Bound DNA would be alternately ordered or not for single strands and stretched and released for double strands as the pitch and helical order of the protein filament changed.

DNA can also be described as a flexible scaffold to hold recombinase molecules at high concentration in a linear array. This suggests a mechanism for recombinase filaments acting as springs tensing and relaxing bound DNA. The flexible and unstructured single-stranded DNA in a filament would be alternately stretched/ordered and relaxed/less-ordered depending on the ATP hydrolysis status and therefore regular arrangement of the bound recombinases. The stiffer, structured double-stranded DNA, resulting from recombinase-mediated homologous pairing, is stretched and unwound within the filament. Disrupting the protein helix when ATP is hydrolyzed allows the DNA to relax, preventing easy reassembly, favoring monomer dissociation, and driving the reaction to favor the recombined DNA product. This, at the moment highly speculative, scenario is also only part of the recombination story. High-resolution information on DNA structures within filaments and description of recombinase dynamics within filaments will soon provide better ideas of how recombination works. Thus, even after more than two decades of intense study, recombinase nucleoprotein filaments are still among the most intriguing molecular machines around.

C. Wyman[1]
[1] Department of Cell Biology and Genetics and
Department of Radiation Oncology
Erasmus University Medical Center
P.O. Box 1738
3000 DR Rotterdam
The Netherlands

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Human CD23: Is It a Lectin in Disguise?

The crystal structure of a low-affinity human IgE receptor, CD23, is reported by Wurzburg et al. (2006) in this issue of *Structure*. This, together with a similar NMR structure by Hibbert et al. (2005) provide some insights into the function of the receptor.

The low-affinity IgE receptor, CD23, is a member of the C-type lectin receptor family that also recognizes CD21 and other ligands. While IgE binding appears to be mainly mediated by protein-protein interactions, it is less clear whether CD23 recognizes CD21 in a carbohydrate-dependent manner. In particular, does CD23 functions as a bona fide calcium-dependent lectin, like the classic mannose binding protein (MBP), selectins, and DC-SIGN, or does it merely folds like a lectin, requiring neither calcium nor carbohydrate for its function, like the natural killer cell-expressed immunoreceptors CD94 and NKG2A–D?

In general, the classic carbohydrate binding C-type lectins possess one to three conserved calcium binding sites and a sugar binding motif, EPN or QPD, specific for either mannose-type or galactose-type carbohydrates. In contrast, the known noncarbohydrate binding C-type lectin-like receptors appear to have lost all functional calcium sites as well as the sugar binding motif. By sequence, CD23 is most similar to DC-SIGN, which retains both the primary and the secondary Ca^{2+} binding sites as well as an EPN motif with preference for mannose-type sugars (Feinberg et al., 2001). At least the primary Ca^{2+} binding site appears conserved in CD23. The putative sugar binding motif appears crippled in human, but not animal, CD23 (Wurzburg et al., 2006). Functionally, both carbohydrate-dependent and -independent binding have been prescribed for this receptor. So, if it smells like a lectin and dresses like a lectin, must it a lectin ?

In this issue of *Structure*, Wurzburg et al. (2006) describe the crystal structures of the lectin domain of human CD23 in both the apo (calcium null) and the calcium bound forms, which may shed light on the function of this receptor (Figure 1). A similar structure was also determined in solution by nuclear magnetic resonance (NMR) (Hibbert et al., 2005). In the crystal structure, the authors found that only the primary Ca^{2+} binding site is occupied in human CD23 and that both Loop L1, the putative secondary calcium binding loop in MBP, and L4, the primary calcium and carbohydrate binding loop in MBP, displayed large conformational changes in response to calcium binding (see Figure 2 of Wurzburg et al. [2006]). They then proposed that this conformational change is necessary for CD23 to bind IgE, since many of the loop

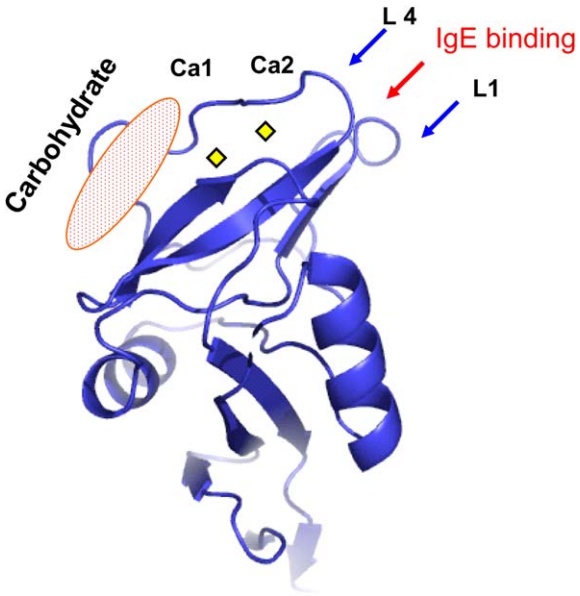

Figure 1. Crystal Structure of the Human Apo-CD23

The primary (Ca1) and secondary (Ca2) calcium binding sites of a classical C-type lectin are labeled as yellow diamonds. The hatched region indicates the putative carbohydrate binding site of a classical C-type lectin. The coordinates for the figure were provided by Ted Jardetzsky.

residues appeared to be implicated in IgE binding, based on mutational work. This model provides a structural explanation for calcium-dependent, but carbohydrate-independent, CD23 recognition of IgE.

Interestingly, an Arg residue was found to serve as a surrogate ligand at the calcium binding site in the apo-CD23 structure. An Arg was also observed to occupy a secondary calcium binding site in the structure of DC-SIGNR in the absence of carbohydrate (Snyder et al., 2005). Calcium-dependent conformational changes in a C-type lectin were also observed in the structure of MBP (Ng et al., 1998). However, the conformational changes in MBP were primarily restricted to the carbohydrate binding Loop L4, whereas both L4 and L1 displayed movement in the CD23 structure. It should be noted that Ca^{2+} appears to play only a limited role in CD23 recognition of IgE as the depletion of Ca^{2+} resulted in only a moderate decrease in IgE binding affinity (Hibbert et al., 2005). Although the crystal structure contains no carbohydrate and thus does not address directly the requirement of carbohydrate in CD23 function, the disorder of Loop L4 in the presence of Ca^{2+} appears to be inconsistent with the role of the bound Ca^{2+} in stabilizing the carbohydrate binding conformation of the loop. In addition, Hibbert and colleagues, using NMR, observed no detectable binding between CD23 and several model carbohydrate compounds (Hibbert et al., 2005). These results, together with the fact that the human CD23 contains a crippled "EPT" motif, make it less likely for human CD23 to function as a carbohydrate receptor, although the possibility remains for the "EPT" motif to recognize altered carbohydrates. A caveat is that CD23s from other species do contain a normal "EPN" motif (see Figure 3 of Wurzburg et al. [2006]), suggesting that human CD23 may be unique in its function when it comes to carbohydrate recognition.

A central issue that remains to be resolved is how CD23 recognizes IgE. Both Wurzburg et al. (2006) and Hibbert et al. (2005) have mapped the IgE binding site, based on either mutational results or NMR titrations, to a region of CD23 distinct from the putative carbohydrate binding site, but involving portions of both Loops L1 and L4 (see Figure 7 of Wurzburg et al. [2006]). On the IgE side, the CD23 binding region has been mapped to the Cε3 domain (Chretien et al., 1988; Ghaderi and Stanworth, 1993). However, the details of the atomic recognition between CD23 and IgE as well as the proposed Ca^{2+} function in this recognition can only be addressed when the complex structure is solved.

Peter D. Sun[1]
[1] Structural Immunology Section
Lab of Immunogenetics
National Institute of Allergy and Infectious Diseases
National Institutes of Health
12441 Parklawn Drive
Rockville, Maryland 20852

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