Corrections

The Complement Regulator C4b-Binding Protein (C4BP) Interacts with both the C4c and C4dg Subfragments of the Parent C4b Ligand: Evidence for Synergy in C4BP Subsite Binding, by Elisa Leung, Anna M. Blom, Liliana Clemenza, and David E. Isenman*, Volume 45, Number 27, July 11, 2006, pages 8378−8392.

Page 8390. Figure 10 is shown here in full.

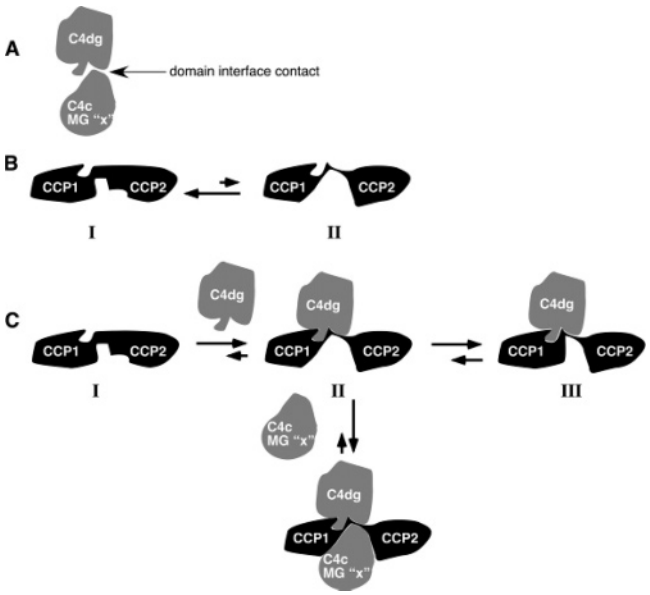

FIGURE 10: Model for the synergies observed in C4BP subsite binding. (A) Within the context of the C4b molecule, the thioester domain−C4d portion of C4dg has a domain interface with a yet to be identified C4c subdomain [denoted MG"x", per the C3 structure nomenclature (*47*)] that mediates a major contact to C4BP. (B) The primary binding site in C4BP is comprised of residues at the interface of CCP1 and CCP2. Within a C4BP subunit, these domains are depicted as existing as an equilibrium mixture of two conformational states (**I** and **II**) that differ predominantly in their intermodular orientations, and thus in the alignment of residues at the interface between the domains. In the absence of ligand, the equilibrium strongly favors conformation **I** (note the relative size of the arrows), but only conformation **II** has a fully formed C4c-binding subsite. (C) For the case corresponding to experiments in which C4dg and C4c were present at the same time, but as separate molecular entities, the first encounter is with C4dg, which either stabilizes conformation **II** or, if it binds to conformation **I**, induces through some additional contacts formed a shift in the equilibrium to conformation **II**. C4c can now bind to a greater number of sites than would have been present in the absence of C4dg. The reestablishment of the relatively small domain interface between C4dg and C4c would enhance the affinity of the binding interaction of C4dg with C4BP; however, given the much larger buried surface area depicted for the contact with C4c, this additional domain interface contact with C4dg has a negligible effect on the overall affinity governing C4c binding. If C4c is not immediately available to bind to the C4dg-liganded conformation **II**, conformational species **III** may form, which is refractory to C4c binding. This species is invoked to explain the observation in Figure 5 that prebinding of C4dg to C4BP renders the latter refractory to binding to a C4c-coupled biosensor chip. However, in the physiologically relevant situation, i.e., the ligand is C4b, the relevant contacting surfaces in C4dg and C4c for C4BP would be present within the same molecular entity. Assuming the same general mechanism for ordered subsite filling in which the initial encounter complex was with the C4dg moiety, the C4c subsite would be immediately filled and little, if any, conformational species **III** would form.

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