Supporting Information for "A Highly Dissociative and Concerted Mechanism for the Nicotinamide Cleavage Reaction in Sir2Tm Enzyme Suggested by ab initio QM/MM Molecular Dynamics Simulations"

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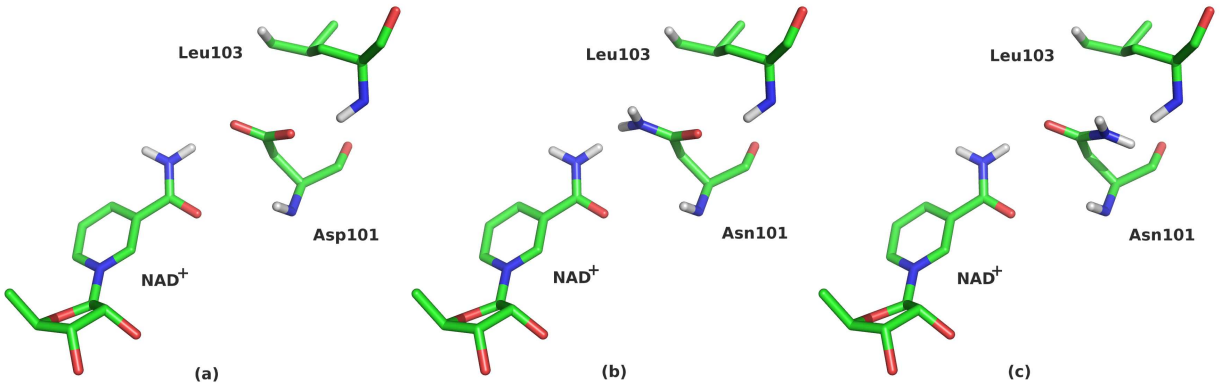

Figure S1: Illustration of two sets of Sir2Tm D101N mutations. (a) Wild-type Sir2Tm enzyme; (b) The first D101N mutation, where the carboxyl oxygen hydrogen-bonding to the NAD^+ was replaced with an amide group; (c) The second D101N mutation, where the carboxyl oxygen hydrogen-bonding to the Leu103 was replaced with an amide group.

Complete list of references 10, 20, 66 and 67.

10. Brunet, A.; Sweeney, L. B.; Sturgill, J. F.; Chua, K. F.; Greer, P. L.; Lin, Y. X.; Tran, H.; Ross, S. E.; Mostoslavsky, R.; Cohen, H. Y.; Hu, L. S.; Cheng, H. L.; Jedrychowski, M. P.; Gygi, S. P.; Sinclair, D. A.; Alt, F. W.; Greenberg, M. E. *Science*, **2004**, *303*, 2011–2015.

20. Mostoslavsky, R.; Chua, K. F.; Lombard, D. B.; Pang, W. W.; Fischer, M. R.; Gellon, L.; Liu, P. F.; Mostoslavsky, G.; Franco, S.; Murphy, M. M.; Mills, K. D.;

Patel, P.; Hsu, J. T.; Hong, A. L.; Ford, E.; Cheng, H. L.; Kennedy, C.; Nunez, N.; Bronson, R.; Frendewey, D.; Auerbach, W.; Valenzuela, D.; Karow, M.; Hottiger, M. O.; Hursting, S.; Barrett, J. C.; Guarente, L.; Mulligan, R.; Demple, B.; Yancopoulos, G. D.; Alt, F. W. *Cell*, **2006**, *124*, 315–329.

66. Shao, Y.; Fusti-Molnar, L.; Jung, Y.; Kussmann, J.; Ochsenfeld, C.; Brown, S. T.; Gilbert, A. T. B.; Slipchenko, L. V.; Levchenko, S. V.; O'Neill, D. P.; Jr., R. A. D.; Lochan, R. C.; Wang, T.; Beran, G. J. O.; Besley, N. A.; Herbert, J. M.; Lin, C. Y.; Voorhis, T. V.; Chien, S. H.; Sodt, A.; Steele, R. P.; Rassolov, V. A.; Maslen, P. E.; Korambath, P. P.; Adamson, R. D.; Austin, B.; Baker, J.; Byrd, E. F. C.; Dachsel, H.; Doerksen, R. J.; Dreuw, A.; Dunietz, B. D.; Dutoi, A. D.; Furlani, T. R.; Gwaltney, S. R.; Heyden, A.; Hirata, S.; Hsu, C.-P.; Kedziora, G.; Khalliulin, R. Z.; Klunzinger, P.; Lee, A. M.; Lee, M. S.; Liang, W.; Lotan, I.; Nair, N.; Peters, B.; Proynov, E. I.; Pieniazek, P. A.; Rhee, Y. M.; Ritchie, J.; Rosta, E.; Sherrill, C. D.; Simmonett, A. C.; Subotnik, J. E.; III, H. L. W.; Zhang, W.; Bell, A. T.; Chakraborty, A. K.; Chipman, D. M.; Keil, F. J.; Warshel, A.; Hehre, W. J.; III, H. F. S.; Kong, J.; Krylov, A. I.; Gill, P. M. W.; Head-Gordon, M. Q-Chem, Version 3.0. Q-Chem, Inc., Pittsburgh, PA 2006.

67. Ponder, J. W. TINKER, Software Tools for Molecular Design, Version 4.2, Jun. 2004. The most updated version for the TINKER program can be obtained from J. W. Ponder's World Wide Web site at http://dasher.wustl.edu/tinker.