development ,table 2 shows the information on the RMSD of the proteins with the respective of C Alpha,Backbone ,side chain ,and all the atoms of the proteins

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