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The cystic fibrosis transmembrane conductance (CFTR), the defective protein in cystic fibrosis, is an anion channel activated by protein kinase A phosphorylation. The regulatory domain of CFTR (RD) has multiple phosphorylation sites, and is responsible for the channel activation. This domain is intrinsically disordered, rendering the structural analysis a difficult task, as high-resolution techniques are barely applicable. In this work, we obtained a biophysical characterization of the native and phosphorylated RD in solution by employing complementary structural methods. The native RD has a gyration radius of the is 3.25 nm, and a maximum molecular dimension of 11.4 nm, larger than expected for a globular protein of the same molecular mass. Phosphorylation causes compaction of the structure, yielding a significant reduction of the gyration radius, to 2.92 nm, and on the maximum molecular dimension to 10.2 nm. Using an ensemble optimization method, we were able to generate a low-resolution, three-dimensional model of the native and the phosphorylated RD based on small-angle x-ray scattering (SAXS) data. We have obtained the first experiment-based model of the CFTR regulatory domain, which will be useful to understand the molecular mechanisms of normal and pathological CFTR functioning.