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Research Article

In silico analysis of Progeria: A genetic disease and natural cardiovascular disorders preventive compounds

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Abstract

Progeria (also known as "Hutchinson–Gilford progeria syndrome"(HGPS) is an extremely rare, severe, genetic condition wherein symptoms resembling aspects of aging are manifested at an early age. The basic objective of this study is how is it responsible for faster ageing than normal? The study of its bioinformatics aspect explaining where the mutation occurs in normal LMNA gene to form mutated Progerin. We explain its sequential and structural aspects in domain and motif. Structural visualization by Marker view software provides the linear structure of LMNA and mutated LMNA. We studied the properties and specificity of Lonafarnib (an edible drug available in market) against Progerin with Docking. Cardiovascular disorders are the major symptoms occurred in Progerin patients. Therefore we found 32 natural compounds with their sources having anti cardiovascular disorders activity. We checked its docking properties and ADMET properties. From this we came to conclude 11 most effective, edible, naturally occurring compounds for cardiovascular disorders in Progerin patients.

INTRODUCTION

Hutchinson–Gilford progeria syndrome is a genetic condition that occurs as a new mutation and is not usually inherited, although there is a uniquely inheritable form (Merideth *et al.*, 2008, Kudlow *et al.*, 2007). As a child ages past infancy, additional conditions become apparent. Limited growth, alopecia, and a distinctive appearance (small face and jaw, pinched nose) are all characteristic of progeria. Later, the condition causes wrinkled skin, atherosclerosis, and cardiovascular problems (Raska I 2010, Eriksson *et al.*, 2007). (HGPS) is a childhood disorder caused by a point mutation in position 1824 of the LMNA gene, replacing cytosine with thymine, creating an unusable form of the protein Lamin A. Lamin A is part of the building blocks of the nuclear envelope (Taimen *et al.*, 2009). No treatments have been proven effective. Most treatment focuses on reducing complications (such as cardiovascular disease) with heart bypass surgery or Growth hormone treatment has been attempted. The most serious aspect of the disease, however, and the cause of death in >90% of cases, is rapid, progressive arterial occlusive disease, with death from myocardial infarction or stroke occurring at an average age of 13 years (range, 8–21 years) (Sagelius *et al.*, 2008).So we tried to find the some natural compounds which can help to ameliorate the life span of progerian patients.

Laminopathies

Laminopathies are a group of rare genetic disorders caused by mutations in genes encoding proteins of the nuclear lamina (Worman and Bonne, 2007). They are included in the more generic term nuclear envelopathies that was coined in 2000 for diseases

associated with defects of the nuclear envelope (Wilson and Foisner, 2010). Mutations causing progeria are defective in splicing LMNA mRNA, therefore producing abnormal lamin A protein, also known as Progerin (McClintock D *et al*., 2007). The mutations activate a cryptic splice site within exon 11 of the gene, thereby causing the deletion of the processing site on prelamin A. This results in an accumulation of progerin that is unable to mature into lamin A, leading to misshapen nuclei. Missplicing also leads to the complete or partial loss of exon 11 and results in a truncated prelamin A protein in the neonatal lethal tight skin contracture syndrome (Rodriguez and Eriksson, 2010). The two major proteins produced from this gene, lamin A and lamin C, are made in most of the body's cells. These proteins have a nearly identical sequence of protein building blocks (amino acids) (Schirmer and Foisner, 2007). In HGPS, the recognition site that the enzyme requires for cleavage of prelamin A to lamin A is mutated. Lamin A cannot be produced, and prelamin A builds up on the nuclear membrane, causing a characteristic nuclear blabbing. This results in the premature aging symptoms of progeria.

Hutchinson-Gilford progeria syndrome (HGPS):

Progeria caused by mutations in the LMNA gene A specific mutation in the LMNA gene has been found in most patients with Hutchinson-Gilford progeria syndrome. This mutation changes a single DNA building block (nucleotide) in the gene (Kudlow BA 2007). Specifically, the mutation replaces the nucleotide cytosine with the nucleotide thymine at position 1824 (written as C1824T). This mutation is also sometimes noted as Gly608Gly (G608G), which refers to the position in the lamin A protein affected by the mutation (Barthélémy *et al*., 2015). The C1824T mutation leads to an abnormal version of the lamin A protein called progerin, which is missing 50 amino acids near one end (Lopez-Mejia *et al*., 2011). The mutations responsible for this disorder result in an abnormal version of lamin A that cannot be processed correctly within the cell. When the altered protein is incorporated into the lamina, it can disrupt the shape of the nuclear envelope (Webster *et al*., 2009). Researchers are working to determine how these changes lead to the signs and symptoms of Hutchinson-Gilford progeria syndrome.

It is an extremely rare, severe, genetic condition wherein symptoms resembling aspects of aging are manifested at an early age (Burke and Stewart, 2014). Those born with progeria typically live about thirteen years, although many have been known to live into their late teens and early twenties and rare individuals may even reach their forties (Stratmann HG 2016). It is a genetic condition that occurs as a new mutation and is not usually inherited, although there is a uniquely inheritable form. In HGPS, the recognition site that the enzyme requires for cleavage of prelamin A to lamin A is mutated. Lamin A cannot be produced, and prelamin A builds up on the nuclear membrane, causing a characteristic nuclear blabbing. This results in the premature aging symptoms of progeria, although the mechanism connecting the misshapen nucleus to the symptoms is not known. A study that compared HGPS patient cells with the skin cells from LMNA young and elderly human subjects found similar defects in the HGPS (McClintock 2007). HGPS is related to aberrant processing of the nuclear envelope protein lamin A and accumulation of farnesylated prelamin A (Dechat *et al*., 2008).The farnesylated preprogerin protein is then incorporated into the nuclear membrane (Capell *et al*., 2005) However, the mutant, truncated protein lacks an important posttranslational processing signal required for cleavage of the preprogerin protein at the carboxyterminus (Reddy and Comai, 2012). This cleavage is required for the release of prelamin A from the nuclear membrane, thus allowing its incorporation into the nuclear lamina. As a result of the absence of lamin A in the nuclear lamina, the cell nuclei from HGPS patients display abnormal nuclear blabbing and aberrant nuclear shapes. Abnormal chromosome segregation and delayed onset and progression of mitosis have also been demonstrated.

Thus, our study aims to determine the point at which the mutation alters the LMNA gene to form Progerin. We was further interested in determination of structural aspects of mutated and non mutated LMNA. The binding specificity of lonafarnib to Progerin was described and some of the natural compounds against cardiovascular diseases were proven to take orally and comfortably fulfilling different Insilco analytical criteria.

MATERIALS AND METHODS

We got sequence of non mutated LMNA and mutated Progerin gene from genbank database. These genes were aligned using ClustalW multiple alignment tool. It is a widely used multiple sequence alignment computer program. The latest version is 2.0. This program is available from the

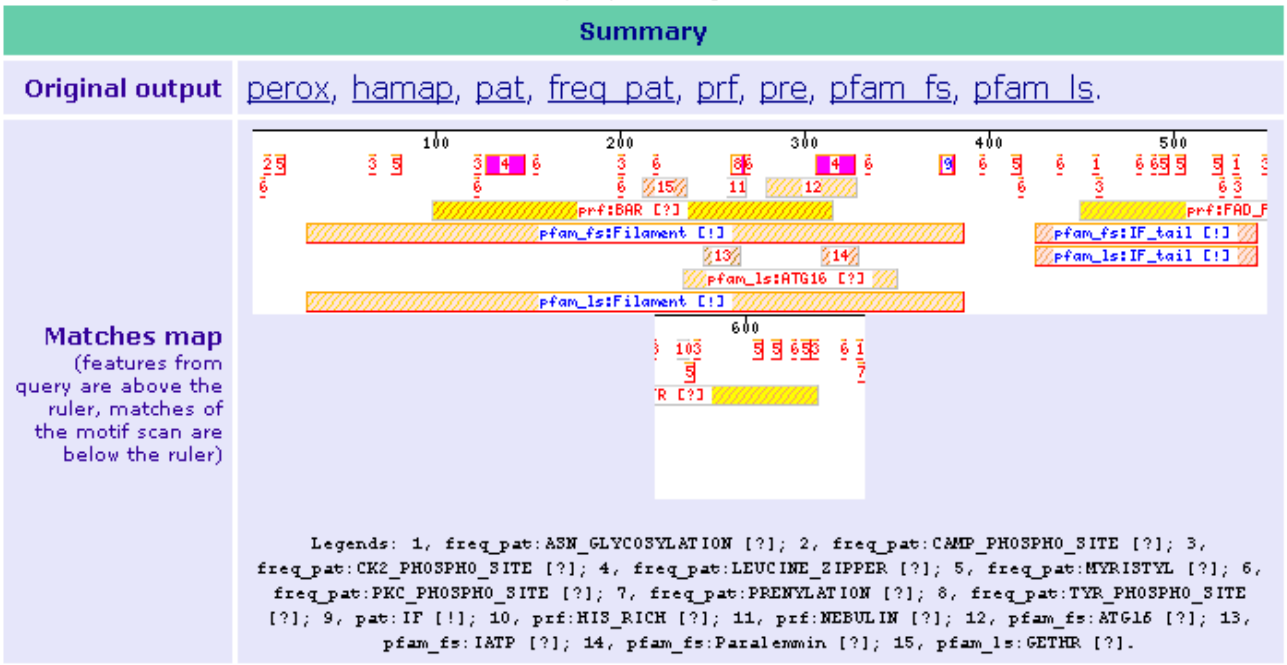
ClustalW Homepage or European Bioinformatics Institute ftp server. The simultaneous alignment of many nucleotide or amino acid sequences is now an essential tool in molecular biology. Multiple alignments are used to find diagnostic Patterns to characterize protein families. Motif Scan was used to get the motif pattern in the protein sequences. Using Geneious we combine all the leading DNA and protein sequence analysis tools into one revolutionary software solution. We also used CLC bio protein work bench to create a software environment enabling users to make a large number of advanced protein sequence analyses, combined with smooth data management, and excellent graphical viewing and output options. For an interactive molecular graphics program we used Marker View software and displaying feasible docking modes of pairs of protein and DNA molecules we used Hex. Hex can also calculate protein-ligand docking, assuming the ligand is rigid, and it can superpose pairs of molecules using only knowledge of their 3D shapes. To determine the ADMET properties of chemical compounds we used ADME Tox from that we concluded how much compound is safe as a drug.

RESULTS AND DISCUSSION

A point mutation in LMNA gene can produce mutated LMNA called progerin. The motif results taken from the Motif Scan gives the region where mutation occurs (Figure 1). The blank area shows deletion area of the Progerin Sequence (Supplementary table 1). We also studied the secondary structure of LMNA and Progerin by CLC-bio3. Comparative alpha helixes and beta sheets were shown in figure 2 where as annotation table of both sequences showed that progrein sequence has absence of 2 beta strands. 3D structure of both LMNA and Progerin was observed in Marker View which results that non mutated lmna is linear in structure where as mutation in LMNA gives rise to form a complex globular structure (Figure 3).

Currently lonafarnib is the only treatments available are used to lessen the strain of living with Progeria and are used on a patient-to patient basis. In lab tests FTIs have been able to reverse an abnormality in Progeria cells. In present study we dock this compound with the help of Hex Doc to check its specificity and binding affinity towards Progerin. We also checked the ADMET property of Lonafarnib which results that it is edible. After administration of lonafarnib a person may have various side effects. Considering this aspect we planned to go for natural compounds which can prevent the cardiovascular disorders occurring in progeria disease.

A) Lmna



B) progerin

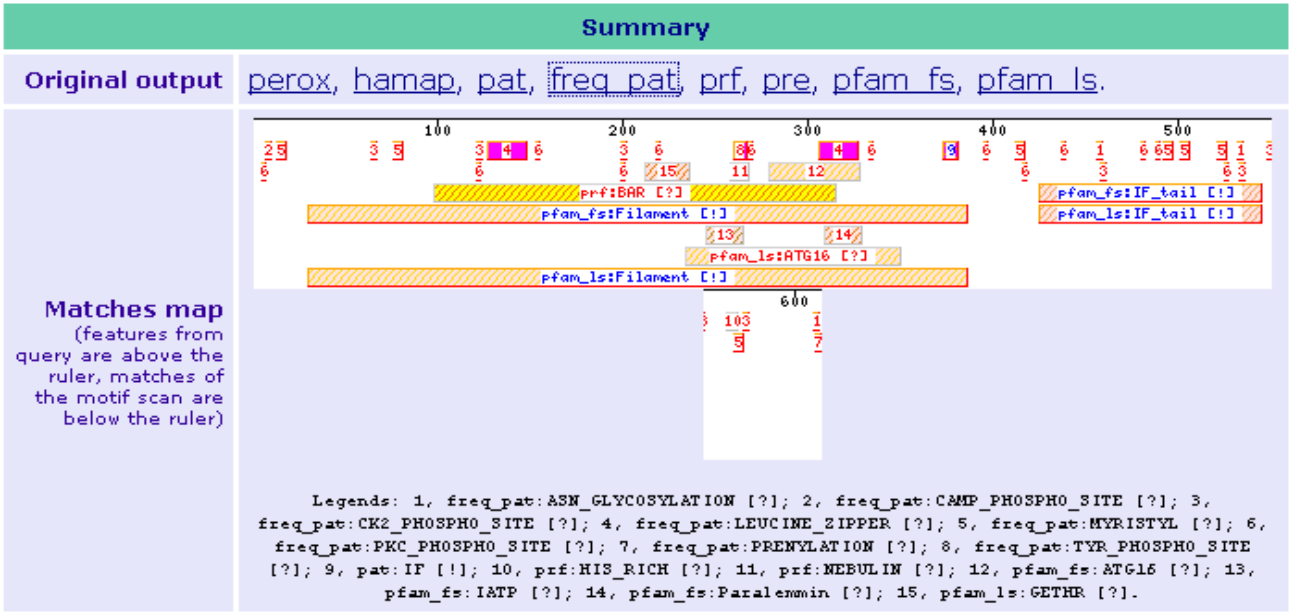


Figure 1: Motif Scan gives the region where mutation occurs. A- Is non mutated LMNA whereas B- is mutated Progerin.

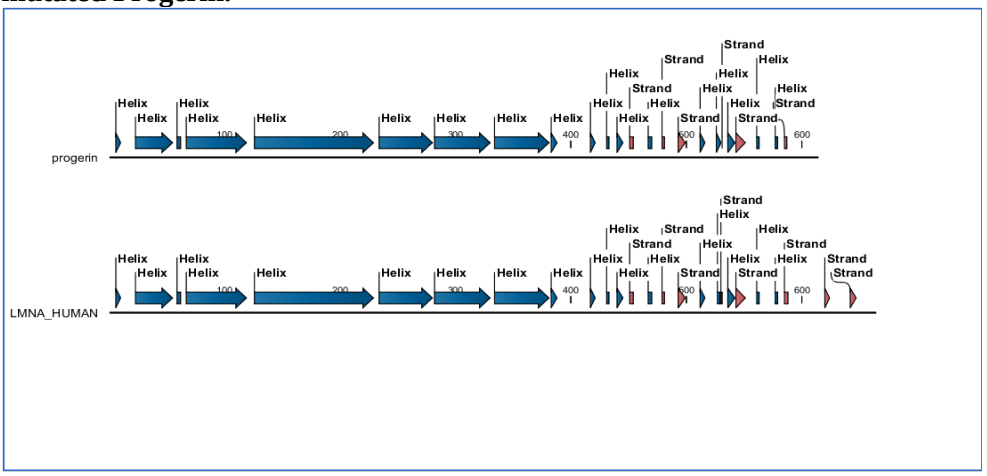
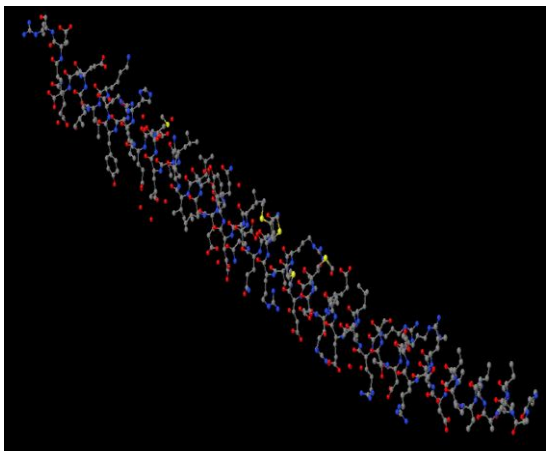


Figure 2: Secondary structures of progerin & lmna It shows the alpha helix & beta strands in the respective proteins. Screen shots of secondary structure prediction in CLC bio workbench.

Non mutated lmna



Mutated lmna (Progerin)

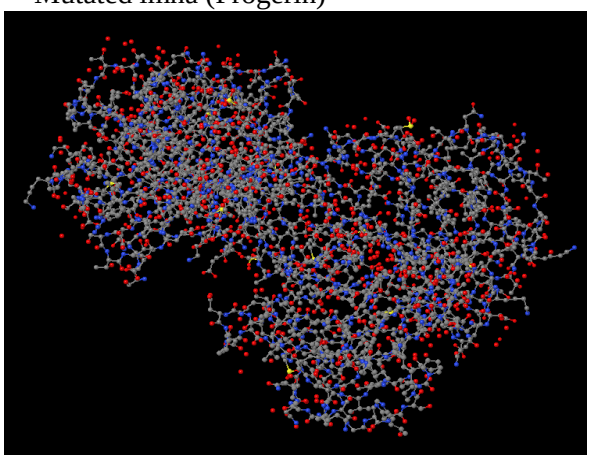


Figure 3: Visualisation of non mutated lmna and mutated lmna (progerin) using Marker View software.

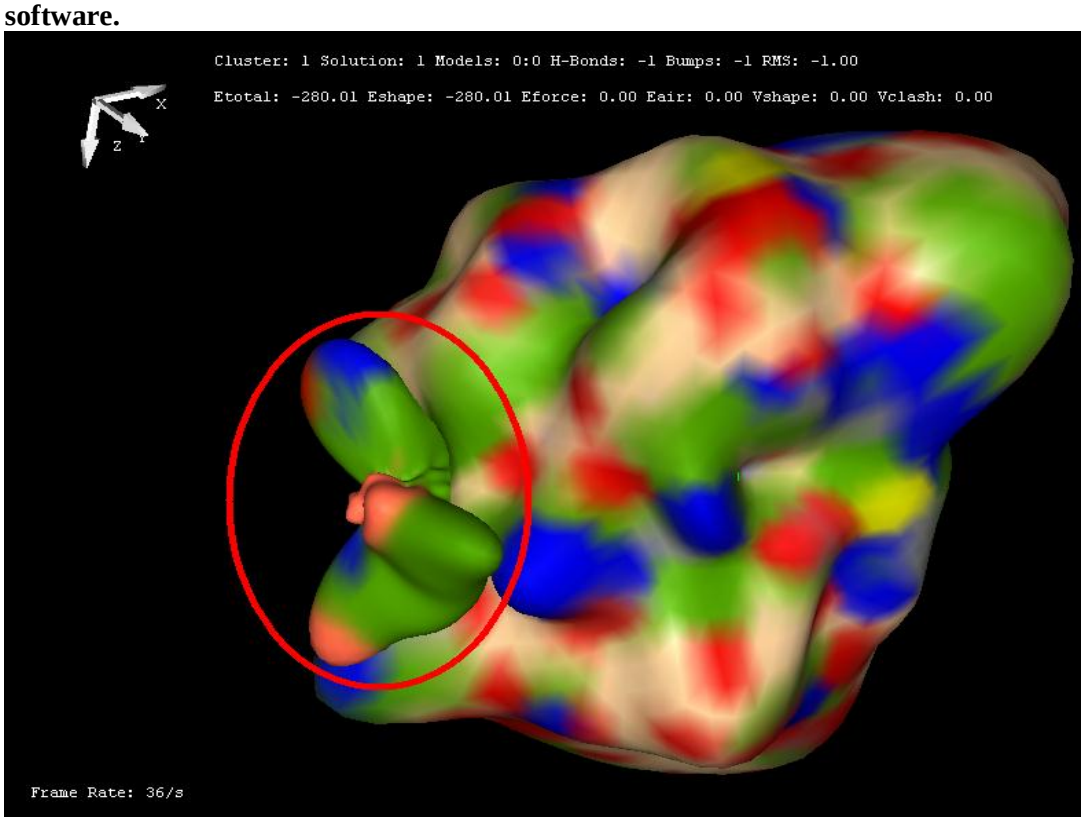


Figure 4: Docking of lonafarnib (Ligand) showed in red circle with Progerin

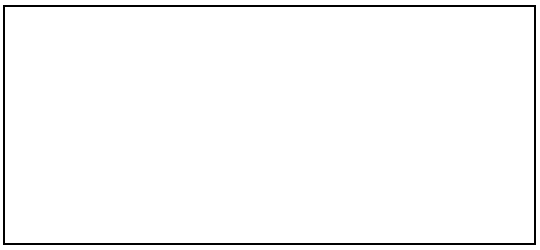
Supplementary table 1: Comparative analysis of non mutated LMNA and mutated Progerin. Blank space indicates where the mutation occurs.

lmna	**progerin**
>LMNA_HUMAN/456-459 motif=freq_pat:ASN_GLYCOSYLATION	>gi/456-459 motif=freq_pat:ASN_GLYCOSYLATION
NKSN	**NKSN**
>LMNA_HUMAN/532-535 motif=freq_pat:ASN_GLYCOSYLATION	>gi/532-535 motif=freq_pat:ASN_GLYCOSYLATION
NSTG	**NSTG**
>LMNA_HUMAN/660-663 motif=freq_pat:ASN_GLYCOSYLATION	>gi/610-613 motif=freq_pat:ASN_GLYCOSYLATION
NCSI	**NCSI**
>LMNA_HUMAN/7-10 motif=freq_pat:CAMP_PHOSPHO_SITE	>gi/7-10 motif=freq_pat:CAMP_PHOSPHO_SITE
RRAT	**RRAT**
>LMNA_HUMAN/5-7 motif=freq_pat:PKC_PHOSPHO_SITE	>gi/5-7 motif=freq_pat:PKC_PHOSPHO_SITE
SQR	**SQR**
>LMNA_HUMAN/121-123 motif=freq_pat:PKC_PHOSPHO_SITE	>gi/121-123 motif=freq_pat:PKC_PHOSPHO_SITE
TKK	**TKK**
>LMNA_HUMAN/153-155 motif=freq_pat:PKC_PHOSPHO_SITE	>gi/153-155 motif=freq_pat:PKC_PHOSPHO_SITE
SEK	**SEK**
>LMNA_HUMAN/199-201	>gi/199-201

motif=freq_pat:PKC_PHOSPHO_SITE	motif=freq_pat:PKC_PHOSPHO_SITE
TMK	**TMK**
>LMNA_HUMAN/218-220 motif=freq_pat:PKC_PHOSPHO_SITE	>gi/218-220 motif=freq_pat:PKC_PHOSPHO_SITE
TKR	**TKR**
>LMNA_HUMAN/268-270 motif=freq_pat:PKC_PHOSPHO_SITE	>gi/268-270 motif=freq_pat:PKC_PHOSPHO_SITE
SAK	**SAK**
>LMNA_HUMAN/333-335 motif=freq_pat:PKC_PHOSPHO_SITE	>gi/333-335 motif=freq_pat:PKC_PHOSPHO_SITE
TSR	**TSR**
>LMNA_HUMAN/395-397 motif=freq_pat:PKC_PHOSPHO_SITE	>gi/395-397 motif=freq_pat:PKC_PHOSPHO_SITE
SQR	**SQR**
>LMNA_HUMAN/416-418 motif=freq_pat:PKC_PHOSPHO_SITE	>gi/416-418 motif=freq_pat:PKC_PHOSPHO_SITE
TKK	**TKK**
>LMNA_HUMAN/437-439 motif=freq_pat:PKC_PHOSPHO_SITE	>gi/437-439 motif=freq_pat:PKC_PHOSPHO_SITE
SGR	**SGR**
>LMNA_HUMAN/480-482 motif=freq_pat:PKC_PHOSPHO_SITE	>gi/480-482 motif=freq_pat:PKC_PHOSPHO_SITE
TYR	**TYR**
>LMNA_HUMAN/488-490 motif=freq_pat:PKC_PHOSPHO_SITE	>gi/488-490 motif=freq_pat:PKC_PHOSPHO_SITE
TLK	**TLK**
>LMNA_HUMAN/525-527 motif=freq_pat:PKC_PHOSPHO_SITE	>gi/525-527 motif=freq_pat:PKC_PHOSPHO_SITE
SLR	**SLR**
>LMNA_HUMAN/625-627 motif=freq_pat:PKC_PHOSPHO_SITE	
SYR	
>LMNA_HUMAN/652-654 motif=freq_pat:PKC_PHOSPHO_SITE	
SPR	>gi/64-67 motif=freq_pat:CK2_PHOSPHO_SITE
>LMNA_HUMAN/64-67 motif=freq_pat:CK2_PHOSPHO_SITE	**TESE**
TESE	>gi/121-124 motif=freq_pat:CK2_PHOSPHO_SITE
>LMNA_HUMAN/121-124 motif=freq_pat:CK2_PHOSPHO_SITE	**TKKE**
TKKE	>gi/199-202 motif=freq_pat:CK2_PHOSPHO_SITE
>LMNA_HUMAN/199-202 motif=freq_pat:CK2_PHOSPHO_SITE	**TMKE**
TMKE	>gi/458-461 motif=freq_pat:CK2_PHOSPHO_SITE
>LMNA_HUMAN/458-461 motif=freq_pat:CK2_PHOSPHO_SITE	**SNED**
SNED	>gi/533-536 motif=freq_pat:CK2_PHOSPHO_SITE
>LMNA_HUMAN/533-536 motif=freq_pat:CK2_PHOSPHO_SITE	**STGE**
STGE	>gi/548-551 motif=freq_pat:CK2_PHOSPHO_SITE
>LMNA_HUMAN/548-551	

motif=freq_pat:CK2_PHOSPHO_SITE
TVVE
>LMNA_HUMAN/572-575 motif=freq_pat:CK2_PHOSPHO_SITE
SSGD
>LMNA_HUMAN/636-639 motif=freq_pat:CK2_PHOSPHO_SITE
SFGD
>LMNA_HUMAN/260-267 motif=freq_pat:TYR_PHOSPHO_SITE
KKElEKTY
>LMNA_HUMAN/13-18 motif=freq_pat:MYRISTYL
GAQASS
>LMNA_HUMAN/76-81 motif=freq_pat:MYRISTYL
GIKAAY
>LMNA_HUMAN/412-417 motif=freq_pat:MYRISTYL
GGSVTK
>LMNA_HUMAN/492-497 motif=freq_pat:MYRISTYL
GQVVTI
>LMNA_HUMAN/501-506 motif=freq_pat:MYRISTYL
GAGATH
>LMNA_HUMAN/521-526 motif=freq_pat:MYRISTYL
GCGNSL
>LMNA_HUMAN/567-572 motif=freq_pat:MYRISTYL
GSHCSS
>LMNA_HUMAN/604-609 motif=freq_pat:MYRISTYL
GAQVGG
>LMNA_HUMAN/614-619 motif=freq_pat:MYRISTYL
GSSASS
>LMNA_HUMAN/630-635 motif=freq_pat:MYRISTYL
GGSGGG
>LMNA_HUMAN/127-148 motif=freq_pat:LEUCINE_ZIPPER
LIAAQARLKDLEALLNSKEAAL
>LMNA_HUMAN/306-327 motif=freq_pat:LEUCINE_ZIPPER
LSQLQKQLAAKEAKLRDLEDSL
>LMNA_HUMAN/661-664 motif=freq_pat:PRENYLATION
CSIM

TVVE
>gi/572-575 motif=freq_pat:CK2_PHOSPHO_SITE
SSGD

>gi/260-267 motif=freq_pat:TYR_PHOSPHO_SITE
KKElEKTY
>gi/13-18 motif=freq_pat:MYRISTYL
GAQASS
>gi/76-81 motif=freq_pat:MYRISTYL
GIKAAY
>gi/412-417 motif=freq_pat:MYRISTYL
GGSVTK
>gi/492-497 motif=freq_pat:MYRISTYL
GQVVTI
>gi/501-506 motif=freq_pat:MYRISTYL
GAGATH
>gi/521-526 motif=freq_pat:MYRISTYL
GCGNSL
>gi/567-572 motif=freq_pat:MYRISTYL
GSHCSS

>gi/127-148 motif=freq_pat:LEUCINE_ZIPPER
LIAAQARLKDLEALLNSKEAAL
>gi/306-327 motif=freq_pat:LEUCINE_ZIPPER
LSQLQKQLAAKEAKLRDLEDSL
>gi/611-614 motif=freq_pat:PRENYLATION
CSIM

Supplementary table 2: The docking score table of selected 18 natural compounds with Progerin.

SR No	Agents	Pub Chem Ligand ID	Lead IT Docking Score	Docking Match	Lipophilic Score	Ambig Score	Clash	Rotational Angle
1	Allyl methyl thiosulfonate	6913086	-13.3609	-14.8397	-3.9760	-5.2213	3.8761	1.4000
2	Magnesium lactate	6536825	-13.1754	-18.6343	-1.8951	-3.6225	2.7765	2.8000
3	Salicylates	450660	-13.0279	-16.9388	-1.7745	-4.2590	3.1445	1.4000
4	γ-L-glutamyl-S-alkyl-L-cysteine	123938	-12.5291	-20.0430	-4.34314	-6.4057	3.1510	9.8000
5	S-allylcysteine (SAC)	98280	-11.6864	-19.5532	-3.6129	-4.1827	3.2624	7.0000
6	Kaempferol	5280863	-11.3815	-13.7362	-4.5889	-5.7918	1.7355	5.6000
7	Isoflavones	25201420	-11.3772	-12.6041	-5.9131	-5.9501	3.4901	4.2000
8	Resveratrol	445154	-11.1511	-13.1147	-5.1044	-3.6870	2.1550	4.2000
9	Anthraquinones	25201450	-9.8032	-11.7712	-4.6837	-6.7862	3.8378	4.2000
10	Epicatechin	72276	-9.1247	-16.9805	-1.9922	-4.4702	0.5182	8.4000
11	Quercetin	5280343	-7.5688	-13.6693	-2.0791	-4.8969	0.6765	7.0000
12	α-Lipoic acid (1,2-dithiolane-3-pentanoic acid)	864	-7.1280	-10.9294	-4.9886	-5.5041	1.8941	7.0000
13	Allixin	86374	-4.7176	-10.8685	-6.0261	-6.0748	4..4517	8.4000
14	S-allylmercaptocysteine	25201750	-4.3408	-8.9747	-3.5953	-5.0567	0.8853	7.0000
15	Hydroxytyrosol (3,4-dihydroxyphenylethanol)	10844647	-4.0577	-8.9649	-3.6920	-4.8005	0.9998	7.0000
16	Hydroxytyrosol	82755	-3.7564	-13.5310	-1.3577	-2.3167	1.0490	7.0000
17	Sulforaphane	5350	-3.0942	-8.7473	-4.4493	-4.6787	2.3811	7.0000
18	1-propenyl allyl thiosulfonate	529388	-2.3764	-9.2798	-4.5352	-4.5173	3.5558	7.0000

We selected 32 compounds from natural sources with Molecular formula and Molecular weight which are satisfying Lipiniski rule. It is a rule of thumb to evaluate drug likeness or determine if a chemical compound with a certain pharmacological or biological activity has properties that would make it a likely orally active drug in humans. We found 32 natural compounds and checked its Lipinski Rule used for cardiovascular diseases listed in Table 1. Out of these 32 we selected 18 molecules as ligand to dock with Progerin to check its affinity of binding (supplementary Table 2). Out of 18, 11 ligands were showing good docking score in expected energy score (Emin and Emax) (Table 2).

The results of this project show that Mutations causing LMNA to form progeria. In splicing LMNA mRNA, therefore producing abnormal lamin A protein, also known as progerin. Hutchinson-Gilford progeria syndrome (HGPS) is caused by a mutant prelamin A that cannot be processed to lamin A (Reddy and Comai, 2012). The hallmark cellular abnormality in HGPS is misshapen nuclei (Worman and Bonne, 2009).

Table 1: Natural compounds satisfying Lipinski Rule:

Sr No.	Natural compound	Natural compound Sources	Molecular Formula	Molecular weight	Lipinskey rule
1	Allicin (allyl 2-propenethiosulfinate or diallyl thiosulfinate)	aqueous garlic extract	$C_6H_{10}OS_2$	162.273	Yes
2	Allyl methyl thiosulfonate	garlic homogenate	$C_{14}H_{15}N_3O_2S$	321.4178	Yes
3	1-propenyl allyl thiosulfonate	garlic homogenate	$C_6H_{14}O_2S_2$	182.30416	Yes
4	γ-L-glutamyl-S-alkyl-L-cysteine	garlic homogenate	$C_8H_{14}N_2O_5S$	250.27216	Yes
5	S-allylcysteine (SAC)	aged garlic extract	$C_6H_{11}NO_2S$	161.22204	Yes
6	S-allylmercaptocysteine	aged garlic extract	$C_5H_9NOS_2$	163.26106	Yes
7	Allixin	aged garlic extract	$C_{12}H_{18}O_4$	226.26892	Yes
8	Selenium	aged garlic extract	Se	78.96	No
9	β-carotene	Carotenoids (fruits and vegetables)	$C_{40}H_{56}$	536.87264	No
10	Lycopene	Carotenoids (fruits and vegetables)	$C_{40}H_{56}$	536.87264	No
11	Resveratrol	Wine	$C_{14}H_{12}O_3$	228.24328	Yes
12	Hydroxytyrosol (3,4-dihydroxyphenylethanol)	Wine	$C_8H_{10}O_3$	157.181685	Yes
13	Isoflavones	Soybeans	$C_{15}H_9O_5$	269.22896	Yes
14	Quercetin	Tea	$C_{15}H_{10}O_7$	302.2357	Yes
15	Kaempferol	Tea	$C_{15}H_{10}O_6$	286.2363	Yes
16	Myrecitin	Tea	$C_{15}H_{10}O_8$	318.2351	No
17	Epigallocatechin gallate	Tea	$C_{22}H_{18}O_{11}$	458.37172	No
18	Hydroxytyrosol	**Olive oil**	$C_8H_{10}O_3$	154.1632	Yes
19	Epicatechin	Chocolate	$C_{15}H_{14}O_6$	290.26806	Yes
20	Salicylates	**Aloe vera**	$C_7H_6O_3$	137.121474	Yes
21	Magnesium lactate	**Aloe vera**	$C_6H_{10}MgO_6$	202.445	Yes
22	Acemannan	**Aloe vera**	$C_{66}H_{100}NO_{49}$	1691.4775	No
23	Lupeol	**Aloe vera**	$C_{30}H_{50}O$	426.7174	No
24	Campestrol	**Aloe vera**	$C_{28}H_{48}O$	400.68012	No
25	b-sitosterol	**Aloe vera**	$C_{29}H_{50}O$	414.7067	No
26	g-linolenic acid	**Aloe vera**	$C_{18}H_{30}O_2$	278.4296	No
27	Anthraquinones	**Aloe vera**	$C_{15}H_9O_5$	269.22896	Yes
28	Policosanols	Sugarcane wax.	$C_{28}H_{58}O$	410.75952	No
29	Pterostilbene	Blueberries	$C_{16}H_{16}O_3$	256.29644	Yes
30	Oligomeric proanthocyanidin	Grape seed extract	$C_{31}H_{28}O_{12}$	592.54682	No
31	Lipoic acid (1,2-dithiolane-3-pentanoic acid)	Yeast	$C_8H_{14}O_2S_2$	206.32556	Yes
32	Sulforaphane	Broccoli	$C_6H_{11}NOS_2$	177.28764	Yes

We hypothesized that the farnesylation of prelamin A is important for its targeting to the nuclear envelope in HGPS and that blocking farnesylation would ameliorate the nuclear shape abnormalities. The FTI (Lonafarnib) can help in blocking the progerin protein which is responsible for progeria. ADMET properties also shows that its safe drug for use. Generally progerian patient's death occurs due to cardiovascular problems in 90% cases so we have gathered some natural compounds which can help progerian patients in their cardiovascular problems (Coutinho *et al*., 2009). The few natural compounds exhibit the antioxidant properties which can help for their longer survival. Out of these 32 we selected 18 molecules as ligand to dock with Progerin to check its affinity of binding and we concluded that 11 compounds listed here can we used as natural compounds for cardiovascular disorders occurred in Hutchinson-Gilford progeria syndrome. Laminopathies are a group of rare genetic disorders caused by mutations in genes encoding proteins of the nuclear lamina (Worman and Bonne, 2007). In future prospective we have to study the other laminopathies disorders Emery-Dreifuss muscular dystrophy because emerins role in muscular dystrophy is unknown moreover, recent research have found that the absence of functional emerin may decrease the infectivity of HIV-1. Thus, it is speculated that patients suffering from Emery-Dreifuss muscular dystrophy may have immunity to or show an irregular infection pattern to HIV-1.So want to study their interaction so from that we could get clue for making drug on AIDS.

Table 2: the docking score table of 18 natural compounds using Hex Dock

Sr No	Natural Agent	Hex Score (Energy range)	Receptor
1.	Quercetin	Emin = -291.61, Emax = -158.76	1BAK
2.	Salicylates	Emin = -215.69, Emax = -134.74	
3.	Allyl methyl thiosulfonate	Emin = -214.21, Emax = -108.88	
4.	Isoflavones	Emin = -203.51, Emax = -103.31	
5.	Anthraquinones	Emin = -203.11, Emax = -106.06	
6.	Kaempferol	Emin = -201.79, Emax = -104.63	
7.	Magnesium lactate	Emin = -199.48, Emax = -91.26	
8.	Epicatechin	Emin = -191.65, Emax = -97.96	
9.	Sulforaphane	Emin = -189.13, Emax = -97.99	
10.	Resveratrol	Emin = -183.81, Emax = -94.70	
11.	Allixin	Emin = -183.50, Emax = -96.57	

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