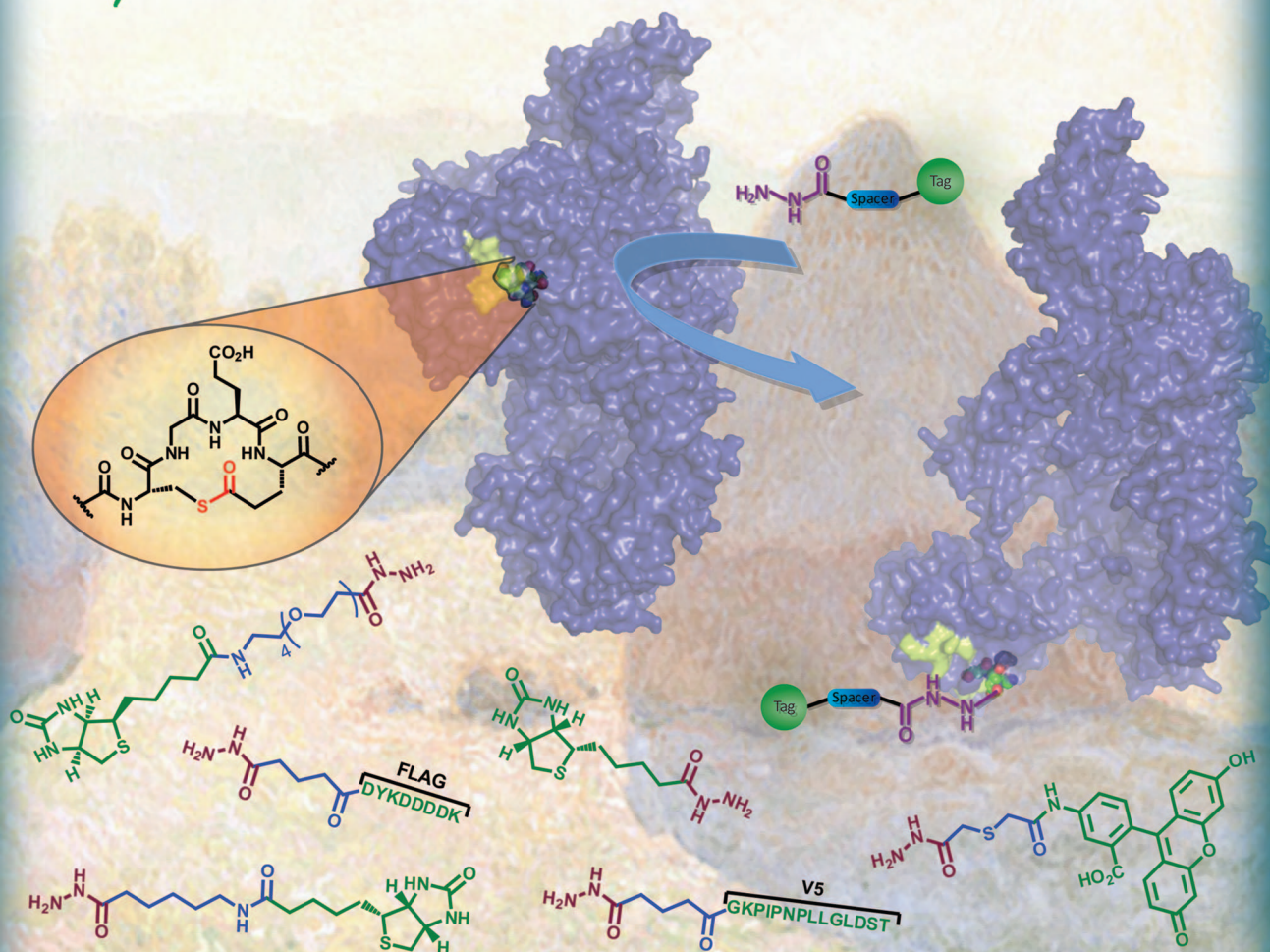


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# CHEM **BIO**CHEM

OF CHEMICAL BIOLOGY

Probing a protein  
haystack



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Chemistry & *Life* Sciences



**Minireview:** Artificial DNA Cutters  
(M. Komiyama)  
**Highlight:** Rolling-Circle Amplification  
(C. Arenz)

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## Cover Picture

**Michael A. Cole, Sarah E. Tully, Alister W. Dodds, James N. Arnold, Grant E. Boldt, Robert B. Sim, John Offer, and Paul Wentworth, Jr.\***

The cover picture shows chemoselective labeling of the “buried” macrocyclic thioester-containing component of complement protein C3 with a variety of hydrazide probes. C3, C4, and  $\alpha_2$ -macroglobulin play crucial roles within the complement system and as blood homeostasis regulators. Given their role in the immune system and disease, these proteins and their resulting processed fragments are highly studied, and the generation of chemically defined conjugates of these proteins offers the potential for significant advances in vaccine design and applied immunological studies. The hydrazide functionalities shown in the lower portion of this image have been used to chemoselectively label the thioester site with molecular tags, thus providing a new bioconjugation approach for thioester proteins and insight into the chemical accessibility of the thioester site. In the background of this cover image is a haystack landscape by Claude Monet representing the ability of these probes to reach these thioester “needles” within their protein scaffold and selectively label them within the complex plasma “haystack”. For further details, see the article by P. Wentworth et al. on p. 1340 ff.

