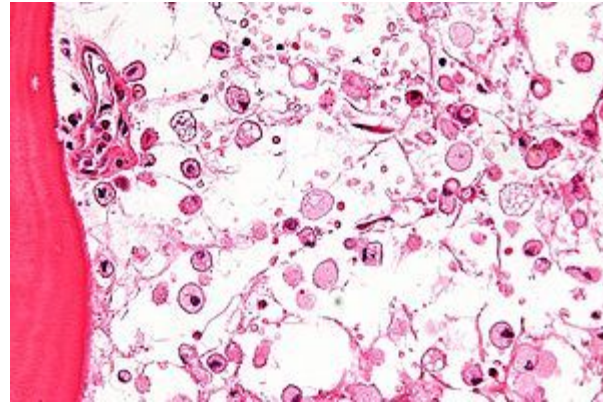


Choroby spichrzeniowe

Lizosomalne choroby spichrzeniowe, choroby lizosomalne, choroby spichrzenia lizosomalnego – grupa chorób uwarunkowanych genetycznie, w których na skutek braku aktywności jednego z enzymów dochodzi do spichrzenia różnych substancji w lizosomach.



UniProt

Information relevant to diseases associated with a given protein are found in the section 'Disease/Phenotypes and variants'. The information given (including the disease name) is consistent with the literature and the OMIM database.

OMIM is a comprehensive, authoritative compendium of human genes and genetic phenotypes that is freely available and updated daily. OMIM is authored and edited at the McKusick-Nathans Institute of Genetic Medicine, Johns Hopkins University School of Medicine, under the direction of Dr. Ada Hamosh. Its official home is omim.org.

The screenshot shows the UniProt website homepage in a web browser. The browser's address bar displays 'uniprot.org'. The page features a dark blue header with the UniProt logo and navigation links: BLAST, Align, Peptide search, ID mapping, and SPARQL. On the right side of the header, it says 'Release 2023_05 | Statistics' and 'Help'. The main content area has a large blue background with the text 'Find your protein' in white. Below this text is a search bar with a placeholder 'UniprotID' and a 'Search' button. Under the search bar, there are examples: 'Insulin', 'APP', 'Human', 'P05067', and 'organism_id 9606'. Below the search bar, there is a statement: 'UniProt is the world's leading high-quality, comprehensive and freely accessible resource of protein sequence and functional information. Cite UniProt™'. At the bottom of the page, there are four colored boxes representing different databases: 'Proteins UniProt Knowledgebase' (blue), 'Species Proteomes' (red), 'Protein Clusters UniRef' (orange), and 'Sequence Archive UniParc' (green). Each box contains a brief description of its content. Below these boxes is a 'Supporting Data' section with four categories: 'Human diseases', 'Cross-referenced databases', 'Subcellular locations', and 'Literature Citations'. Each category has a list of links to related resources.

*lysosomal storage diseases

UniProt

BLAST Align Peptide search ID mapping SPARQL Human diseases Lysosomal

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1 UniProtKB entry · 1 reviewed UniProtKB entry

☐ **Gaucher disease**

An autosomal recessive lysosomal storage disease due to deficient activity of lysosomal beta-glucocerebrosidase, and characterized by accumulation of glucosylceramide in the reticulo-endothelial system. GD is a multisystem disease historically divided into three main subtypes on the basis of the presence of neurologic involvement, age at onset and progression rate: type 1 is the non-neuropathic form, type 2 is the acute neuropathic form with early onset and rapid neurologic deterioration, type 3 is the chronic neuropathic form with slow progression of neurologic features. GD shows a marked phenotypic diversity ranging from adult asymptomatic forms, at the mild end, to perinatal lethal forms at the severe end of the disease spectrum. Formal diagnosis of Gaucher disease is based on the measurement of glucocerebrosidase levels in circulating leukocytes and molecular genetic analysis.

1 UniProtKB entry · 1 reviewed UniProtKB entry

☐ **Gaucher disease, atypical, due to saposin C deficiency**

A disease characterized by marked glucosylceramide accumulation in the spleen without having a deficiency of glucosylceramide-beta glucosidase characteristic of classic Gaucher disease. Gaucher disease is a lysosomal storage disorder characterized by skeletal deterioration, hepatosplenomegaly, and organ dysfunction. There are several subtypes based on the presence and severity of neurological involvement.

1 UniProtKB entry · 1 reviewed UniProtKB entry

☐ **Ceroid lipofuscinosis, neuronal, 10**

A form of neuronal ceroid lipofuscinosis with onset at birth or early childhood. Neuronal ceroid lipofuscinoses are progressive neurodegenerative, lysosomal storage diseases characterized by intracellular accumulation of autofluorescent liposomal material, and clinically by seizures, dementia, visual loss, and/or cerebral atrophy.

1 UniProtKB entry · 1 reviewed UniProtKB entry

☐ **Farber lipogranulomatosis**

An autosomal recessive lysosomal storage disorder characterized by subcutaneous lipid-loaded nodules, excruciating pain in the joints and extremities, and marked accumulation of ceramide in lysosomes. Disease severity is variable. The most severe disease subtype is a rare neonatal form with death occurring before 1 year of age.

1 UniProtKB entry · 1 reviewed UniProtKB entry

☐ **Mucopolidosis type III complementation group A**

Autosomal recessive disease of lysosomal enzyme targeting. Clinically MLI is characterized by restricted joint mobility, skeletal dysplasia, and short stature. Mildly coarsened facial features and thickening of the skin have been described. Cardiac valvular disease and corneal clouding may also occur. Half of the reported patients show learning disabilities or intellectual disability.

1 UniProtKB entry · 1 reviewed UniProtKB entry

☐ **Ceroid lipofuscinosis, neuronal, 13 (Kufs type)**

A form of neuronal ceroid lipofuscinosis characterized by adult onset of progressive cognitive decline and motor dysfunction leading to dementia and often early death. Some patients develop seizures. Neuronal ceroid lipofuscinoses are progressive neurodegenerative, lysosomal storage diseases characterized by intracellular accumulation of autofluorescent liposomal material. CLN13 inheritance is autosomal recessive.

☐ **Ceroid lipofuscinosis, neuronal, 4B (Kufs type), autosomal dominant**

An adult-onset neuronal ceroid lipofuscinosis. Neuronal ceroid lipofuscinoses are progressive neurodegenerative, lysosomal storage diseases characterized by intracellular accumulation of autofluorescent liposomal material, and clinically by seizures, dementia, visual loss, and/or cerebral atrophy. CLN4B has no visual involvement and is characterized by seizures and other neurologic symptoms.

☐ **Hermansky-Pudlak syndrome 11**

A form of Hermansky-Pudlak syndrome, a genetically heterogeneous autosomal recessive disorder characterized by oculocutaneous albinism, bleeding due to platelet storage pool deficiency, and lysosomal storage defects. This syndrome results from defects of diverse cytoplasmic organelles including

Gaucher disease

An autosomal recessive lysosomal storage disease due to deficient activity of lysosomal beta-glucocerebrosidase, and characterized by accumulation of glucosylceramide in the reticulo-endothelial system. GD is a multisystem disease historically divided into three main subtypes on the basis of the presence of neurologic involvement, age at onset and progression rate: type 1 is the non-neuropathic form, type 2 is the acute neuropathic form with early onset and rapid neurologic deterioration, type 3 is the chronic neuropathic form with slow progression of neurologic features. GD shows a marked phenotypic diversity ranging from adult asymptomatic forms, at the mild end, to perinatal lethal forms at the severe end of the disease spectrum. Formal diagnosis of Gaucher disease is based on the measurement of glucocerebrosidase levels in circulating leukocytes and molecular genetic analysis.

Disease - Gaucher disease

Definition
An autosomal recessive lysosomal storage disease due to deficient activity of lysosomal beta-glucocerebrosidase, and characterized by accumulation of glucosylceramide in the reticulo-endothelial system. GD is a multisystem disease historically divided into three main subtypes on the basis of the presence of neurologic involvement, age at onset and progression rate: type 1 is the non-neuropathic form, type 2 is the acute neuropathic form with early onset and rapid neurologic deterioration, type 3 is the chronic neuropathic form with slow progression of neurologic features. GD shows a marked phenotypic diversity ranging from adult asymptomatic forms, at the mild end, to perinatal lethal forms at the severe end of the disease spectrum. Formal diagnosis of Gaucher disease is based on the measurement of glucocerebrosidase levels in circulating leukocytes and molecular genetic analysis.

Acronym
GD

Alternative names
Acid beta-glucosidase deficiency
GBA deficiency
Glucocerebrosidase deficiency

Cross references
MIM: 230400 (phenotype)
MeSH: C061720 (D)
MeSH: D005776 (T)

Disclaimer
Any medical or genetic information present in this entry is provided for research, educational and informational purposes only. It is not in any way intended to be used as a substitute for professional medical advice, diagnosis, treatment or care. Our staff consists of biologists and biochemists that are not trained to give medical advice.

Related UniProtKB entry
Browse 1 entry

P04062 - GBA1_HUMAN
Lysosomal acid glucosylceramidase | Gene: GBA1 (GBA, GC, GLUC) | Homo sapiens (Human) | EC:3.2.1.45 | 536 amino acids | Evidence at protein level | Annotation score: 50

Keywords
#Glycosidase #Glycosyltransferase #Hydrolase #Transferase #Cholesterol metabolism #Lipid metabolism #Sphingolipid metabolism #Steroid metabolism #Steroid metabolism #Disease variant #Gaucher disease

Richitype
#Neurodegeneration #Parkinson disease #Parkinsonism

178 reviewed variants · 2 active sites · 5 isoforms · 1 interaction · 7 diseases · 42 3D structures · 119 reviewed publications

Lysosomal acid glucosylceramidase

Glucosylceramidase that catalyzes, within the lysosomal compartment, the hydrolysis of glucosylceramides/GlcCers (such as beta-D-glucosyl-(1<->1')-N-acylsphing-4-enine) into free ceramides (such as N-acylsphing-4-enine) and glucose (PubMed:9201993, PubMed:24211208, PubMed:15916907, PubMed:32144204).

GBA1 - Lysosomal acid gli x +

uniprot.org/uniprotkb/P04062/entry

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UniProt BLAST Align Peptide search ID mapping SPARQL UniProtKB

Advanced | Search | Help

P04062 · GBA1_HUMAN

Protein¹ Lysosomal acid glucosylceramidase
Gene¹ GBA1
Status¹ UniProtKB reviewed (Swiss-Prot)
Organism¹ Homo sapiens (Human)

Amino acids 536 (go to sequence)
Protein existence¹ Evidence at protein level
Annotation score¹

Entry Variant viewer Feature viewer Genomic coordinates Publications External links History

BLAST Align Download Add Add a publication Entry feedback

Function¹

Glucosylceramidase that catalyzes, within the lysosomal compartment, the hydrolysis of glucosylceramides/GlcCers (such as beta-D-glucosyl-(1<->1')-N-acylsphing-4-enine) into free ceramides (such as N-acylsphing-4-enine) and glucose (PubMed:9201993, PubMed:24211208, PubMed:15916907, PubMed:32144204).
Plays a central role in the degradation of complex lipids and the turnover of cellular membranes (PubMed:27378688).
Through the production of ceramides, participates in the PKC-activated salvage pathway of ceramide formation (PubMed:19279011).
Catalyzes the glucosylation of cholesterol, through a transglucosylation reaction where glucose is transferred from GlcCer to cholesterol (PubMed:24211208, PubMed:26724485, PubMed:32144204).
GlcCer containing mono-unsaturated fatty acids (such as beta-D-glucosyl-N-(2'-octadecenoylethyl)-sphing-4-enine) are preferred as glucose donors for cholesterol glucosylation when compared with GlcCer containing same chain length of saturated fatty acids (such as beta-D-glucosyl-N-octadecanoyl-sphing-4-enine) (PubMed:24211208).
Under specific conditions, may alternatively catalyze the reverse reaction, transferring glucose from cholesteryl 3-beta-D-glucoside to ceramide (PubMed:26724485) (Probable). Can also hydrolyze cholesteryl 3-beta-D-glucoside producing glucose and cholesterol (PubMed:24211208, PubMed:26724485).
Catalyzes the hydrolysis of galactosylceramides/GalCers (such as beta-D-galactosyl-(1<->1')-N-acylsphing-4-enine), as well as the transfer of galactose between GalCers and cholesterol in vitro, but with lower activity than with GlcCers (PubMed:32144204).
Contrary to GlcCer and GalCer, xyllosylceramide/XylCer (such as beta-D-xylosyl-(1<->1')-N-acylsphing-4-enine) is not a good substrate for hydrolysis, however it is a good xylose donor for transxylosylation activity to form cholesteryl 3-beta-D-xyloside (PubMed:33361282) (2 Publications) (1 Publication).
Source: Rhea 15269 (2)

Catalytic activity¹

a beta-D-glucosyl-(1<->1')-N-acylsphing-4-enine + H₂O = an N-acylsphing-4-enine + D-glucose (3 Publications)
This reaction proceeds in the forward direction (2 Publications)
EC 3.2.1.45 (UniProtKB) ENZYME (2) Rhea (2)
Source: Rhea 15269 (2)

Hide Rhea reaction

a beta-D-glucosyl-(1<->1')-N-acylsphing-4-enine
CHEBI:22601

H₂O
CHEBI:15377

an N-acylsphing-4-enine
CHEBI:52639

D-glucose
CHEBI:4167

Disease & Variants

Disease & Variants

Gaucher disease 1 (GD1)

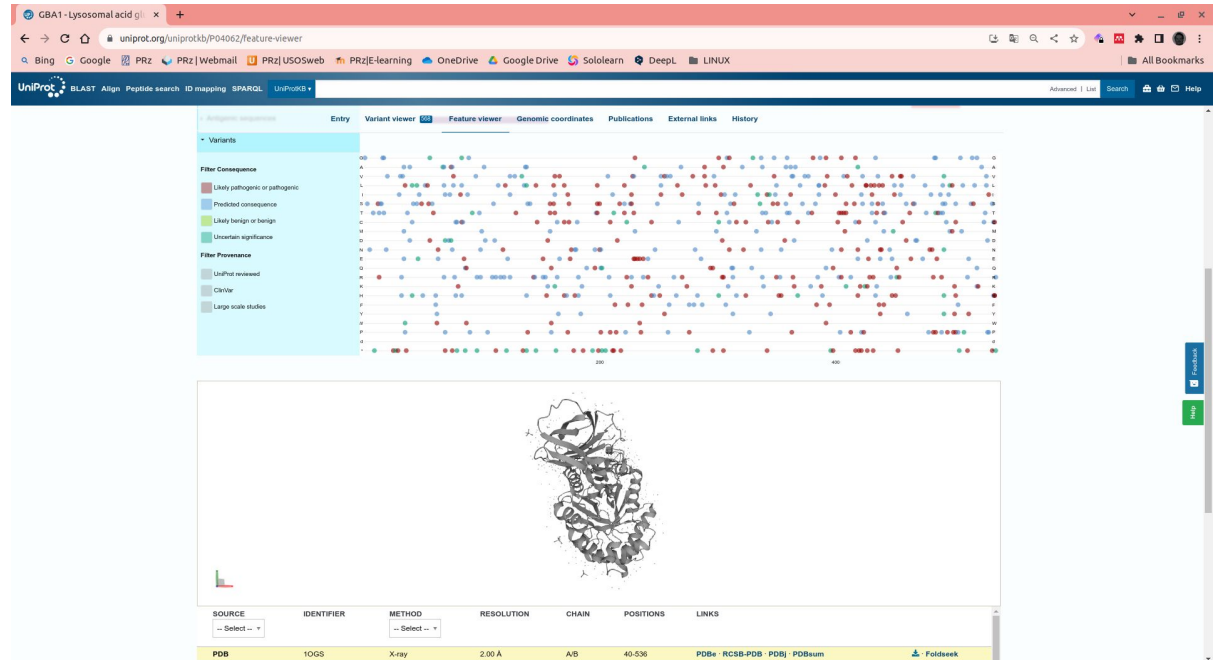
Gaucher disease 2 (GD2)

Gaucher disease 3 (GD3)

Gaucher disease 3C (GD3C)

Gaucher disease perinatal lethal
(GDPL)

Parkinson disease (PARK)



Structure disease relationship

GBA1 - Lysosomal acid g | X

uniprot.org/uniprotkb/P04062/entry#structure

Bing Google PRZ PRZ | Webmail PRZ | USOSweb PRZ | E-learning OneDrive Google Drive Sololearn DeepL LINUX

UniProt BLAST Align Peptide search ID mapping SPARQL UnProtB

Advanced | Log Search

Function
Names & Taxonomy
Subcellular Location
Disease & Variants
PTM/Processing
Expression
Interaction
Structure
Family & Domains
Sequence & Isoforms
Similar Proteins

Entry Variant viewer Feature viewer Genomic coordinates Publications External links History

Structure



SOURCE	IDENTIFIER	METHOD	RESOLUTION	CHAIN	POSITIONS	LINKS
PDB	1OGS	X-ray	2.00 Å	A/B	40-536	PDB: RCSB-PDB: PDB: PDBeum Foldseek
PDB	1Y7V	X-ray	2.40 Å	A/B	40-536	PDB: RCSB-PDB: PDB: PDBeum Foldseek
PDB	2F61	X-ray	2.50 Å	A/B	40-536	PDB: RCSB-PDB: PDB: PDBeum Foldseek
PDB	2J25	X-ray	2.90 Å	A/B	40-536	PDB: RCSB-PDB: PDB: PDBeum Foldseek
PDB	2NSX	X-ray	2.11 Å	A/B/C/D	40-536	PDB: RCSB-PDB: PDB: PDBeum Foldseek
PDB	2NT0	X-ray	1.79 Å	A/B/C/D	40-536	PDB: RCSB-PDB: PDB: PDBeum Foldseek
PDB	2NT1	X-ray	2.30 Å	A/B/C/D	40-536	PDB: RCSB-PDB: PDB: PDBeum Foldseek
PDB	2V3D	X-ray	1.96 Å	A/B	40-536	PDB: RCSB-PDB: PDB: PDBeum Foldseek
PDB	2V3E	X-ray	2.00 Å	A/B	40-536	PDB: RCSB-PDB: PDB: PDBeum Foldseek
PDB	2V3F	X-ray	1.95 Å	A/B	40-536	PDB: RCSB-PDB: PDB: PDBeum Foldseek

Features

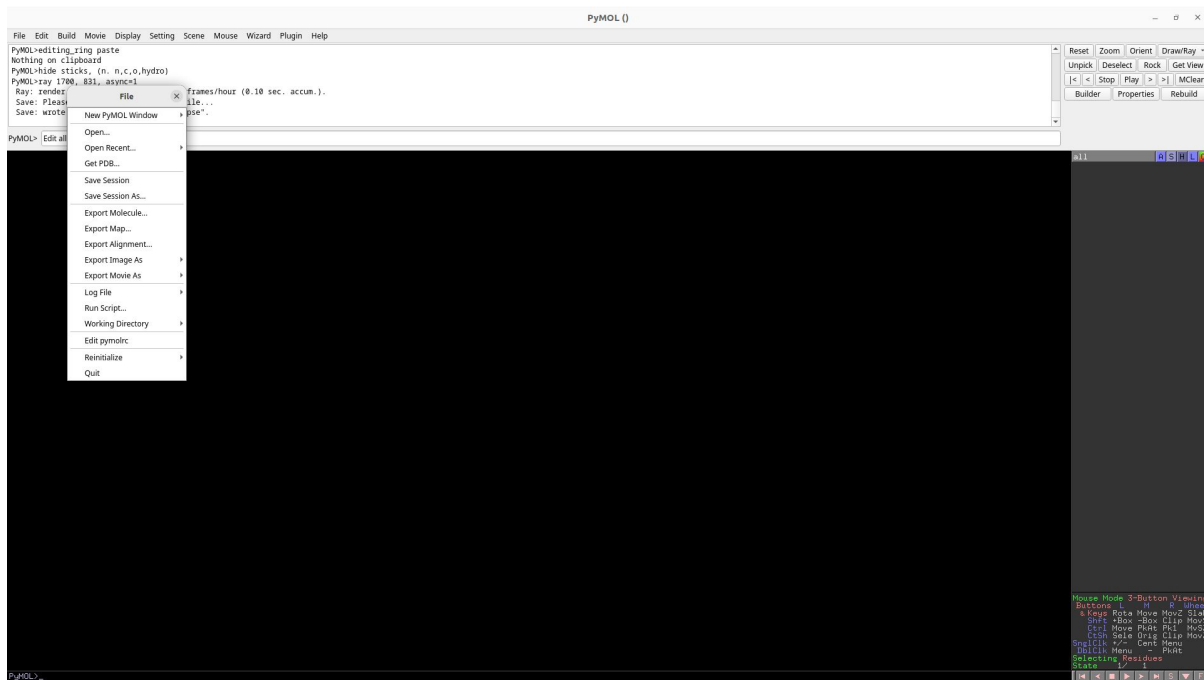
Showing features for beta strand', helix', turn'.



PyMOL

Przed rozpoczęciem pracy warto pamiętać by:

- zapisać plik sesji:
File|Save Session
- zapisać plik log:
File|Log File|Open...
- Właściwości obiektów modyfikowane są w sekcji po prawej stronie i kontrolowane przez przyciski w DEDYKOWANYM wierszu.
- Domyślne ustawienia myszki to (sprawdź w razie problemów):
3-Button Viewing
Residues



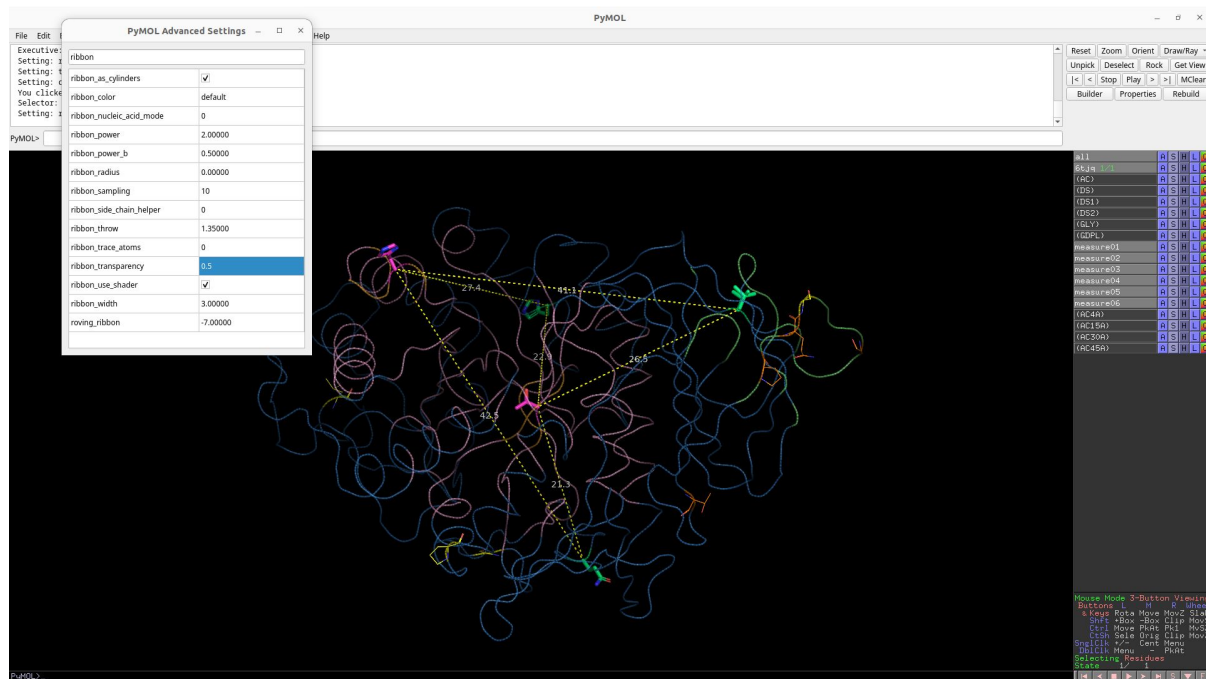
Analiza strukturalna

- Załaduj wybraną strukturę do programu PyMOL (uzasadnij swój wybór).
- Zaznacz aminokwasy tworzące:
 - miejsce aktywne (sekcja 'Function')
 - wiązania dwusiarczkowe oraz ulegające glikozylacji (sekcja 'PTM/Processing')
- Przykładowe polecenia:
`>fetch 6tjq`
`>select AC, 6tjq and (resi 274,379)`
- Pomoc dla wiersza poleceń jest dostępna za pomocą polecenia:
`>help`
`>help fetch`
`>help select`
`>help selection`



Analiza wariantu GDPL

- Zaznacz ulegające mutacji aminokwasy.
- Przygotuj wizualizację.
- Wykonaj pomiary odległości aminokwasy AC-aminokwasy GDPL. Wizard|Measurement
- W oparciu o wyniki podziel strukturę na 4 strefy oddziaływań:
 - > AC +4Å
 - > max. pomiar odległości/3, np.: $42.5/3=14.2$
 - >strefy AC +15Å, +30Å, +45Å
- Przykładowe polecenia:
hide sticks, (n. n,c,o,hydro)
select AC4A, 6tjq and AC around 4
- Dodatkowe ustawienia dotyczące np. przezroczystości elementów dostępne są w Setting|Transparency lub Setting|Edit All...



Przygotowanie wizualizacji

- Obrazki do raportu przygotuj za pomocą przycisku Draw/Ray.
...by wygenerować kolejne obrazki należy użyć przycisku Back.
- Zadbaj o numerację i opis każdego obrazku w raporcie.
- Proszę przeprowadzić prostą analizę:
 - dla wybranego wariantu choroby (GD1 lub GD2 lub GD3) jaka min, max, średnia odległość mutacji od miejsca aktywnego (dla min 5 wybranych mutacji)
 - jaka jest dystrybucja mutacji w poszczególnych strefach (ile aminokwasów przypada na każdą strefę?)
 - ile mutacji i jakiego rodzaju zlokalizowanych jest na powierzchni?