

Crystal Structure Studies on Native Fibrinogen from Chicken Blood

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Beamline(s): **X12C, X12B**

The search for crystals of native fibrinogen molecules is longstanding. One of the main problems has been the presence of mobile α C domains, which in most species also contain a number of repeated sequences that are thought to contribute to the flexibility. As it happens, chicken fibrinogen lacks these repeats; accordingly, we purified chicken fibrinogen, and, for whatever reason, managed to obtain diffraction-grade crystals in short order. Nonetheless, even in chicken, the fibrinogen molecule is large and ungangly, and it has not been an easy structure to determine. Finding suitable conditions for flash-freezing that minimized mosaicity was also a formidable problem, and our early data sets were collected at room temperature. Crosslinking with glutaraldehyde proved advantageous in that a reasonably complete low resolution data set could be obtained from a single crystal. The unit cell for the crosslinked material was virtually the same as non-crosslinked ($a = 114.6$, $b = 104.8$, $c = 207.2$, $\beta = 105.9$, space group P21). We were able to obtain a 5.5 Å structure from these data that encompassed the full-length molecule and elucidated the nature of the central domain (1). The amino-terminal segments of the α and β chains, including the fibrinopeptides A and B and the knobs they protect, were not apparent in electron density maps, nor were the α C domains, all features that must remain flexible in the crystal.

Recently we have found conditions for reproducible flash-freezing and have managed to collect data at 2.9 Å. Although a generally improved structure for the coiled coil regions is emerging, the flexible regions are still not apparent.

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References: Z. Yang, I. Mochalkin, L. Veerapandian, M. Riley and R.F. Doolittle, "Crystal Structure of Native Chicken Fibrinogen at 5.5 Å Resolution. Proc. Natl. Acad. Sci., U.S.A. 97:3903-3912, 2000.