
Thank you for your attention!
Predoc at EMBL Hamburg
SAXS
Bioinformatics
IDP by NMR
Dmitri Svergun's Lab
Visiting scientist at EMBL Heidelberg
Project description:
Systems Biology
Kiran Patil's Lab
Master's degree
Bioinformatics
University of Rome "Tor Vergata"
Thesis title:
"Computational analisys of the Cyclophilin-Cyclosporin A complex in Lesihmania and Human"
Bachelor degree
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Small Thesis Project:
"The Genetic Drift and its Mathematical Modeling"


Valencia
• Microbiology
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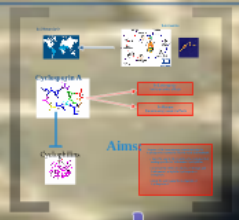

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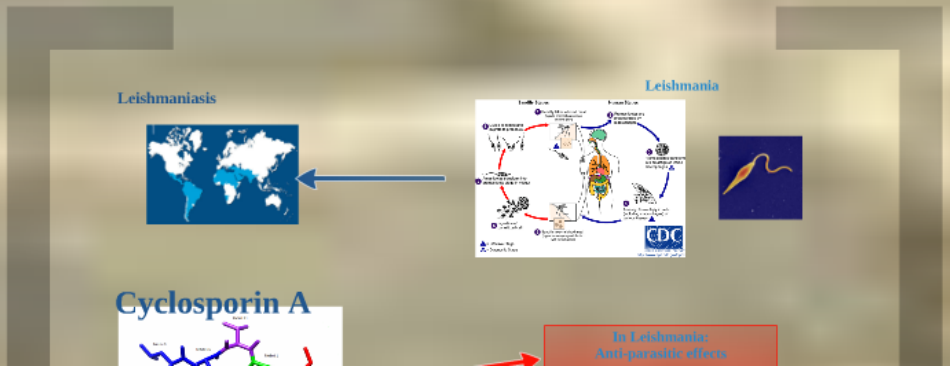

Cyclosporin A compl

Center for Molecular Bioinformatics, Department of Biology

Manuela Helmer Citterich

Leishmaniasis

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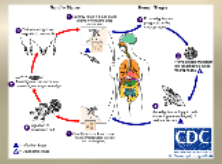
Leishmaniasis

Leishmania



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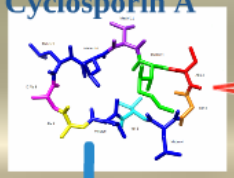
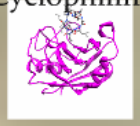


In Leishmania:
Anti-parasitic effects

In Human:
Immunosuppressant effects

Cyclophilins



Aims:

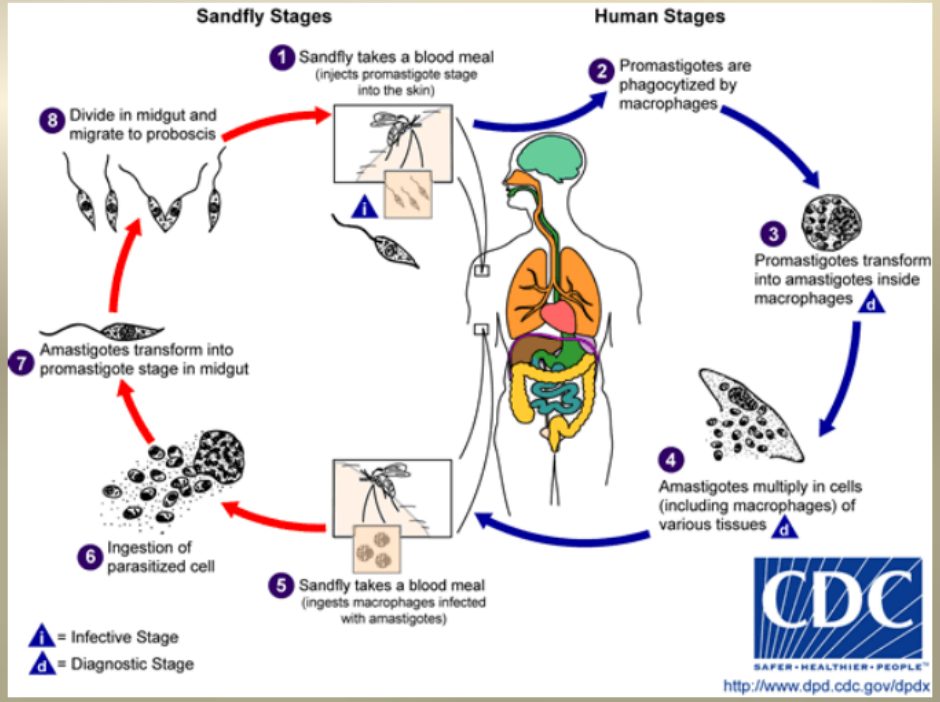
Because of the immunosuppressant activity, the Cyclosporin A cannot be used to treat leishmaniasis.

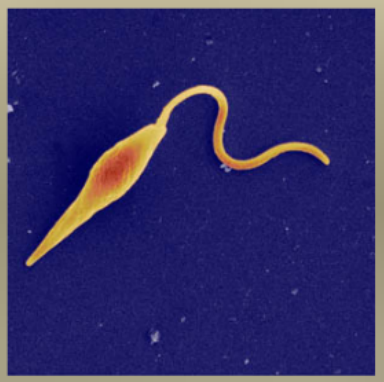
- Pave the way to the creation of a Cyclosporin A analog specific for leishmania Cyclophilins
- Detect all the differences between human and leishmania Cyclophilin A / Cyclosporin A complexes.
- Study the anti-parasitic mechanism of Cyclosporin A.

Leishmaniasis

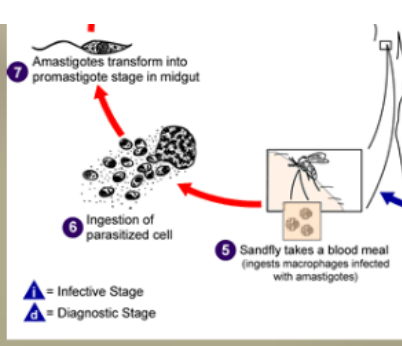
Cyclosporin A

Leishmania

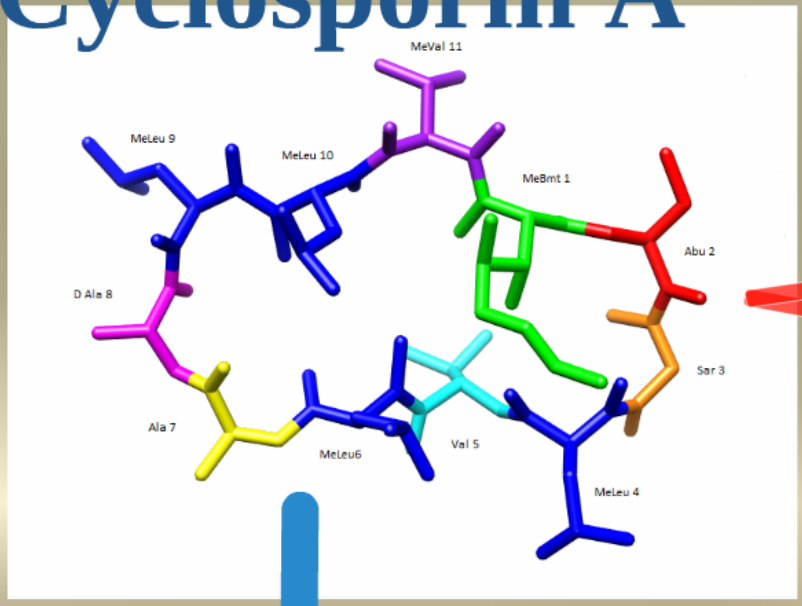




In Leishmania:



Cyclosporin A



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In Leishmania:
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Because of the immunosuppressant activity the

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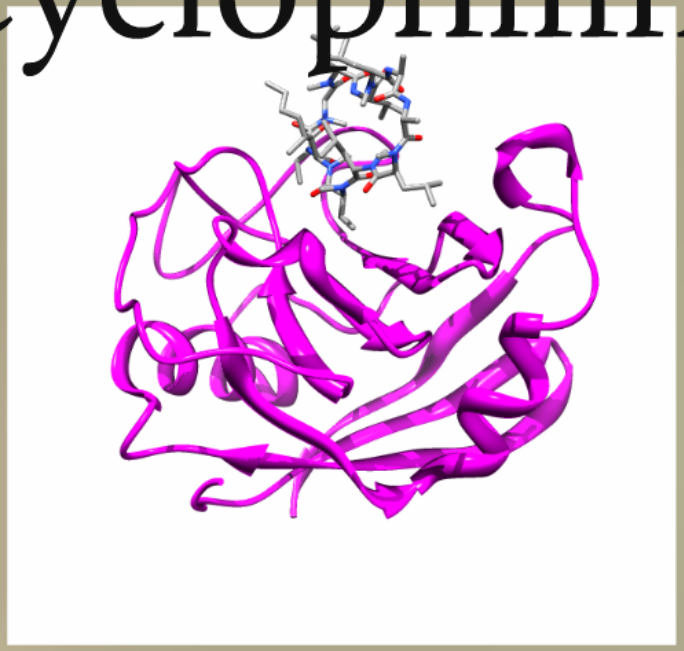

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Because of the immunosuppressant activity the Cyclosporin A cannot be used to treat leishmaniasis

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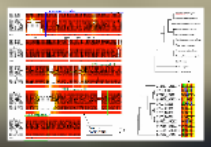
Cyclophilins

Aims:

Conclusions:

Cyclophilin 40:



Cyclophilin 40 seemed to be highly interesting because is the only Cyclophilin that get phosphorylated at the amastigote stage and binds to HSPs.

We searched for paralogues and proposed two Leishmania infantum proteins that, if mutated toghether with the Cyclophilin 40, could generate a lethal phenotipe in the parasite: A4I935_LEIIN (CYP 4) and A4HSQ3_LEIIN (CYP 2).

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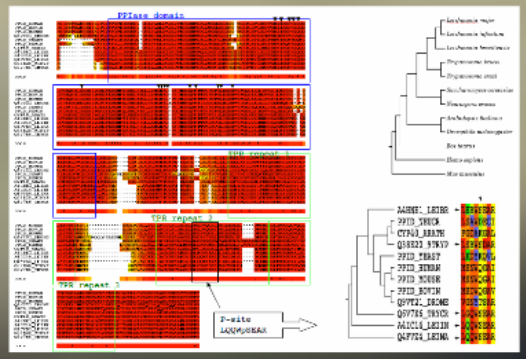

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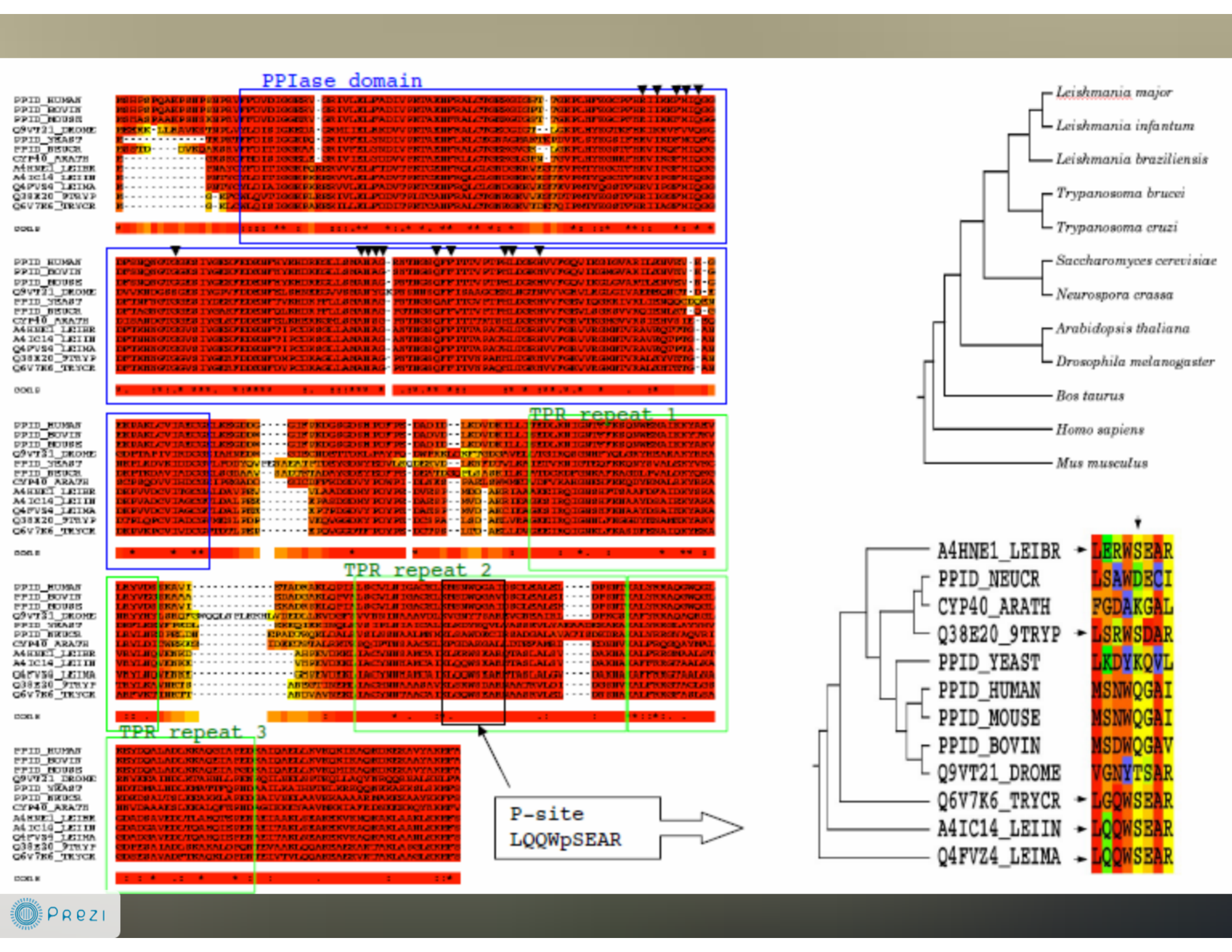
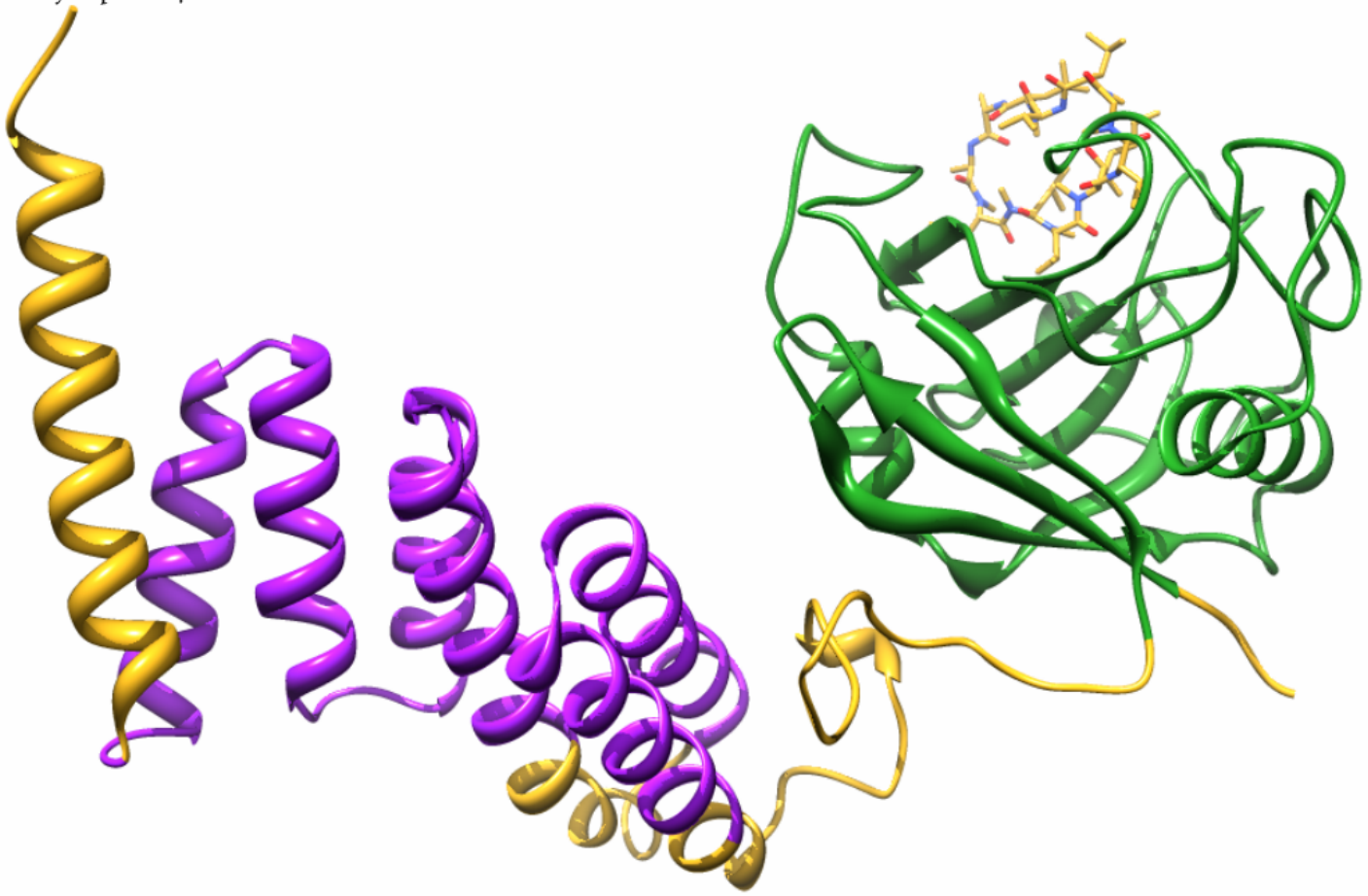
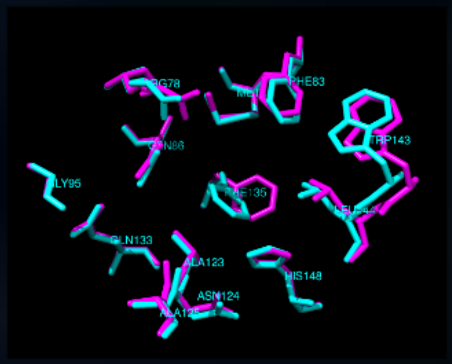

PPIase domain
TPR repeat 1
TPR repeat 2
TPR repeat 3
P-site
LQQWpSEAR
Leishmania major
Leishmania infantum
Leishmania braziliensis
Trypanosoma brucei
Trypanosoma cruzi
Saccharomyces cerevisiae
Neurospora crassa
Arabidopsis thaliana
Drosophila melanogaster
Bos taurus
Homo sapiens
Mus musculus
A4HNE1_LEIBR LERWSEAR
PPID_NEUCR LSAWDECI
CYP40_ARATH FGDAKGAL
Q38E20_9TRYP LSRWSDAR
PPID_YEAST LKDYKQVL
PPID_HUMAN MSNWQGAI
PPID_MOUSE MSNWQGAI
PPID_BOVIN MSDWQGAV
Q9VT21_DROME VGNYTSAR
Q6V7K6_TRYCR LGQWSEAR
A4IC14_LEIIN LQQWSEAR
Q4FVZ4_LEIMA LQQWSEAR

Leishmania infantum model of Cyclophilin 40



Superimposition of two structures: 3EOV and 3HAQ



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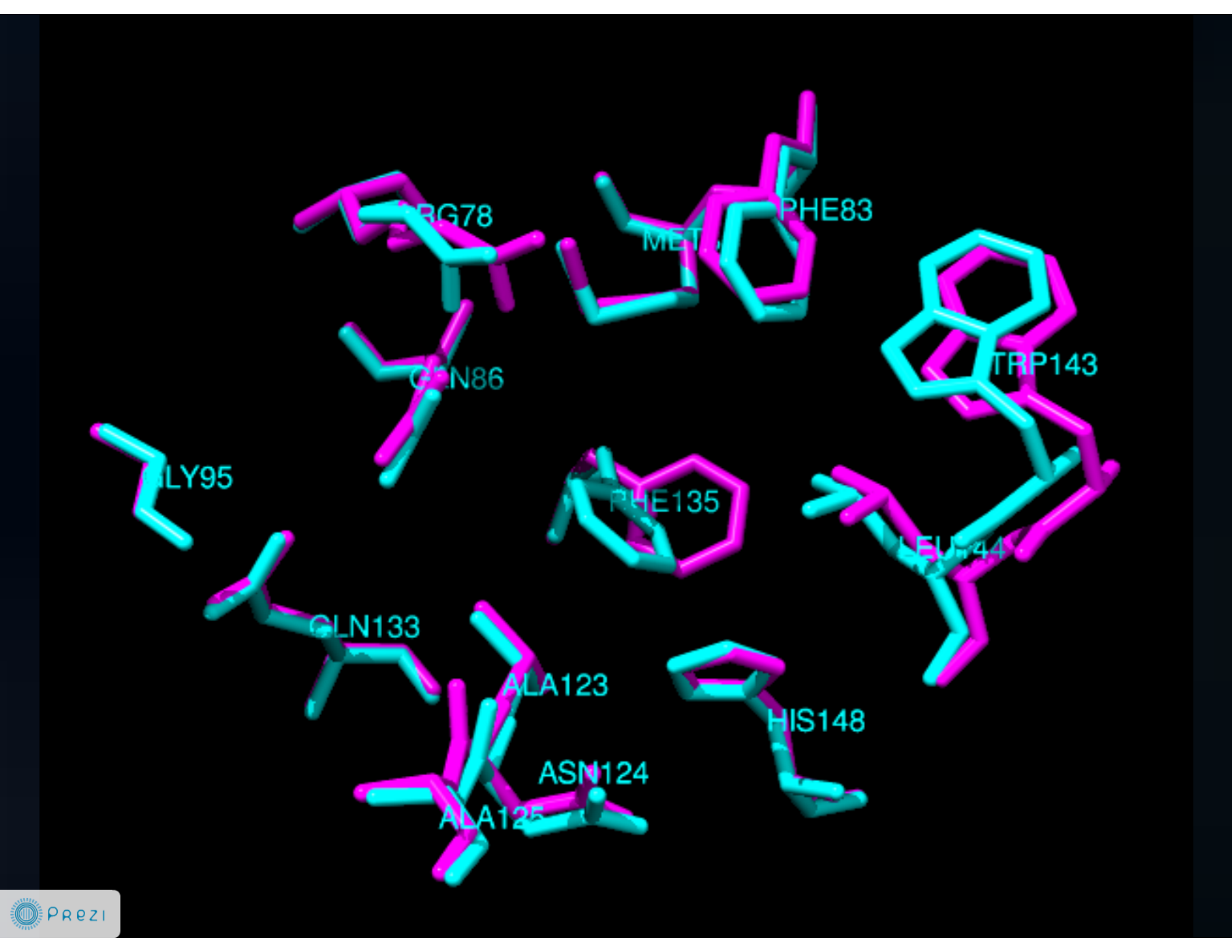
PHE83
TRP143
PHE135
GLN133
ALA123
HIS148
ASN124

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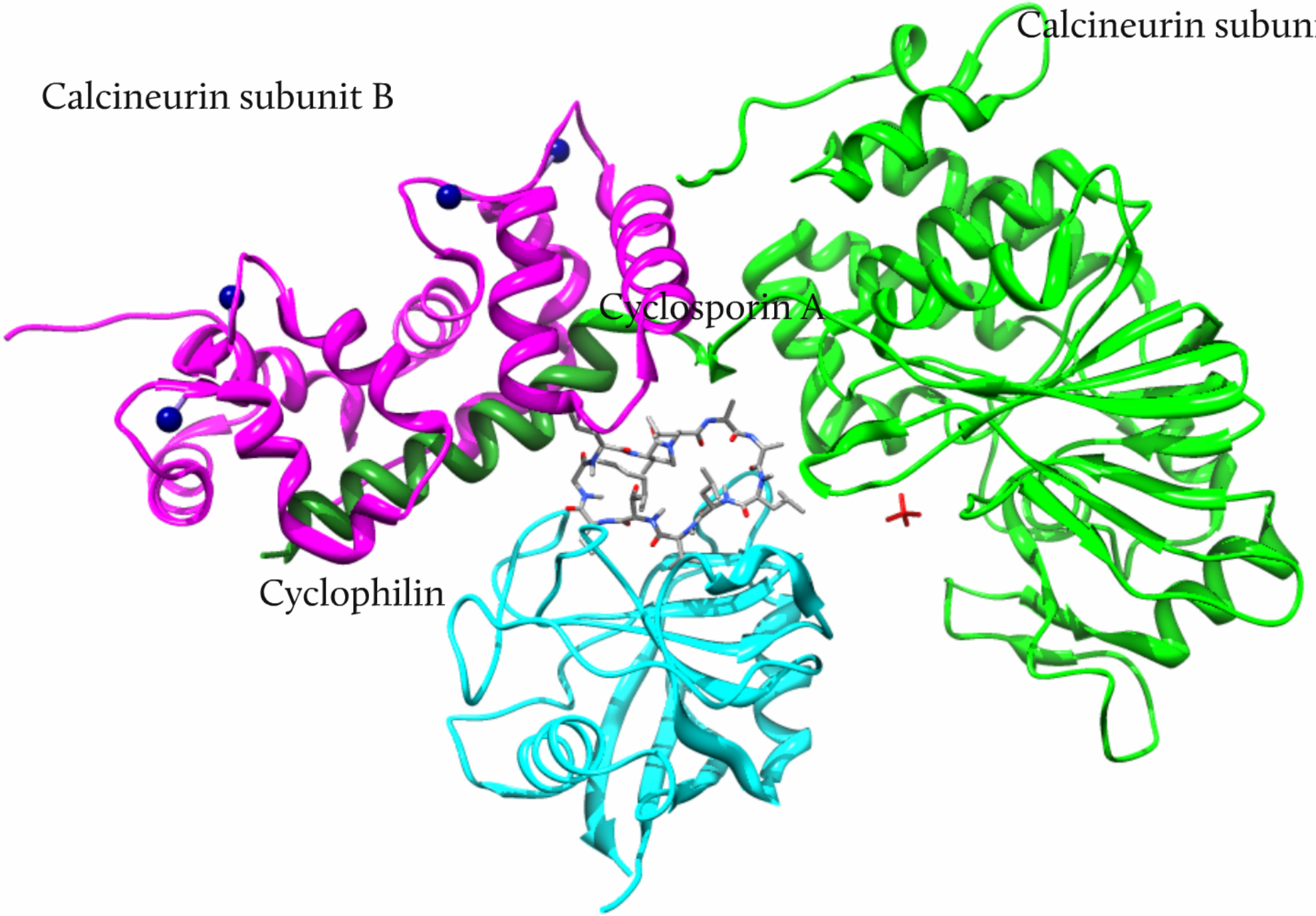
Calcineurin subunit A
Calcineurin subunit B
Cyclosporin A
Cyclophilin

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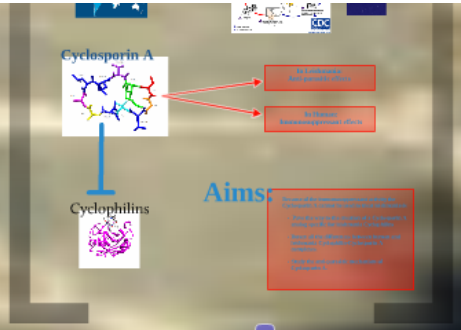

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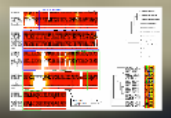

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Cyclosporin A

Cyclophilins

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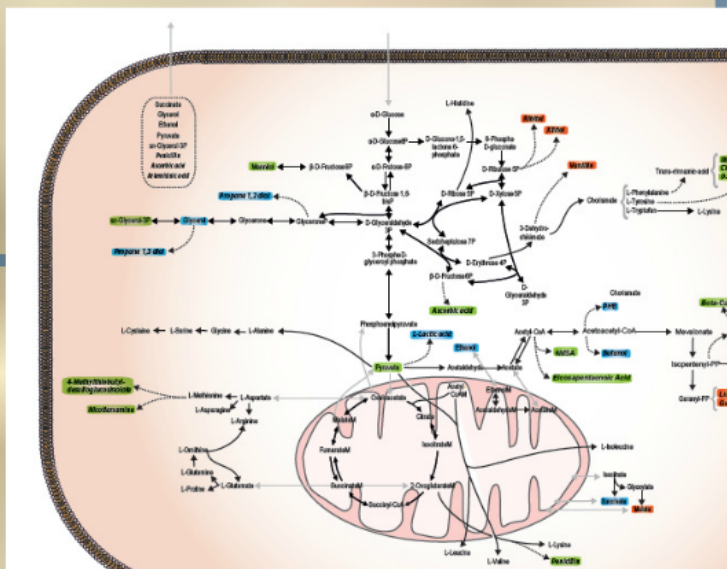

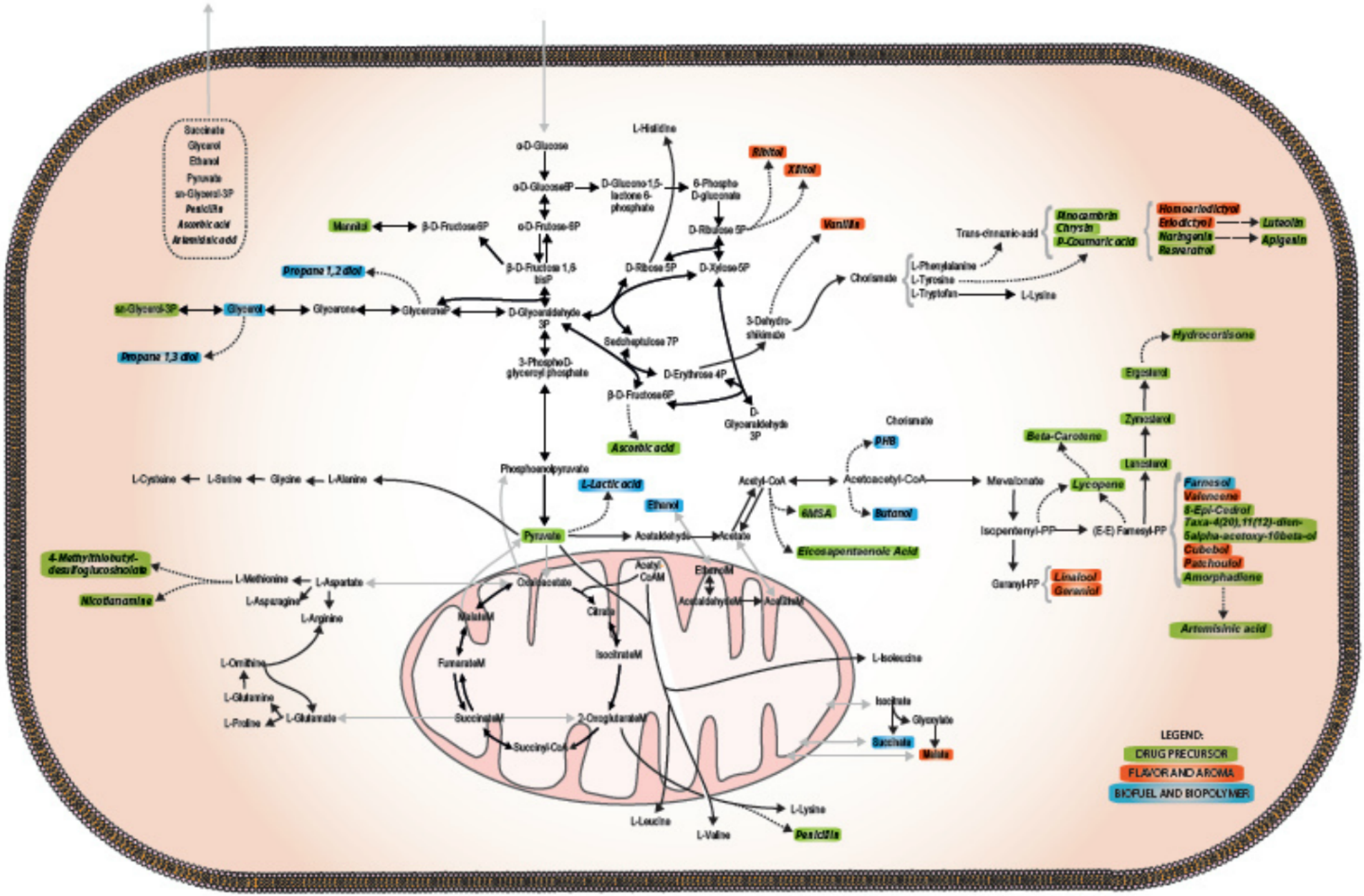
Succinate
Glycerol
Ethanol
Pyruvate
sn-Glycerol-3P
Penicillin
Ascorbic acid
Artemisinic acid
α-D-Glucose
α-D-Glucose6P
D-Glucono-1,5-lactone 6-phosphate
6-Phospho D-gluconate
L-Histidine
Ribitol
Xilitol
Mannitol
β-D-Fructose6P
α-D-Fructose-6P
β-D-Fructose 1,6-bisP
Propane 1,2 diol
D-Ribose 5P
D-Xylose 5P
Vanillin
Trans-cinnamic-acid
Rhinocanthin
Chrysin
p-Coumaric acid
Homoeriodictyol
Eriodictyol
Naringenin
Resveratrol
Luteolin
Apigenin
Chorismate
L-Phenylalanine
L-Tyrosine
L-Tryptofan
L-Lysine
sn-Glycerol-3P
Glycerol
Glycerone
Glycerone-P
D-Glyceraldehyde 3P
Propane 1,3 diol
Sedoheptulose 7P
3-Dehydro-shikimate
3-PhosphoD-glyceroyl phosphate
D-Erythrose 4P
β-D-Fructose6P
D-Glyceraldehyde 3P
Ascorbic acid
Hydrocortisone
Ergosterol
Zymosterol
Lanosterol
Beta-Carotene
Lycopene
Chorismate
PHB
Acetyl-CoA
Acetoacetyl-CoA
Mevalonate
6MSA
Butanol
Eicosapentaenoic Acid
Isopentenyl-PP
(E-E) Farnesyl-PP
Geranyl-PP
Linalool
Geraniol
Farnesol
Valencene
8-Epi-Cedrol
Taxa-4(20),11(12)-dien-5alpha-acetoxy-10beta-ol
Cubebol
Patchoulol
Amorphadiene
Artemisinic acid
Phosphoenolpyruvate
L-Lactic acid
Ethanol
Pyruvate
Acetaldehyde
Acetate
L-Cysteine
L-Serine
Glycine
L-Alanine
4-Methylthiobutyl-desulfoglucosinolate
Nicotianamine
L-Methionine
L-Aspartate
L-Asparagine
L-Arginine
L-Ornithine
L-Glutamine
L-Proline
L-Glutamate
Oxaloacetate
Acetyl-CoAM
EthanolM
AcetaldehydeM
AcetateM
MalateM
CitrateM
FumarateM
IsocitrateM
SuccinateM
2-OxoglutarateM
Succinyl-CoA
L-Isoleucine
Isocitrate
Glyoxylate
Succinate
Malate
L-Leucine
L-Valine
L-Lysine
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LEGEND:
DRUG PRECURSOR
FLAVOR AND AROMA
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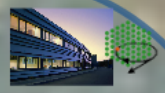

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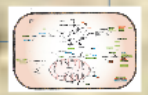

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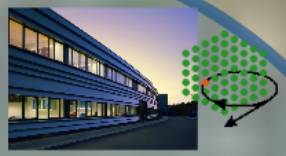

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