

# Proteomic Translation of Chronic Granulomatous Disease (CGD)

**Keywords:** CGD; NADPH oxidase; Mulch pneumonitis

## Abstract

Chronic granulomatous disease considered as one of the congenital hereditary disease that present due to mutation in one of these following genes; CYBA, CYBB, NCF1, NCF2, or NCF4 gene in X chromosome, that lead to lack a body defense mechanisms against infections specially bacterial & fungal infections due to absence of NADPH oxidase productions in phagocytic cells; lungs is the most common site of infections. Sometimes the causes of CGD is unknown & we did not have a scientific explanation for this; the main aim of this study is to identify the CYBB gene SNPs change in a way to predict mutation effects of this gene at the proteomic level; through in silico tools by using sift, polyphen-2, I mutant suite-3, SNPs & GO software prediction programs for SNPs detections. A according to these predictions tools & their confirmations tools I found that CYBB gene SNPs mutation showed damaging predictions which was considered as clinical manifestation of this study beside this; a lots of those SNPs illustrate decreasing in protein functionality even those that were predicted benign by polyphen-2.

## Introduction

CGD is a congenital immune deficiency disease that is genetically inherited in an X-linked manner; these means only men can be infected; also both sexes can be infected in case of autosomal recessive forms. CGD manifested by recurrent severe infections including; pneumonia, lymphadenitis, skin and hepatic abscesses, osteomyelitis and septicemia; inflammation of these tissue areas in various organs (granulomas) can result on tissue damaging. Usually infections become apparent during the first year of life; in this disease phagocytic neutrophils are unable to produce a bactericidal respiratory burst due to a deficiency of one of the proteins component of the NADPH oxidase complex [1-8].

The features of chronic granulomatous disease usually first appear in childhood, although some individuals do not show symptoms until later on in their life; they may have at least one serious bacterial or fungal infections every 3 to 4 years, especially in the lungs (pneumonia) or fungal pneumonia (mulch pneumonitis; which causes fever and shortness of breath after exposure to decaying organic materials such as mulch, hay, or dead leaves). Other common areas of infection include; the skin, liver, and lymph nodes; so the most common area of inflammation are gastrointestinal tract; ( in many cases the intestinal wall is inflamed, causing a form of inflammatory bowel disease that varies in severity but can lead to stomach pain, diarrhea, bloody stool, nausea, and vomiting) and the genitourinary tract, in addition to the stomach, colon, and rectum, as well as the mouth, throat, and skin inflammations; also, inflammation in the stomach can prevent food from passing through esophagus to the intestines (gastric outlet obstruction), leading to an inability to digest food, vomiting after eating and weight loss. In the genitourinary tract, inflammation can occur in the kidneys and bladder [2].

Inflammation of the lymph nodes (lymphadenitis) and bone marrow (osteomyelitis), which both produce immune cells,



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can lead to further impairment of the immune system; rarely those people with chronic granulomatous disease develop autoimmune disorders. Repeated episodes of infection and inflammation reduce the life expectancy of individuals with chronic granulomatous disease; however, with the treatment, they can live until mid to late adult hood. The disease can occur in 1 in 200,000 to 250,000 people worldwide, due to mutation in the CYBA, CYBB, NCF1, NCF2, or NCF4 gene, which leads to the presence of five types of this condition. The proteins which produced from those affected genes are parts (subunits) of an enzyme complex called NADPH oxidase, that plays an essential role in the immune system, specifically in phagocytes; by production of superoxide that is used to generate other toxic substances, which play a role in killing foreign invaders and preventing them from reproducing in the body and causing illness. NADPH oxidase is also thought to regulate the activity of neutrophils, which play a critical role in adjusting the inflammatory response to optimize healing and reduce injury to the body. Beside the above, mutation in those genes can lead to production of proteins with little or no function or the productions of no protein at all [1-8].

Chronic granulomatous disease that caused by mutations in the CYBB gene is inherited in an X-linked recessive pattern. The CYBB gene is located on the X chromosome, which is one of the two sex chromosomes. When chronic granulomatous disease is caused by CYBA, NCF1, NCF2, or NCF4 gene mutations, the condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations [2].

Therapeutic options for CGD included prophylactic antibiotics and antifungal medications, interferon-gamma injections, and aggressive management of acute infections. Bone marrow transplantation can cure CGD, however this therapy is complex and transplant candidates and donors must be carefully selected, weighing the risks and benefits carefully. Researchers are investigating other approaches including gene therapy as a future option [1-8].

In this study I used different computational methods to identify the CYBB gene SNPs to predict mutation effects at the proteomic level.

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Table 1: Illustrate SIFT & Polyphen-2 predictions results.

SNP	Organism/Build	Amino acid change	Sift score	Sift prediction	Polyphen result	Polyphen score
rs137854585	<i>Homo_sapiens</i> /GRCh37.74	P415H	0	Deleterious	Probably damaging	1
rs137854585	<i>Homo_sapiens</i> /GRCh37.74	P148H	0	Deleterious	Probably damaging	1
rs137854585	<i>Homo_sapiens</i> /GRCh37.74	P383H	0	Deleterious	Probably damaging	1
rs137854585	<i>Homo_sapiens</i> /GRCh37.74	P415L	0	Deleterious	Probably damaging	1
rs137854585	<i>Homo_sapiens</i> /GRCh37.74	P148L	0	Deleterious	Probably damaging	1
rs137854585	<i>Homo_sapiens</i> /GRCh37.74	P383L	0	Deleterious	Probably damaging	1
rs137854586	<i>Homo_sapiens</i> /GRCh37.74	G389E	0	Deleterious	Probably damaging	1
rs137854586	<i>Homo_sapiens</i> /GRCh37.74	G122E	0	Deleterious	Probably damaging	1
rs137854586	<i>Homo_sapiens</i> /GRCh37.74	G357E	0	Deleterious	Probably damaging	1
rs137854586	<i>Homo_sapiens</i> /GRCh37.74	G389A	0	Deleterious	Probably damaging	1
rs137854586	<i>Homo_sapiens</i> /GRCh37.74	G122A	0	Deleterious	Probably damaging	1
rs137854586	<i>Homo_sapiens</i> /GRCh37.74	G357A	0	Deleterious	Probably damaging	1
rs137854587	<i>Homo_sapiens</i> /GRCh37.74	H209Y	0	Deleterious	Probably damaging	1
rs137854587	<i>Homo_sapiens</i> /GRCh37.74	H177Y	0	Deleterious	Probably damaging	1
rs137854589	<i>Homo_sapiens</i> /GRCh37.74	C212Y	0.015	Deleterious	Probably damaging	1
rs137854589	<i>Homo_sapiens</i> /GRCh37.74	C244Y	0.034	Deleterious	Probably damaging	1
rs137854591	<i>Homo_sapiens</i> /GRCh37.74	H101R	0	Deleterious	Probably damaging	1
rs137854591	<i>Homo_sapiens</i> /GRCh37.74	H69R	0	Deleterious	Probably damaging	1
rs137854593	<i>Homo_sapiens</i> /GRCh37.74	D500G	0.004	Deleterious	Probably damaging	1
rs137854593	<i>Homo_sapiens</i> /GRCh37.74	D233G	0.004	Deleterious	Probably damaging	1
rs137854593	<i>Homo_sapiens</i> /GRCh37.74	D468G	0.005	Deleterious	Probably damaging	1
rs137854594	<i>Homo_sapiens</i> /GRCh37.74	H101Y	0	Deleterious	Probably damaging	1
rs137854594	<i>Homo_sapiens</i> /GRCh37.74	H69Y	0	Deleterious	Probably damaging	1
rs137854595	<i>Homo_sapiens</i> /GRCh37.74	H36N	0.002	Deleterious	Probably damaging	0.995
rs137854595	<i>Homo_sapiens</i> /GRCh37.74	H303N	0.003	Deleterious	Probably damaging	0.987
rs137854595	<i>Homo_sapiens</i> /GRCh37.74	H271N	0.003	Deleterious	Probably damaging	0.996
rs137854596	<i>Homo_sapiens</i> /GRCh37.74	P37R	0.002	Deleterious	Probably damaging	1
rs137854596	<i>Homo_sapiens</i> /GRCh37.74	P304R	0.004	Deleterious	Probably damaging	1
rs137854596	<i>Homo_sapiens</i> /GRCh37.74	P272R	0.005	Deleterious	Probably damaging	1
rs139670417	<i>Homo_sapiens</i> /GRCh37.74	R229H	0.004	Deleterious	Probably damaging	1
rs139670417	<i>Homo_sapiens</i> /GRCh37.74	R197H	0.004	Deleterious	Probably damaging	1
rs140677309	<i>Homo_sapiens</i> /GRCh37.74	S258C	0.013	Deleterious	Possibly damaging	0.648
rs140677309	<i>Homo_sapiens</i> /GRCh37.74	S525C	0.037	Deleterious	Probably damaging	0.965
rs140677309	<i>Homo_sapiens</i> /GRCh37.74	S493C	0.037	Deleterious	Possibly damaging	0.775
rs141798777	<i>Homo_sapiens</i> /GRCh37.74	L75M	0.035	Deleterious	Probably damaging	1
rs141798777	<i>Homo_sapiens</i> /GRCh37.74	L43M	0.036	Deleterious	Probably damaging	1
rs146275471	<i>Homo_sapiens</i> /GRCh37.74	R198Q	0.002	Deleterious	Probably damaging	1
rs146275471	<i>Homo_sapiens</i> /GRCh37.74	R166Q	0.002	Deleterious	Probably damaging	0.997
rs151344453	<i>Homo_sapiens</i> /GRCh37.74	Y41D	0.031	Deleterious	Probably damaging	1
rs151344454	<i>Homo_sapiens</i> /GRCh37.74	C537R	0	Deleterious	Probably damaging	1
rs151344454	<i>Homo_sapiens</i> /GRCh37.74	C270R	0	Deleterious	Probably damaging	1

rs151344454	<i>Homo_sapiens</i> /GRCh37.74	C505R	0	Deleterious	Probably damaging	1
rs151344456	<i>Homo_sapiens</i> /GRCh37.74	R54S	0.001	Deleterious	Probably damaging	0.996
rs151344456	<i>Homo_sapiens</i> /GRCh37.74	R22S	0.001	Deleterious	Probably damaging	0.997
rs151344457	<i>Homo_sapiens</i> /GRCh37.74	C59R	0.003	Deleterious	Probably damaging	0.999
rs151344457	<i>Homo_sapiens</i> /GRCh37.74	C27R	0.004	Deleterious	Probably damaging	0.999
rs151344458	<i>Homo_sapiens</i> /GRCh37.74	H119R	0	Deleterious	Probably damaging	1
rs151344458	<i>Homo_sapiens</i> /GRCh37.74	H87R	0	Deleterious	Probably damaging	1
rs151344459	<i>Homo_sapiens</i> /GRCh37.74	H209Q	0	Deleterious	Probably damaging	1
rs151344459	<i>Homo_sapiens</i> /GRCh37.74	H177Q	0	Deleterious	Probably damaging	1
rs151344460	<i>Homo_sapiens</i> /GRCh37.74	H222N	0	Deleterious	Probably damaging	0.998
rs151344460	<i>Homo_sapiens</i> /GRCh37.74	H190N	0	Deleterious	Probably damaging	1
rs151344460	<i>Homo_sapiens</i> /GRCh37.74	H222Y	0	Deleterious	Probably damaging	1
rs151344460	<i>Homo_sapiens</i> /GRCh37.74	H190Y	0	Deleterious	Probably damaging	1
rs151344462	<i>Homo_sapiens</i> /GRCh37.74	H222R	0	Deleterious	Probably damaging	1
rs151344462	<i>Homo_sapiens</i> /GRCh37.74	H190R	0	Deleterious	Probably damaging	1
rs151344465	<i>Homo_sapiens</i> /GRCh37.74	C212R	0.013	Deleterious	Probably damaging	1
rs151344465	<i>Homo_sapiens</i> /GRCh37.74	C244R	0.02	Deleterious	Probably damaging	1
rs151344466	<i>Homo_sapiens</i> /GRCh37.74	E42K	0.002	Deleterious	Probably damaging	1
rs151344466	<i>Homo_sapiens</i> /GRCh37.74	E309K	0.003	Deleterious	Probably damaging	1
rs151344466	<i>Homo_sapiens</i> /GRCh37.74	E277K	0.003	Deleterious	Probably damaging	1
rs151344467	<i>Homo_sapiens</i> /GRCh37.74	G322E	0	Deleterious	Probably damaging	1
rs151344467	<i>Homo_sapiens</i> /GRCh37.74	G55E	0	Deleterious	Probably damaging	1
rs151344467	<i>Homo_sapiens</i> /GRCh37.74	G290E	0	Deleterious	Probably damaging	1
rs151344468	<i>Homo_sapiens</i> /GRCh37.74	I325F	0.002	Deleterious	Probably damaging	0.99
rs151344468	<i>Homo_sapiens</i> /GRCh37.74	I58F	0.002	Deleterious	Probably damaging	0.987
rs151344468	<i>Homo_sapiens</i> /GRCh37.74	I293F	0.002	Deleterious	Probably damaging	0.993
rs151344469	<i>Homo_sapiens</i> /GRCh37.74	S66P	0.003	Deleterious	Probably damaging	1
rs151344469	<i>Homo_sapiens</i> /GRCh37.74	S333P	0.004	Deleterious	Probably damaging	1
rs151344469	<i>Homo_sapiens</i> /GRCh37.74	S301P	0.004	Deleterious	Probably damaging	1
rs151344470	<i>Homo_sapiens</i> /GRCh37.74	P339H	0	Deleterious	Probably damaging	0.994
rs151344470	<i>Homo_sapiens</i> /GRCh37.74	P72H	0	Deleterious	Probably damaging	1
rs151344470	<i>Homo_sapiens</i> /GRCh37.74	P307H	0	Deleterious	Probably damaging	0.999
rs151344471	<i>Homo_sapiens</i> /GRCh37.74	R89P	0.001	Deleterious	Probably damaging	1
rs151344471	<i>Homo_sapiens</i> /GRCh37.74	R356P	0.002	Deleterious	Probably damaging	1
rs151344471	<i>Homo_sapiens</i> /GRCh37.74	R324P	0.002	Deleterious	Probably damaging	1
rs151344472	<i>Homo_sapiens</i> /GRCh37.74	M138R	0.002	Deleterious	Probably damaging	0.997
rs151344472	<i>Homo_sapiens</i> /GRCh37.74	M373R	0.002	Deleterious	Probably damaging	0.999
rs151344472	<i>Homo_sapiens</i> /GRCh37.74	M405R	0.003	Deleterious	Probably damaging	0.999
rs151344473	<i>Homo_sapiens</i> /GRCh37.74	G408R	0.001	Deleterious	Probably damaging	1
rs151344473	<i>Homo_sapiens</i> /GRCh37.74	G141R	0.001	Deleterious	Probably damaging	1
rs151344473	<i>Homo_sapiens</i> /GRCh37.74	G376R	0.001	Deleterious	Probably damaging	1
rs151344474	<i>Homo_sapiens</i> /GRCh37.74	G408E	0.001	Deleterious	Probably damaging	1
rs151344474	<i>Homo_sapiens</i> /GRCh37.74	G141E	0.001	Deleterious	Probably damaging	1
rs151344474	<i>Homo_sapiens</i> /GRCh37.74	G376E	0.001	Deleterious	Probably damaging	1
rs151344475	<i>Homo_sapiens</i> /GRCh37.74	S422P	0.006	Deleterious	Probably damaging	1

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rs151344475	<i>Homo_sapiens</i> /GRCh37.74	S390P	0.007	Deleterious	Probably damaging	1
rs151344475	<i>Homo_sapiens</i> /GRCh37.74	S155P	0.013	Deleterious	Probably damaging	1
rs151344477	<i>Homo_sapiens</i> /GRCh37.74	W516C	0	Deleterious	Probably damaging	1
rs151344477	<i>Homo_sapiens</i> /GRCh37.74	W249C	0	Deleterious	Probably damaging	1
rs151344477	<i>Homo_sapiens</i> /GRCh37.74	W484C	0	Deleterious	Probably damaging	1
rs151344478	<i>Homo_sapiens</i> /GRCh37.74	V534D	0	Deleterious	Probably damaging	0.998
rs151344478	<i>Homo_sapiens</i> /GRCh37.74	V267D	0	Deleterious	Probably damaging	0.998
rs151344478	<i>Homo_sapiens</i> /GRCh37.74	V502D	0	Deleterious	Probably damaging	0.999
rs151344479	<i>Homo_sapiens</i> /GRCh37.74	R54M	0	Deleterious	Probably damaging	1
rs151344479	<i>Homo_sapiens</i> /GRCh37.74	R22M	0	Deleterious	Probably damaging	1
rs151344480	<i>Homo_sapiens</i> /GRCh37.74	A55D	0.001	Deleterious	Probably damaging	1
rs151344480	<i>Homo_sapiens</i> /GRCh37.74	A23D	0.002	Deleterious	Probably damaging	1
rs151344481	<i>Homo_sapiens</i> /GRCh37.74	A57E	0.001	Deleterious	Probably damaging	1
rs151344481	<i>Homo_sapiens</i> /GRCh37.74	A25E	0.001	Deleterious	Probably damaging	1
rs151344482	<i>Homo_sapiens</i> /GRCh37.74	H209R	0	Deleterious	Probably damaging	1
rs151344482	<i>Homo_sapiens</i> /GRCh37.74	H177R	0	Deleterious	Probably damaging	1
rs151344484	<i>Homo_sapiens</i> /GRCh37.74	H338Y	0.001	Deleterious	Probably damaging	1
rs151344484	<i>Homo_sapiens</i> /GRCh37.74	H71Y	0.001	Deleterious	Probably damaging	0.999
rs151344484	<i>Homo_sapiens</i> /GRCh37.74	H306Y	0.001	Deleterious	Probably damaging	1
rs151344485	<i>Homo_sapiens</i> /GRCh37.74	S312F	0.001	Deleterious	Probably damaging	1
rs151344485	<i>Homo_sapiens</i> /GRCh37.74	S344F	0.004	Deleterious	Probably damaging	1
rs151344485	<i>Homo_sapiens</i> /GRCh37.74	S77F	0.005	Deleterious	Probably damaging	1
rs151344486	<i>Homo_sapiens</i> /GRCh37.74	L420P	0	Deleterious	Probably damaging	1
rs151344486	<i>Homo_sapiens</i> /GRCh37.74	L153P	0	Deleterious	Probably damaging	1
rs151344486	<i>Homo_sapiens</i> /GRCh37.74	L388P	0	Deleterious	Probably damaging	1
rs151344487	<i>Homo_sapiens</i> /GRCh37.74	W516R	0	Deleterious	Probably damaging	0.996
rs151344487	<i>Homo_sapiens</i> /GRCh37.74	W249R	0	Deleterious	Probably damaging	0.999
rs151344487	<i>Homo_sapiens</i> /GRCh37.74	W484R	0	Deleterious	Probably damaging	0.999
rs151344488	<i>Homo_sapiens</i> /GRCh37.74	C59W	0.001	Deleterious	Probably damaging	1
rs151344488	<i>Homo_sapiens</i> /GRCh37.74	C27W	0.027	Deleterious	Probably damaging	1
rs151344489	<i>Homo_sapiens</i> /GRCh37.74	T307P	0.002	Deleterious	Probably damaging	0.999
rs151344489	<i>Homo_sapiens</i> /GRCh37.74	T40P	0.002	Deleterious	Probably damaging	0.997
rs151344489	<i>Homo_sapiens</i> /GRCh37.74	T275P	0.002	Deleterious	Probably damaging	0.999
rs151344490	<i>Homo_sapiens</i> /GRCh37.74	L505R	0.001	Deleterious	Probably damaging	0.999
rs151344490	<i>Homo_sapiens</i> /GRCh37.74	L238R	0.001	Deleterious	Probably damaging	1
rs151344490	<i>Homo_sapiens</i> /GRCh37.74	L473R	0.001	Deleterious	Probably damaging	1
rs151344491	<i>Homo_sapiens</i> /GRCh37.74	G179R	0	Deleterious	Probably damaging	1
rs151344491	<i>Homo_sapiens</i> /GRCh37.74	G147R	0	Deleterious	Probably damaging	1
rs151344492	<i>Homo_sapiens</i> /GRCh37.74	L546P	0	Deleterious	Probably damaging	1
rs151344492	<i>Homo_sapiens</i> /GRCh37.74	L279P	0	Deleterious	Probably damaging	1
rs151344492	<i>Homo_sapiens</i> /GRCh37.74	L514P	0	Deleterious	Probably damaging	1
rs151344493	<i>Homo_sapiens</i> /GRCh37.74	S193F	0.001	Deleterious	Probably damaging	1
rs151344493	<i>Homo_sapiens</i> /GRCh37.74	S161F	0.002	Deleterious	Probably damaging	1
rs151344495	<i>Homo_sapiens</i> /GRCh37.74	L342Q	0.001	Deleterious	Probably damaging	0.999
rs151344495	<i>Homo_sapiens</i> /GRCh37.74	L75Q	0.001	Deleterious	Probably damaging	1
rs151344495	<i>Homo_sapiens</i> /GRCh37.74	L310Q	0.001	Deleterious	Probably damaging	1

rs151344496	<i>Homo_sapiens</i> /GRCh37.74	F205I	0	Deleterious	Probably damaging	1
rs151344496	<i>Homo_sapiens</i> /GRCh37.74	F173I	0	Deleterious	Probably damaging	1
rs151344497	<i>Homo_sapiens</i> /GRCh37.74	T178P	0.001	Deleterious	Probably damaging	1
rs151344497	<i>Homo_sapiens</i> /GRCh37.74	T146P	0.001	Deleterious	Probably damaging	1
rs151344498	<i>Homo_sapiens</i> /GRCh37.74	Q231P	0.006	Deleterious	Probably damaging	0.992
rs151344498	<i>Homo_sapiens</i> /GRCh37.74	Q199P	0.006	Deleterious	Probably damaging	0.997
rs200614534	<i>Homo_sapiens</i> /GRCh37.74	V407A	0.001	Deleterious	Probably damaging	0.995
rs200614534	<i>Homo_sapiens</i> /GRCh37.74	V140A	0.002	Deleterious	Probably damaging	0.988
rs200614534	<i>Homo_sapiens</i> /GRCh37.74	V375A	0.002	Deleterious	Probably damaging	0.994
rs267606451	<i>Homo_sapiens</i> /GRCh37.74	S66F	0	Deleterious	Probably damaging	1
rs267606451	<i>Homo_sapiens</i> /GRCh37.74	S333F	0.001	Deleterious	Probably damaging	1
rs267606451	<i>Homo_sapiens</i> /GRCh37.74	S301F	0.001	Deleterious	Probably damaging	1

**Table 2:** Illustrate I-mutant 3 prediction results for protein activity.

SNP	Organism/Build	Amino Acid Change	WT	MT	DDG	RI	I Mutant Result
rs137854585	<i>Homo_sapiens</i> /GRCh37.74	P415H	P	H	-1.69	9	Decrease
rs137854585	<i>Homo_sapiens</i> /GRCh37.74	P148H	P	H	-1.69	9	Decrease
rs137854585	<i>Homo_sapiens</i> /GRCh37.74	P383H	P	H	-1.69	9	Decrease
rs137854585	<i>Homo_sapiens</i> /GRCh37.74	P415L	P	L	-0.77	6	Decrease
rs137854585	<i>Homo_sapiens</i> /GRCh37.74	P148L	P	L	-0.77	6	Decrease
rs137854585	<i>Homo_sapiens</i> /GRCh37.74	P383L	P	L	-0.77	6	Decrease
rs137854586	<i>Homo_sapiens</i> /GRCh37.74	G389E	G	E	-0.69	3	Decrease
rs137854586	<i>Homo_sapiens</i> /GRCh37.74	G122E	G	E	-0.69	3	Decrease
rs137854586	<i>Homo_sapiens</i> /GRCh37.74	G357E	G	E	-0.69	3	Decrease
rs137854586	<i>Homo_sapiens</i> /GRCh37.74	G389A	G	A	-0.93	8	Decrease
rs137854586	<i>Homo_sapiens</i> /GRCh37.74	G122A	G	A	-0.93	8	Decrease
rs137854586	<i>Homo_sapiens</i> /GRCh37.74	G357A	G	A	-0.93	8	Decrease
rs137854587	<i>Homo_sapiens</i> /GRCh37.74	H209Y	H	Y	0.49	8	Increase
rs137854587	<i>Homo_sapiens</i> /GRCh37.74	H177Y	H	Y	0.49	8	Increase
rs137854589	<i>Homo_sapiens</i> /GRCh37.74	C212Y	C	Y	-0.15	0	Decrease
rs137854589	<i>Homo_sapiens</i> /GRCh37.74	C244Y	C	Y	-0.15	0	Decrease
rs137854591	<i>Homo_sapiens</i> /GRCh37.74	H101R	H	R	-0.09	2	Decrease
rs137854591	<i>Homo_sapiens</i> /GRCh37.74	H69R	H	R	-0.09	2	Decrease
rs137854593	<i>Homo_sapiens</i> /GRCh37.74	D500G	D	G	-0.57	2	Decrease
rs137854593	<i>Homo_sapiens</i> /GRCh37.74	D233G	D	G	-0.57	2	Decrease
rs137854593	<i>Homo_sapiens</i> /GRCh37.74	D468G	D	G	-0.57	2	Decrease
rs137854594	<i>Homo_sapiens</i> /GRCh37.74	H101Y	H	Y	0.24	3	Increase
rs137854594	<i>Homo_sapiens</i> /GRCh37.74	H69Y	H	Y	0.24	3	Increase
rs137854595	<i>Homo_sapiens</i> /GRCh37.74	H36N	H	N	-0.38	3	Decrease
rs137854595	<i>Homo_sapiens</i> /GRCh37.74	H303N	H	N	-0.38	3	Decrease
rs137854595	<i>Homo_sapiens</i> /GRCh37.74	H271N	H	N	-0.38	3	Decrease
rs137854596	<i>Homo_sapiens</i> /GRCh37.74	P37R	P	R	-0.65	4	Decrease
rs137854596	<i>Homo_sapiens</i> /GRCh37.74	P304R	P	R	-0.65	4	Decrease
rs137854596	<i>Homo_sapiens</i> /GRCh37.74	P272R	P	R	-0.65	4	Decrease
rs139670417	<i>Homo_sapiens</i> /GRCh37.74	R229H	R	H	-1.07	8	Decrease
rs139670417	<i>Homo_sapiens</i> /GRCh37.74	R197H	R	H	-1.07	8	Decrease

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rs140677309	<i>Homo_sapiens</i> /GRCh37.74	S258C	S	C	-0.54	3	Decrease
rs140677309	<i>Homo_sapiens</i> /GRCh37.74	S525C	S	C	-0.54	3	Decrease
rs140677309	<i>Homo_sapiens</i> /GRCh37.74	S493C	S	C	-0.54	3	Decrease
rs141798777	<i>Homo_sapiens</i> /GRCh37.74	L75M	L	M	-1.09	4	Decrease
rs141798777	<i>Homo_sapiens</i> /GRCh37.74	L43M	L	M	-1.09	4	Decrease
rs146275471	<i>Homo_sapiens</i> /GRCh37.74	R198Q	R	Q	-1.22	8	Decrease
rs146275471	<i>Homo_sapiens</i> /GRCh37.74	R166Q	R	Q	-1.22	8	Decrease
rs151344453	<i>Homo_sapiens</i> /GRCh37.74	Y41D	Y	D	-1.25	4	Decrease
rs151344454	<i>Homo_sapiens</i> /GRCh37.74	C537R	C	R	-0.31	4	Decrease
rs151344454	<i>Homo_sapiens</i> /GRCh37.74	C270R	C	R	-0.31	4	Decrease
rs151344454	<i>Homo_sapiens</i> /GRCh37.74	C505R	C	R	-0.31	4	Decrease
rs151344456	<i>Homo_sapiens</i> /GRCh37.74	R54S	R	S	-0.66	7	Decrease
rs151344456	<i>Homo_sapiens</i> /GRCh37.74	R22S	R	S	-0.66	7	Decrease
rs151344457	<i>Homo_sapiens</i> /GRCh37.74	C59R	C	R	-0.25	1	Decrease
rs151344457	<i>Homo_sapiens</i> /GRCh37.74	C27R	C	R	-0.25	1	Decrease
rs151344458	<i>Homo_sapiens</i> /GRCh37.74	H119R	H	R	-0.02	4	Decrease
rs151344458	<i>Homo_sapiens</i> /GRCh37.74	H87R	H	R	-0.02	4	Decrease
rs151344459	<i>Homo_sapiens</i> /GRCh37.74	H209Q	H	Q	-0.15	3	Decrease
rs151344459	<i>Homo_sapiens</i> /GRCh37.74	H177Q	H	Q	-0.15	3	Decrease
rs151344460	<i>Homo_sapiens</i> /GRCh37.74	H222N	H	N	-0.64	3	Decrease
rs151344460	<i>Homo_sapiens</i> /GRCh37.74	H190N	H	N	-0.64	3	Decrease
rs151344460	<i>Homo_sapiens</i> /GRCh37.74	H222Y	H	Y	0.15	4	Increase
rs151344460	<i>Homo_sapiens</i> /GRCh37.74	H190Y	H	Y	0.15	4	Increase
rs151344462	<i>Homo_sapiens</i> /GRCh37.74	H222R	H	R	-0.16	4	Decrease
rs151344462	<i>Homo_sapiens</i> /GRCh37.74	H190R	H	R	-0.16	4	Decrease
rs151344465	<i>Homo_sapiens</i> /GRCh37.74	C212R	C	R	-0.16	2	Decrease
rs151344465	<i>Homo_sapiens</i> /GRCh37.74	C244R	C	R	-0.16	2	Decrease
rs151344466	<i>Homo_sapiens</i> /GRCh37.74	E42K	E	K	-0.35	7	Decrease
rs151344466	<i>Homo_sapiens</i> /GRCh37.74	E309K	E	K	-0.35	7	Decrease
rs151344466	<i>Homo_sapiens</i> /GRCh37.74	E277K	E	K	-0.35	7	Decrease
rs151344467	<i>Homo_sapiens</i> /GRCh37.74	G322E	G	E	-0.8	4	Decrease
rs151344467	<i>Homo_sapiens</i> /GRCh37.74	G55E	G	E	-0.8	4	Decrease
rs151344467	<i>Homo_sapiens</i> /GRCh37.74	G290E	G	E	-0.8	4	Decrease
rs151344468	<i>Homo_sapiens</i> /GRCh37.74	I325F	I	F	-1.19	4	Decrease
rs151344468	<i>Homo_sapiens</i> /GRCh37.74	I58F	I	F	-1.19	4	Decrease
rs151344468	<i>Homo_sapiens</i> /GRCh37.74	I293F	I	F	-1.19	4	Decrease
rs151344469	<i>Homo_sapiens</i> /GRCh37.74	S66P	S	P	-0.18	0	Decrease
rs151344469	<i>Homo_sapiens</i> /GRCh37.74	S333P	S	P	-0.18	0	Decrease
rs151344469	<i>Homo_sapiens</i> /GRCh37.74	S301P	S	P	-0.18	0	Decrease
rs151344470	<i>Homo_sapiens</i> /GRCh37.74	P339H	P	H	-1.32	7	Decrease
rs151344470	<i>Homo_sapiens</i> /GRCh37.74	P72H	P	H	-1.32	7	Decrease
rs151344470	<i>Homo_sapiens</i> /GRCh37.74	P307H	P	H	-1.32	7	Decrease
rs151344471	<i>Homo_sapiens</i> /GRCh37.74	R89P	R	P	-0.66	6	Decrease
rs151344471	<i>Homo_sapiens</i> /GRCh37.74	R356P	R	P	-0.66	6	Decrease
rs151344471	<i>Homo_sapiens</i> /GRCh37.74	R324P	R	P	-0.66	6	Decrease
rs151344472	<i>Homo_sapiens</i> /GRCh37.74	M138R	M	R	-0.62	2	Decrease

rs151344472	<i>Homo_sapiens</i> /GRCh37.74	M373R	M	R	-0.62	2	Decrease
rs151344472	<i>Homo_sapiens</i> /GRCh37.74	M405R	M	R	-0.62	2	Decrease
rs151344473	<i>Homo_sapiens</i> /GRCh37.74	G408R	G	R	-0.51	3	Decrease
rs151344473	<i>Homo_sapiens</i> /GRCh37.74	G141R	G	R	-0.51	3	Decrease
rs151344473	<i>Homo_sapiens</i> /GRCh37.74	G376R	G	R	-0.51	3	Decrease
rs151344474	<i>Homo_sapiens</i> /GRCh37.74	G408E	G	E	-0.54	1	Increase
rs151344474	<i>Homo_sapiens</i> /GRCh37.74	G141E	G	E	-0.54	1	Increase
rs151344474	<i>Homo_sapiens</i> /GRCh37.74	G376E	G	E	-0.54	1	Increase
rs151344475	<i>Homo_sapiens</i> /GRCh37.74	S422P	S	P	-0.31	1	Increase
rs151344475	<i>Homo_sapiens</i> /GRCh37.74	S390P	S	P	-0.31	1	Increase
rs151344475	<i>Homo_sapiens</i> /GRCh37.74	S155P	S	P	-0.31	1	Increase
rs151344477	<i>Homo_sapiens</i> /GRCh37.74	W516C	W	C	-1.77	9	Decrease
rs151344477	<i>Homo_sapiens</i> /GRCh37.74	W249C	W	C	-1.77	9	Decrease
rs151344477	<i>Homo_sapiens</i> /GRCh37.74	W484C	W	C	-1.77	9	Decrease
rs151344478	<i>Homo_sapiens</i> /GRCh37.74	V534D	V	D	-1.49	9	Decrease
rs151344478	<i>Homo_sapiens</i> /GRCh37.74	V267D	V	D	-1.49	9	Decrease
rs151344478	<i>Homo_sapiens</i> /GRCh37.74	V502D	V	D	-1.49	9	Decrease
rs151344479	<i>Homo_sapiens</i> /GRCh37.74	R54M	R	M	-0.2	1	Decrease
rs151344479	<i>Homo_sapiens</i> /GRCh37.74	R22M	R	M	-0.2	1	Decrease
rs151344480	<i>Homo_sapiens</i> /GRCh37.74	A55D	A	D	-0.58	6	Decrease
rs151344480	<i>Homo_sapiens</i> /GRCh37.74	A23D	A	D	-0.58	6	Decrease
rs151344481	<i>Homo_sapiens</i> /GRCh37.74	A57E	A	E	-0.36	4	Decrease
rs151344481	<i>Homo_sapiens</i> /GRCh37.74	A25E	A	E	-0.36	4	Decrease
rs151344482	<i>Homo_sapiens</i> /GRCh37.74	H209R	H	R	0.12	1	Decrease
rs151344482	<i>Homo_sapiens</i> /GRCh37.74	H177R	H	R	0.12	1	Decrease
rs151344484	<i>Homo_sapiens</i> /GRCh37.74	H338Y	H	Y	0.47	7	Increase
rs151344484	<i>Homo_sapiens</i> /GRCh37.74	H71Y	H	Y	0.47	7	Increase
rs151344484	<i>Homo_sapiens</i> /GRCh37.74	H306Y	H	Y	0.47	7	Increase
rs151344485	<i>Homo_sapiens</i> /GRCh37.74	S312F	S	F	0.4	5	Increase
rs151344485	<i>Homo_sapiens</i> /GRCh37.74	S344F	S	F	0.4	5	Increase
rs151344485	<i>Homo_sapiens</i> /GRCh37.74	S77F	S	F	0.4	5	Increase
rs151344486	<i>Homo_sapiens</i> /GRCh37.74	L420P	L	P	-1.64	7	Decrease
rs151344486	<i>Homo_sapiens</i> /GRCh37.74	L153P	L	P	-1.64	7	Decrease
rs151344486	<i>Homo_sapiens</i> /GRCh37.74	L388P	L	P	-1.64	7	Decrease
rs151344487	<i>Homo_sapiens</i> /GRCh37.74	W516R	W	R	-1.3	9	Decrease
rs151344487	<i>Homo_sapiens</i> /GRCh37.74	W249R	W	R	-1.3	9	Decrease
rs151344487	<i>Homo_sapiens</i> /GRCh37.74	W484R	W	R	-1.3	9	Decrease
rs151344488	<i>Homo_sapiens</i> /GRCh37.74	C59W	C	W	-0.14	2	Decrease
rs151344488	<i>Homo_sapiens</i> /GRCh37.74	C27W	C	W	-0.14	2	Decrease
rs151344489	<i>Homo_sapiens</i> /GRCh37.74	T307P	T	P	-0.59	6	Decrease
rs151344489	<i>Homo_sapiens</i> /GRCh37.74	T40P	T	P	-0.59	6	Decrease
rs151344489	<i>Homo_sapiens</i> /GRCh37.74	T275P	T	P	-0.59	6	Decrease
rs151344490	<i>Homo_sapiens</i> /GRCh37.74	L505R	L	R	-1.63	8	Decrease
rs151344490	<i>Homo_sapiens</i> /GRCh37.74	L238R	L	R	-1.63	8	Decrease
rs151344490	<i>Homo_sapiens</i> /GRCh37.74	L473R	L	R	-1.63	8	Decrease
rs151344491	<i>Homo_sapiens</i> /GRCh37.74	G179R	G	R	-0.44	5	Decrease

rs151344491	<i>Homo_sapiens</i> /GRCh37.74	G147R	G	R	-0.44	5	Decrease
rs151344492	<i>Homo_sapiens</i> /GRCh37.74	L546P	L	P	-1.32	5	Decrease
rs151344492	<i>Homo_sapiens</i> /GRCh37.74	L279P	L	P	-1.32	5	Decrease
rs151344492	<i>Homo_sapiens</i> /GRCh37.74	L514P	L	P	-1.32	5	Decrease
rs151344493	<i>Homo_sapiens</i> /GRCh37.74	S193F	S	F	-0.03	1	Decrease
rs151344493	<i>Homo_sapiens</i> /GRCh37.74	S161F	S	F	-0.03	1	Decrease
rs151344495	<i>Homo_sapiens</i> /GRCh37.74	L342Q	L	Q	-1.81	8	Decrease
rs151344495	<i>Homo_sapiens</i> /GRCh37.74	L75Q	L	Q	-1.81	8	Decrease
rs151344495	<i>Homo_sapiens</i> /GRCh37.74	L310Q	L	Q	-1.81	8	Decrease
rs151344496	<i>Homo_sapiens</i> /GRCh37.74	F205I	F	I	-0.84	8	Decrease
rs151344496	<i>Homo_sapiens</i> /GRCh37.74	F173I	F	I	-0.84	8	Decrease
rs151344497	<i>Homo_sapiens</i> /GRCh37.74	T178P	T	P	-0.38	5	Decrease
rs151344497	<i>Homo_sapiens</i> /GRCh37.74	T146P	T	P	-0.38	5	Decrease
rs151344498	<i>Homo_sapiens</i> /GRCh37.74	Q231P	Q	P	-0.46	5	Decrease
rs151344498	<i>Homo_sapiens</i> /GRCh37.74	Q199P	Q	P	-0.46	5	Decrease
rs200614534	<i>Homo_sapiens</i> /GRCh37.74	V407A	V	A	-2.02	10	Decrease
rs200614534	<i>Homo_sapiens</i> /GRCh37.74	V140A	V	A	-2.02	10	Decrease
rs200614534	<i>Homo_sapiens</i> /GRCh37.74	V375A	V	A	-2.02	10	Decrease
rs267606451	<i>Homo_sapiens</i> /GRCh37.74	S66F	S	F	0.35	4	Increase
rs267606451	<i>Homo_sapiens</i> /GRCh37.74	S333F	S	F	0.35	4	Increase
rs267606451	<i>Homo_sapiens</i> /GRCh37.74	S301F	S	F	0.35	4	Increase

## Methods

Chronic granulomatous disease sequence (CGD) was retrieved from NCBI [https://www.ncbi.nlm.nih.gov/projects/SNP/snp\\_ref.cgi?geneId=1536;rs141756032](https://www.ncbi.nlm.nih.gov/projects/SNP/snp_ref.cgi?geneId=1536;rs141756032) [*Homo sapiens*], in chromosome X: 37804069; Gene: CYBB.

### Sift prediction

(SIFT - Predict effects of non synonymous /missense variants) (<http://sift.bii.a-star.edu.sg/>) SIFT dbSNP 138 was selected from batch tools from SIFT Sorting Intolerant From Tolerant software to predict whether an amino acid substitution affects protein function, based on the sequence homology and the physical properties of amino acids. SIFT can be applied to naturally occurring non synonymous polymorphisms and laboratory-induced missense mutations.

### PolyPhen-2 (Polymorphism phenotyping v2)

PolyPhen-2 prediction of functional effects of human nsSNPs (<http://genetics.bwh.harvard.edu/pph2/index.shtml>) was used to predict the impact of an amino acid substitution on the structure and function of a human protein using straight forward physical and comparative consideration [9-12].

### I-Mutant suite

I mutant.3 (<http://gpcr2.biocomp.unibo.it/cgi/predictors/IMutant3.0/I-Mutant3.0.cgi>) was used to predict the effect of single point protein mutation with disease association from Protein Sequence [13-15].

### SNPs and GO

SNPs & GO (<http://snps.biofold.org/snps-and-go/snps-and-go.html>) was used to predicting a disease associated variations by GO terms through SVM-based classifier to confirm SNPs results, by putting protein sequence, profile and functional information to give output inform of disease/neutral with RI & scores [16-21].

## Results and Discussions

141 out of 150 showed probably damaging by polyphen-2, while 3 showed possibly damaging and 6 were benign; that is why considered out of this study, all of them were considered deleterious by sift prediction including those showed benign predictions.

All those SNPs below showed deleterious, probably damaging with score predictions equal or slightly less than 1 according to sift & polyphen-2 prediction sequential (see Table 1) rs137854585, rs137854586, rs137854587, rs137854589, rs137854591, rs137854593, rs137854594, rs137854595, rs137854596, rs139670417, rs141798777, rs146275471, rs151344453, rs151344454, rs151344456, rs151344457, rs151344458, rs151344459, rs151344460, rs151344462, rs151344465, rs151344466, rs151344467, rs151344468, rs151344469, rs151344470, rs151344471, rs151344472, rs151344473, rs151344474, rs151344475, rs151344477, rs151344478, rs151344479, rs151344480, rs151344481, rs151344482, rs151344484, rs151344485, rs151344486, rs151344487, rs151344488, rs151344489, rs151344490, rs151344491, rs151344492, rs151344493, rs151344495, rs151344496, rs151344497, rs151344498, rs200614534, rs267606451; except rs140677309 SNPs that showed both probably & possibly damaging predictions.

### I mutant-3 prediction

The total number of 150 SNPs showed 21 with increased protein activity while the remaining 129 showed decreased in protein activity, also the same SNPs had the same wide types but different mutant



**Table 3:** Illustrate SNPs & GO predictions for CGD.

SNP	Organism/Build	Amino acid change	PhD-SNP prediction	PhD-SNP IR	PhD-SNP probability	SNPS & GO prediction	SNPS & GO IR	SNPS & GO probability
rs137854585	<i>Homo_sapiens</i> /GRCh37.74	P415H	Disease	9	0.946	Disease	7	0.852
rs137854585	<i>Homo_sapiens</i> /GRCh37.74	P148H	Disease	9	0.945	Disease	7	0.851
rs137854585	<i>Homo_sapiens</i> /GRCh37.74	P383H	Disease	9	0.946	Disease	7	0.852
rs137854585	<i>Homo_sapiens</i> /GRCh37.74	P415L	Disease	9	0.952	Disease	8	0.897
rs137854585	<i>Homo_sapiens</i> /GRCh37.74	P148L	Disease	9	0.95	Disease	8	0.896
rs137854585	<i>Homo_sapiens</i> /GRCh37.74	P383L	Disease	9	0.951	Disease	8	0.896
rs137854586	<i>Homo_sapiens</i> /GRCh37.74	G389E	Disease	8	0.917	Disease	8	0.882
rs137854586	<i>Homo_sapiens</i> /GRCh37.74	G122E	Disease	8	0.917	Disease	8	0.882
rs137854586	<i>Homo_sapiens</i> /GRCh37.74	G357E	Disease	8	0.918	Disease	8	0.883
rs137854586	<i>Homo_sapiens</i> /GRCh37.74	G389A	Disease	7	0.833	Disease	6	0.819
rs137854586	<i>Homo_sapiens</i> /GRCh37.74	G122A	Disease	7	0.834	Disease	6	0.819
rs137854586	<i>Homo_sapiens</i> /GRCh37.74	G357A	Disease	7	0.835	Disease	6	0.821
rs137854587	<i>Homo_sapiens</i> /GRCh37.74	H209Y	Disease	9	0.974	Disease	8	0.89
rs137854587	<i>Homo_sapiens</i> /GRCh37.74	H177Y	Disease	9	0.974	Disease	8	0.89
rs137854589	<i>Homo_sapiens</i> /GRCh37.74	C212Y	Disease	8	0.894	Disease	1	0.563
rs137854589	<i>Homo_sapiens</i> /GRCh37.74	C244Y	Disease	8	0.891	Disease	1	0.555
rs137854591	<i>Homo_sapiens</i> /GRCh37.74	H101R	Disease	9	0.933	Disease	8	0.911
rs137854591	<i>Homo_sapiens</i> /GRCh37.74	H69R	Disease	9	0.933	Disease	8	0.91
rs137854593	<i>Homo_sapiens</i> /GRCh37.74	D500G	Disease	5	0.852	Disease	7	0.728
rs137854593	<i>Homo_sapiens</i> /GRCh37.74	D233G	Disease	7	0.849	Disease	4	0.721
rs137854593	<i>Homo_sapiens</i> /GRCh37.74	D468G	Disease	7	0.851	Disease	5	0.726
rs137854594	<i>Homo_sapiens</i> /GRCh37.74	H101Y	Disease	9	0.93	Disease	7	0.862
rs137854594	<i>Homo_sapiens</i> /GRCh37.74	H69Y	Disease	9	0.929	Disease	7	0.862
rs137854595	<i>Homo_sapiens</i> /GRCh37.74	H36N	Disease	0	0.523	Disease	3	0.67
rs137854595	<i>Homo_sapiens</i> /GRCh37.74	H303N	Disease	0	0.517	Disease	3	0.667
rs137854595	<i>Homo_sapiens</i> /GRCh37.74	H271N	Disease	0	0.519	Disease	3	0.668
rs137854596	<i>Homo_sapiens</i> /GRCh37.74	P37R	Disease	8	0.889	Disease	6	0.815
rs137854596	<i>Homo_sapiens</i> /GRCh37.74	P304R	Disease	8	0.89	Disease	6	0.817
rs137854596	<i>Homo_sapiens</i> /GRCh37.74	P272R	Disease	8	0.889	Disease	6	0.816
rs139670417	<i>Homo_sapiens</i> /GRCh37.74	R229H	Disease	3	0.635	Neutral	6	0.204
rs139670417	<i>Homo_sapiens</i> /GRCh37.74	R197H	Disease	3	0.637	Neutral	6	0.205
rs140677309	<i>Homo_sapiens</i> /GRCh37.74	S258C	Neutral	1	0.463	Neutral	2	0.403
rs140677309	<i>Homo_sapiens</i> /GRCh37.74	S525C	Neutral	0	0.483	Neutral	2	0.416
rs140677309	<i>Homo_sapiens</i> /GRCh37.74	S493C	Neutral	1	0.47	Neutral	2	0.412
rs141798777	<i>Homo_sapiens</i> /GRCh37.74	L75M	Neutral	1	0.456	Neutral	7	0.133
rs141798777	<i>Homo_sapiens</i> /GRCh37.74	L43M	Neutral	1	0.441	Neutral	7	0.129
rs146275471	<i>Homo_sapiens</i> /GRCh37.74	R198Q	Disease	9	0.94	Disease	7	0.87
rs146275471	<i>Homo_sapiens</i> /GRCh37.74	R166Q	Disease	9	0.94	Disease	7	0.87
rs151344453	<i>Homo_sapiens</i> /GRCh37.74	Y41D	Disease	7	0.852	Disease	7	0.829
rs151344454	<i>Homo_sapiens</i> /GRCh37.74	C537R	Disease	9	0.964	Disease	8	0.919
rs151344454	<i>Homo_sapiens</i> /GRCh37.74	C270R	Disease	9	0.964	Disease	8	0.918
rs151344454	<i>Homo_sapiens</i> /GRCh37.74	C505R	Disease	9	0.964	Disease	8	0.918
rs151344456	<i>Homo_sapiens</i> /GRCh37.74	R54S	Disease	7	0.849	Disease	4	0.703

rs151344456	<i>Homo_sapiens</i> /GRCh37.74	R22S	Disease	8	0.899	Disease	6	0.781
rs151344457	<i>Homo_sapiens</i> /GRCh37.74	C59R	Disease	8	0.902	Disease	7	0.852
rs151344457	<i>Homo_sapiens</i> /GRCh37.74	C27R	Disease	8	0.899	Disease	7	0.848
rs151344458	<i>Homo_sapiens</i> /GRCh37.74	H119R	Disease	9	0.937	Disease	8	0.909
rs151344458	<i>Homo_sapiens</i> /GRCh37.74	H87R	Disease	9	0.937	Disease	8	0.908
rs151344459	<i>Homo_sapiens</i> /GRCh37.74	H209Q	Disease	9	0.95	Disease	7	0.827
rs151344459	<i>Homo_sapiens</i> /GRCh37.74	H177Q	Disease	9	0.949	Disease	7	0.828
rs151344460	<i>Homo_sapiens</i> /GRCh37.74	H222N	Disease	9	0.957	Disease	7	0.869
rs151344460	<i>Homo_sapiens</i> /GRCh37.74	H190N	Disease	9	0.956	Disease	7	0.868
rs151344460	<i>Homo_sapiens</i> /GRCh37.74	H222Y	Disease	9	0.972	Disease	8	0.909
rs151344460	<i>Homo_sapiens</i> /GRCh37.74	H190Y	Disease	9	0.971	Disease	8	0.908
rs151344462	<i>Homo_sapiens</i> /GRCh37.74	H222R	Disease	9	0.968	Disease	9	0.928
rs151344462	<i>Homo_sapiens</i> /GRCh37.74	H190R	Disease	9	0.967	Disease	9	0.928
rs151344465	<i>Homo_sapiens</i> /GRCh37.74	C212R	Disease	7	0.874	Disease	1	0.544
rs151344465	<i>Homo_sapiens</i> /GRCh37.74	C244R	Disease	7	0.871	Disease	1	0.537
rs151344466	<i>Homo_sapiens</i> /GRCh37.74	E42K	Disease	4	0.683	Disease	4	0.714
rs151344466	<i>Homo_sapiens</i> /GRCh37.74	E309K	Disease	4	0.704	Disease	5	0.727
rs151344466	<i>Homo_sapiens</i> /GRCh37.74	E277K	Disease	4	0.702	Disease	5	0.725
rs151344467	<i>Homo_sapiens</i> /GRCh37.74	G322E	Disease	7	0.845	Disease	5	0.742
rs151344467	<i>Homo_sapiens</i> /GRCh37.74	G55E	Disease	7	0.842	Disease	5	0.737
rs151344467	<i>Homo_sapiens</i> /GRCh37.74	G290E	Disease	7	0.844	Disease	5	0.74
rs151344468	<i>Homo_sapiens</i> /GRCh37.74	I325F	Disease	5	0.735	Neutral	0	0.486
rs151344468	<i>Homo_sapiens</i> /GRCh37.74	I58F	Disease	5	0.732	Neutral	0	0.481
rs151344468	<i>Homo_sapiens</i> /GRCh37.74	I293F	Disease	5	0.738	Neutral	0	0.488
rs151344469	<i>Homo_sapiens</i> /GRCh37.74	S66P	Disease	9	0.938	Disease	8	0.878
rs151344469	<i>Homo_sapiens</i> /GRCh37.74	S333P	Disease	9	0.94	Disease	8	0.88
rs151344469	<i>Homo_sapiens</i> /GRCh37.74	S301P	Disease	9	0.939	Disease	8	0.879
rs151344470	<i>Homo_sapiens</i> /GRCh37.74	P339H	Disease	6	0.789	Neutral	0	0.477
rs151344470	<i>Homo_sapiens</i> /GRCh37.74	P72H	Disease	6	0.783	Neutral	1	0.471
rs151344470	<i>Homo_sapiens</i> /GRCh37.74	P307H	Disease	6	0.788	Neutral	0	0.476
rs151344471	<i>Homo_sapiens</i> /GRCh37.74	R89P	Disease	9	0.953	Disease	8	0.923
rs151344471	<i>Homo_sapiens</i> /GRCh37.74	R356P	Disease	9	0.945	Disease	8	0.925
rs151344471	<i>Homo_sapiens</i> /GRCh37.74	R324P	Disease	9	0.954	Disease	8	0.924
rs151344472	<i>Homo_sapiens</i> /GRCh37.74	M138R	Disease	7	0.863	Disease	7	0.853
rs151344472	<i>Homo_sapiens</i> /GRCh37.74	M373R	Disease	7	0.856	Disease	7	0.851
rs151344472	<i>Homo_sapiens</i> /GRCh37.74	M405R	Disease	7	0.856	Disease	7	0.851
rs151344473	<i>Homo_sapiens</i> /GRCh37.74	G408R	Disease	9	0.948	Disease	7	0.872
rs151344473	<i>Homo_sapiens</i> /GRCh37.74	G141R	Disease	9	0.947	Disease	7	0.87
rs151344473	<i>Homo_sapiens</i> /GRCh37.74	G376R	Disease	9	0.947	Disease	7	0.871
rs151344474	<i>Homo_sapiens</i> /GRCh37.74	G408E	Disease	9	0.939	Disease	7	0.863
rs151344474	<i>Homo_sapiens</i> /GRCh37.74	G141E	Disease	9	0.938	Disease	7	0.861
rs151344474	<i>Homo_sapiens</i> /GRCh37.74	G376E	Disease	9	0.938	Disease	7	0.862
rs151344475	<i>Homo_sapiens</i> /GRCh37.74	S422P	Disease	9	0.941	Disease	8	0.9
rs151344475	<i>Homo_sapiens</i> /GRCh37.74	S390P	Disease	9	0.939	Disease	8	0.899
rs151344475	<i>Homo_sapiens</i> /GRCh37.74	S155P	Disease	9	0.937	Disease	8	0.896
rs151344477	<i>Homo_sapiens</i> /GRCh37.74	W516C	Disease	8	0.916	Disease	7	0.857

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rs151344477	<i>Homo_sapiens</i> /GRCh37.74	W249C	Disease	8	0.91	Disease	7	0.856
rs151344477	<i>Homo_sapiens</i> /GRCh37.74	W484C	Disease	8	0.916	Disease	7	0.856
rs151344478	<i>Homo_sapiens</i> /GRCh37.74	V534D	Disease	9	0.936	Disease	8	0.892
rs151344478	<i>Homo_sapiens</i> /GRCh37.74	V267D	Disease	9	0.935	Disease	8	0.891
rs151344478	<i>Homo_sapiens</i> /GRCh37.74	V502D	Disease	9	0.936	Disease	8	0.892
rs151344479	<i>Homo_sapiens</i> /GRCh37.74	R54M	Disease	7	0.827	Disease	2	0.595
rs151344479	<i>Homo_sapiens</i> /GRCh37.74	R22M	Disease	7	0.862	Disease	3	0.668
rs151344480	<i>Homo_sapiens</i> /GRCh37.74	A55D	Disease	8	0.918	Disease	7	0.863
rs151344480	<i>Homo_sapiens</i> /GRCh37.74	A23D	Disease	9	0.935	Disease	8	0.901
rs151344481	<i>Homo_sapiens</i> /GRCh37.74	A57E	Disease	8	0.924	Disease	6	0.798
rs151344481	<i>Homo_sapiens</i> /GRCh37.74	A25E	Disease	8	0.923	Disease	6	0.798
rs151344482	<i>Homo_sapiens</i> /GRCh37.74	H209R	Disease	9	0.974	Disease	8	0.904
rs151344482	<i>Homo_sapiens</i> /GRCh37.74	H177R	Disease	9	0.974	Disease	8	0.904
rs151344484	<i>Homo_sapiens</i> /GRCh37.74	H338Y	Disease	6	0.805	Disease	6	0.803
rs151344484	<i>Homo_sapiens</i> /GRCh37.74	H71Y	Disease	6	0.804	Disease	6	0.802
rs151344484	<i>Homo_sapiens</i> /GRCh37.74	H306Y	Disease	6	0.804	Disease	6	0.803
rs151344485	<i>Homo_sapiens</i> /GRCh37.74	S312F	Disease	7	0.871	Disease	5	0.768
rs151344485	<i>Homo_sapiens</i> /GRCh37.74	S344F	Disease	7	0.872	Disease	5	0.769
rs151344485	<i>Homo_sapiens</i> /GRCh37.74	S77F	Disease	7	0.856	Disease	5	0.752
rs151344486	<i>Homo_sapiens</i> /GRCh37.74	L420P	Disease	9	0.958	Disease	8	0.89
rs151344486	<i>Homo_sapiens</i> /GRCh37.74	L153P	Disease	9	0.959	Disease	8	0.892
rs151344486	<i>Homo_sapiens</i> /GRCh37.74	L388P	Disease	9	0.958	Disease	8	0.891
rs151344487	<i>Homo_sapiens</i> /GRCh37.74	W516R	Disease	8	0.913	Disease	7	0.858
rs151344487	<i>Homo_sapiens</i> /GRCh37.74	W249R	Disease	9	0.91	Disease	7	0.856
rs151344487	<i>Homo_sapiens</i> /GRCh37.74	W484R	Disease	9	0.913	Disease	7	0.859
rs151344488	<i>Homo_sapiens</i> /GRCh37.74	C59W	Disease	8	0.879	Disease	5	0.785
rs151344488	<i>Homo_sapiens</i> /GRCh37.74	C27W	Disease	7	0.869	Disease	5	0.745
rs151344489	<i>Homo_sapiens</i> /GRCh37.74	T307P	Disease	5	0.747	Neutral	4	0.288
rs151344489	<i>Homo_sapiens</i> /GRCh37.74	T40P	Disease	5	0.747	Neutral	5	0.287
rs151344489	<i>Homo_sapiens</i> /GRCh37.74	T275P	Disease	5	0.75	Neutral	4	0.29
rs151344490	<i>Homo_sapiens</i> /GRCh37.74	L505R	Disease	8	0.894	Disease	7	0.864
rs151344490	<i>Homo_sapiens</i> /GRCh37.74	L238R	Disease	8	0.898	Disease	7	0.866
rs151344490	<i>Homo_sapiens</i> /GRCh37.74	L473R	Disease	8	0.894	Disease	7	0.864
rs151344491	<i>Homo_sapiens</i> /GRCh37.74	G179R	Disease	9	0.955	Disease	8	0.884
rs151344491	<i>Homo_sapiens</i> /GRCh37.74	G147R	Disease	9	0.955	Disease	8	0.883
rs151344492	<i>Homo_sapiens</i> /GRCh37.74	L546P	Disease	6	0.8	Disease	4	0.689
rs151344492	<i>Homo_sapiens</i> /GRCh37.74	L279P	Disease	6	0.802	Disease	4	0.689
rs151344492	<i>Homo_sapiens</i> /GRCh37.74	L514P	Disease	6	0.8	Disease	4	0.689
rs151344493	<i>Homo_sapiens</i> /GRCh37.74	S193F	Disease	7	0.867	Disease	5	0.768
rs151344493	<i>Homo_sapiens</i> /GRCh37.74	S161F	Disease	7	0.866	Disease	5	0.767
rs151344495	<i>Homo_sapiens</i> /GRCh37.74	L342Q	Disease	6	0.775	Disease	5	0.747
rs151344495	<i>Homo_sapiens</i> /GRCh37.74	L75Q	Disease	6	0.779	Disease	5	0.747
rs151344495	<i>Homo_sapiens</i> /GRCh37.74	L310Q	Disease	6	0.775	Disease	5	0.746
rs151344496	<i>Homo_sapiens</i> /GRCh37.74	F205I	Disease	9	0.971	Disease	8	0.913
rs151344496	<i>Homo_sapiens</i> /GRCh37.74	F173I	Disease	9	0.971	Disease	8	0.914
rs151344497	<i>Homo_sapiens</i> /GRCh37.74	T178P	Disease	9	0.952	Disease	8	0.859

rs151344497	Homo_sapiens/GRCh37.74	T146P	Disease	9	0.952	Disease	7	0.857
rs151344498	Homo_sapiens/GRCh37.74	Q231P	Disease	8	0.882	Neutral	1	0.428
rs151344498	Homo_sapiens/GRCh37.74	Q199P	Disease	8	0.882	Neutral	1	0.428
rs200614534	Homo_sapiens/GRCh37.74	V407A	Disease	6	0.808	Disease	1	0.541
rs200614534	Homo_sapiens/GRCh37.74	V140A	Disease	6	0.808	Disease	1	0.539
rs200614534	Homo_sapiens/GRCh37.74	V375A	Disease	6	0.808	Disease	1	0.541
rs267606451	Homo_sapiens/GRCh37.74	S66F	Disease	9	0.938	Disease	8	0.878
rs267606451	Homo_sapiens/GRCh37.74	S333F	Disease	8	0.918	Disease	7	0.845
rs267606451	Homo_sapiens/GRCh37.74	S301F	Disease	8	0.917	Disease	7	0.853

types, instead of these some of them shared the same mutant types; as illustrated in Table 2 below.

**SNPs & GO predictions**

The total numbers of 126 SNPs were showed disease prediction by both PhD-SNP prediction and SNPs & GO prediction they are: rs137854585, rs137854586, rs137854587, rs137854589, rs137854591, rs137854593, rs137854594, rs137854595, rs137854596, rs139670417, rs141798777, rs146275471, rs151344453, rs151344454, rs151344456, rs151344457, rs151344458, rs151344459, rs151344460, rs151344462, rs151344465, rs151344466, rs151344467, rs151344468, rs151344469, rs151344470, rs151344471, rs151344472, rs151344473, rs151344474,rs151344475, rs151344477, rs151344478, rs151344479, rs151344480, rs151344481, rs151344482, rs151344484, rs151344485, rs151344486, rs151344487, rs151344488, rs151344489, rs151344490, rs151344491, rs151344492, rs151344493, rs151344495, rs151344496, rs151344497, rs151344498, rs200614534, rs267606451, except 13 SNPs they were showed both diseases & neutrals according to PhD-SNP prediction and SNPs & GO prediction sequential; they are: rs139670417, rs151344468, rs151344470, rs151344489, rs151344498 while 5 SNPs were showed neutral for both PhD-SNP prediction and SNPs & GO prediction they are; rs140677309 and rs141798777 (see Table 3).

**Conclusions**

The output of this study were explained and confirmed the damaging effect of those selected CGD SNPs. Although due to some protein ID problems in ENSP00000441958 & ENSP00000441896; I used UPI00020654B0 & UPI00020654AF instead of them; which were suggested by uniprot web site to complete polyphen-2 prediction, also I faced error prediction with some sequences in meta-snps prediction, that is explains why I exclude them from this study, so on I suggest to check this program again to know where is the problem.

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