## **A4**

## Probing the Movement of Helix F of $\alpha_1$ -Antitrypsin

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 $\alpha_1$ -Antitrypsin is a member of the serine protease inhibitor (serpin) family that share a common tertiary structure. The reactive site loop (RSL) of serpins is exposed at one end of the molecule for protease binding. Upon cleavage by a target protease, the RSL is inserted into the major  $\beta$ -sheet A, which is a necessary process for formation of a tight inhibitory complex. It is thought that helix F region (thFs3A and helix F) located in front of  $\beta$ -sheet A, should be lifted for the loop insertion during complex formation. As a preliminary step to test this possibility, movement of helix F region of  $\alpha_1$ -antitrypsin was examined by spin labeling EPR spectroscopy. Some activity-affecting stabilizing mutations (G117F and K335V, at near helix F) caused broadening of EPR spectra. The results strongly suggest that helix F region is more closely located towards  $\beta$ -sheet A in mutant  $\alpha_1$ -antitrypsin. The increased stability at near helix F in the mutant protein may interrupt the loop insertion during the complex formation.

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