

Colored PROMALS3D alignment (sequences in aligned order)

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Conservation:          55          55 599959  59995995          595 5 5 9 9
1yc2_chainB_p004     1 MEDEIRKAAEILA--KSKHAVVFTGAGISAESGIPTFRG-----EDGLWR---KYDPEEVASISGFKRN 60
2h4f_chainA_p001     1 --MKMKEFLDLLN--ESRLTVTLTGAGISTPSGIPDFRGPNGIYKK-----YSQ---NVFDIDFFYSHP 57
4fvt_chainA_p003    122 -KLSLQDVAELIRARACQRVVVMVGAGISTPSGIPDFR-SPGSGLYSNLQOYDLPYPEAIFELPFFFHNP 189
4i5i_chainA_p002    241 --NTIEDAVKLLQ--ECKKIIVLTGAGVSVSCGIPDFRSRDGIYARLAVDFPDLDPQAMFDIEYFRKDP 306
Consensus aa:        ...phpchhc11...tp.h1hhhGAG1Sh.tGIPsFRt.....hp.....Pp.hhp1..F.ppP
Consensus ss:        hhhhhhhhh h eeeee hhh h hhh hhhhhh h

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Conservation:          9 5559          95 9 5 5 9 99999 9 5 59          5 99 9
1yc2_chainB_p004     61 RAFWEFSMEM-KDKLFAEPNPAHYAIAELERMGIVKAVITQNI DMLHQ RAGS--RVLELHGSM DKL DCL 127
2h4f_chainA_p001     58 EEFYRFAKEGIFPMLQAKPNLAHVLLAKLEEKGLIEAVITQNI DRLHQ RAGS--KKVIELHGNVVEEYYCV 125
4fvt_chainA_p003    190 KPFFTLAKE--LYPGNYKPNVTHYFLRLLLDKGLLLRLY TQNI DGLERVSGIPASKLVEAHGT FASATCT 257
4i5i_chainA_p002    307 RPFFKFAKE--IYPGQFQPSLCHKFI ALS DKEGKLLRNY TQNI DTLEQVAGI--QRIIQCHGS FATASCL 372
Consensus aa:        c.F@phtbE..b....hpPs.hH.h1.b.ccbGblb..htQNI D.Lcp.tG...p+llpHGsh.ph.Ch
Consensus ss:        hhhhhhhhhh hhhh hhhhhhhhhh eeeee hhhh eeeeeeeeeeee

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Conservation:          9 5 5 5959 9 59 595999 995 5 55 5 959
1yc2_chainB_p004    128 DCHETYDWSEFVEDFNKGEI PRCRKC----GSYYVKPRV VLFGEPLPQRTLFEAIEEAKHCD AFM VVGSS 193
2h4f_chainA_p001    126 RCEKKYTVEDVIKKLESSDVPLCDDC-----NSLIRPNIVFFGENLPQDALREAI GLSSRASLMIVL GSS 190
4fvt_chainA_p003    258 VCQRPFPGEDIRADVMADRVPRCPVC-----TGVVKPDIVFFGEPLPQRF-LLHVVD FPMAD LLLILGTS 321
4i5i_chainA_p002    373 ICKYKVDCEAVRGDIFNQVVP RCP RCPA DEPLA IMKPEIVFFGENLP EQFH RAMKYDKDEVDLLIVIGSS 442
Consensus aa:        .Cp..hs.p.h..ch....lP.C..C.....hh+Pp1VhFGEsLPpphh..h.....hshhh1lGoS
Consensus ss:        hhhhhhhh ee ee hhhhhhhhhhhh eeeee

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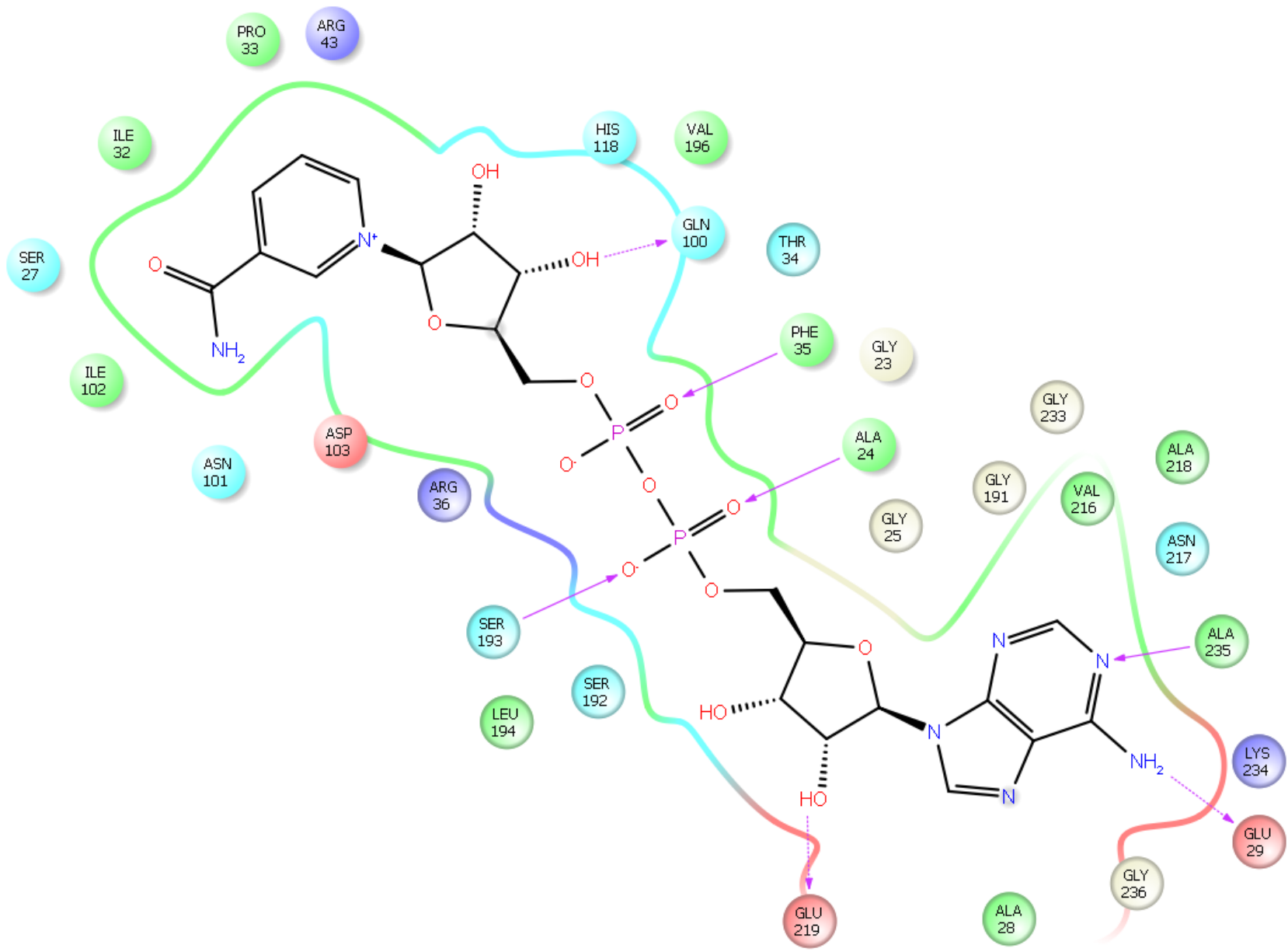
Conservation:          9 9 9 9 55          9 55 55 5 5 5
1yc2_chainB_p004    194 LVVYPAAELPYIAKKAGAKMIIVNAEPTMADP--IF--DVKII GKAGEVLPKIVEEVK-RLRSE----- 252
2h4f_chainA_p001    191 LVVYPAAELPLITVRSGGKLVIVNLGETPFDD--IA--TLKYNMDVVEFARRVMEEGGIS----- 246
4fvt_chainA_p003    322 LEVEPFASL TEAVR-SSVPRLLINRDLVGPLAWHPRSRDVAQLGDVVHGVESLV LLLGWT--EEMRDLVQ 388
4i5i_chainA_p002    443 LKVRPVALIPSSIP-HEVPQILINREPLPHL---HF--DVELLGD CDVI INELCHRLGGEY-AKLCCNP- 504
Consensus aa:        L.V.PhA.lS..h....s...lllN...h...s.....sl.b..chs..h.plhc...p...c.....
Consensus ss:        hhhhhhhhhhhh eeee eeee hhhhhhhhhhhh h hhhh h

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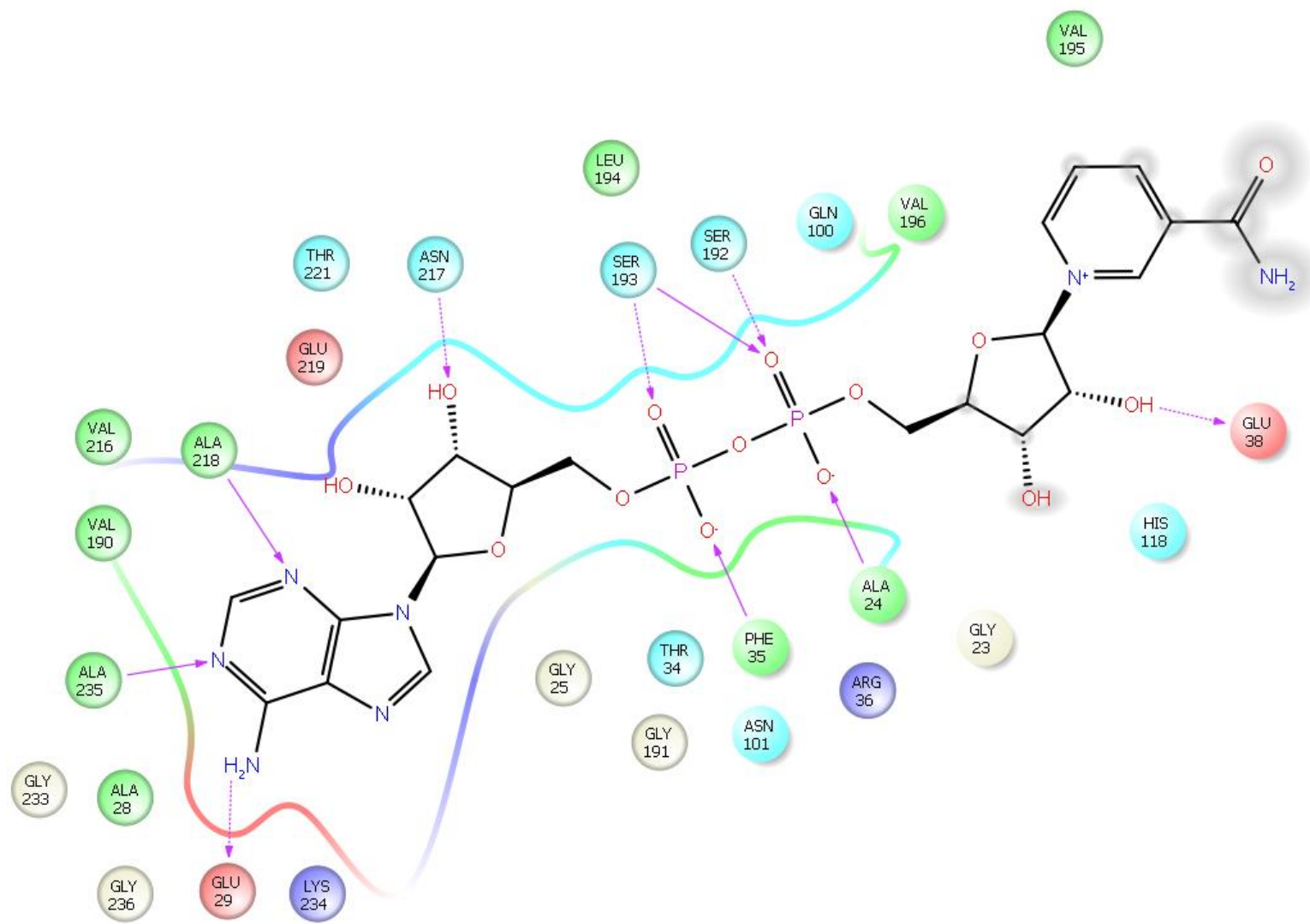
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Conservation:
1yc2_chainB_p004     -----
2h4f_chainA_p001     -----
4fvt_chainA_p003    389 RETGKLD--- 395
4i5i_chainA_p002    505 --VKLSEITE 512
Consensus aa:        .....
Consensus ss:        hh

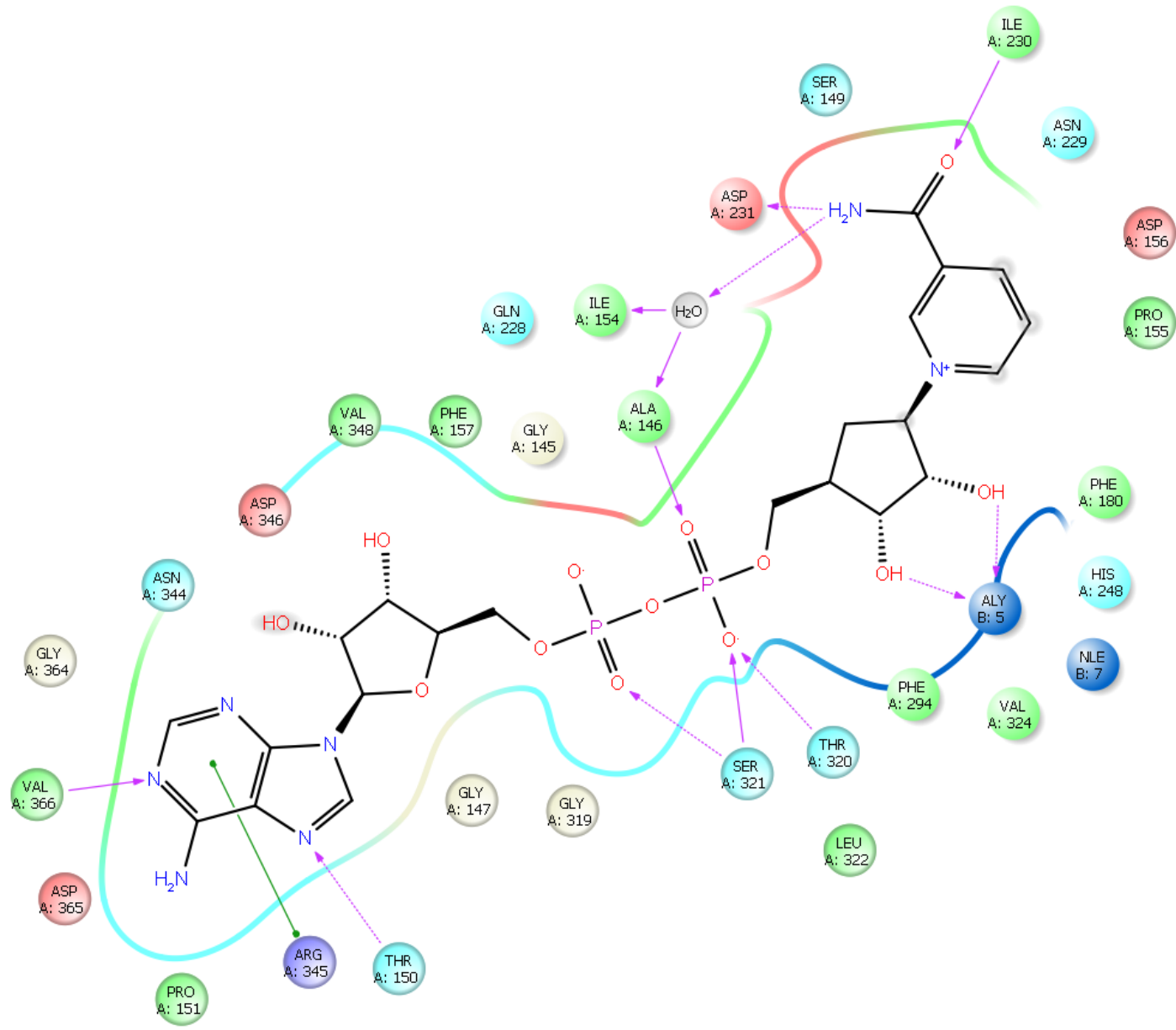
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NAD⁺ in Sir2Af2 (1YC2:B)



NAD⁺ in Sir2Af2 (1YC2:A)



NAD⁺ in SIRT3 (4FVT)

Residues in the binding pocket of A and C are mostly conserved.

The first conserved section (G23-G37 in 1Sir2Af2) is part of both A and C pockets:

```
99959 59995995  
'GAGISAESGIPTFRG-  
'GAGISTPSGIPDFRGI  
'GAGISTPSGIPDFR-  
'GAGVSVSCGIPDFRSI
```

e.g. for 1YC2:B;

A Pocket: Gly23, Ala24, Gly25, Ala28, Glu29,

C Pocket: Ser27, Ile32, Pro33,

The second conserved section (Q100-D103 in Sir2Af2) is part of C pocket:

```
9999  
'QNIDI  
'QNIDI  
'QNIDI  
'QNIDI
```

The third conserved section (G191-S193 in Sir2Af2) is part of A pocket phosphate binding site:

```
959  
'GSS  
'GSS  
'GTS  
'GSS
```

The fourth section (N217-A218 in Sir2Af2) is part of A pocket:

```
9  
'NAEI  
'NLGI  
'NRDI  
'NREI
```

The fifth section (K234-G236 in Sir2Af2) is part of A pocket:

55

.GKA(

IMDV

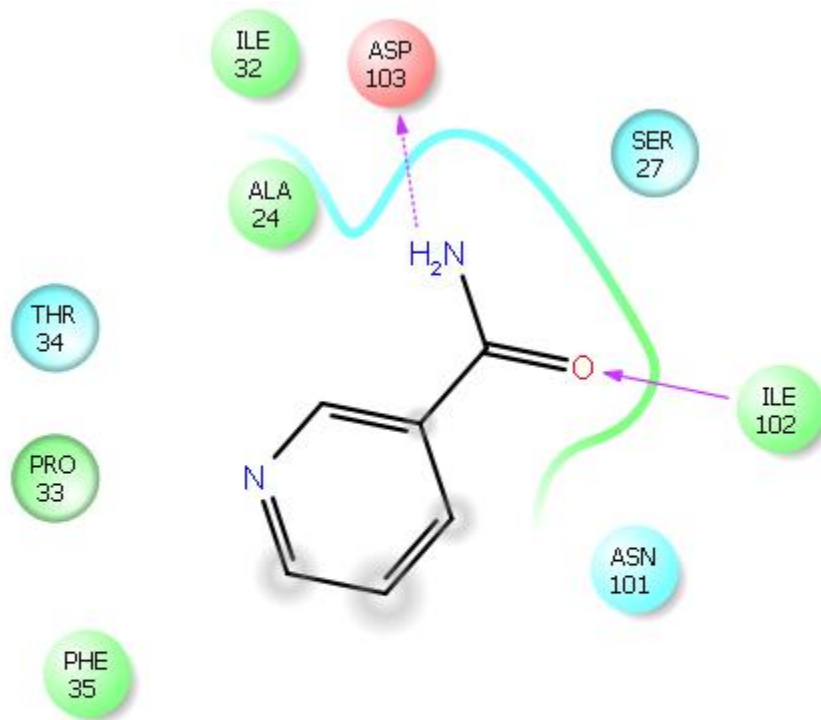
.GDV

.GDCI

The B pocket actually doesn't have much contact between NAD⁺ and Sirtuins. And we found only Val195 in 1YC2:A

In SIRT1 structure (4I5I), the nicotinamide moiety is in a different pocket (similar to what identified by Marmorstein's group as D pocket).

NAM binding pocket is consistent with the C pocket.



NAM in Sir2Af2 (1YC2:A)