

Fig S6. Biochemical association of the previously identified HIV Gag sectors listed in the Supporting Information of [1]. These sectors were inferred in [1] using the HIV Gag sequence data available at the time of publication. For all structural interfaces, the contact-defining distance between the alpha-carbon atoms was set to d=7Å. The inference method in [1] is similar to the PCA approach [2] tested in this paper, mainly differing in the procedure to form sectors from eigenvectors; specifically, the method in [1] formed sectors from visual inspection of eigenvector biplots, whereas an automated procedure was applied in [2]. Similar to [2], the method in [1] produced relatively large sectors that did not show the highly resolved and modular biochemical association revealed by RoCA (Fig 3). Importantly, no sector reported in [1] was found to be associated with RP. This was due to the fact that the residues in the biochemical domain important in this case (p24-SP1 interface; see Results) were mixed up with the epitope residues associated with LTNP in sector 3.

## References

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- 2. Quadeer AA, Louie RHY, Shekhar K, Chakraborty AK, Hsing IM, McKay MR. Statistical linkage analysis of substitutions in patient-derived sequences of genotype 1a hepatitis C virus nonstructural protein 3 exposes targets for immunogen design. J Virol. 2014;88(13):7628–44. doi:10.1128/JVI.03812-13.