Cytoplasmic dynein is a massive multisubunit motor protein that together with its activator dynactin is responsible for the majority of minus-end microtubule-based motility. Both macromolecular complexes are connected by a direct interaction between dynactin’s largest subunit, p150Glued, and dynein intermediate chain IC. The nuclear distribution protein E, NUDE, is also involved in regulating dynein function and localization. A common structural feature between NUDE and p150Glued is that they contain long parallel homodimeric coiled coils. Here, we demonstrate using coupling constants, amide-amide sequential NOEs, secondary chemical shifts, residual dipolar coupling, and various dynamics measurements that apo IC is natively disordered except for a short helical structure (Region 1), and a nascent helix (Region 2) separated from Region 1 by a disordered linker. When bound to p150Glued, different patterns of spectral exchange broadening suggest that Region 1 forms a coiled-coil and Region 2 a packed stable helix, with the intervening and subsequent residues remaining disordered. Interestingly, p150Glued and NUDE share a common site on dynein IC but whereas the binding footprint of p150Glued on IC involves two noncontiguous recognition regions (Regions 1 and 2), the binding of NUDE is restricted to Region 1. The multi-region IC binding interface, the partial disorder and posttranslational modification of Region 2, and the modulation of the length of the linker by alternative splicing may provide elegant and multi-faceted regulation of dynein by p150Glued and NUDE.