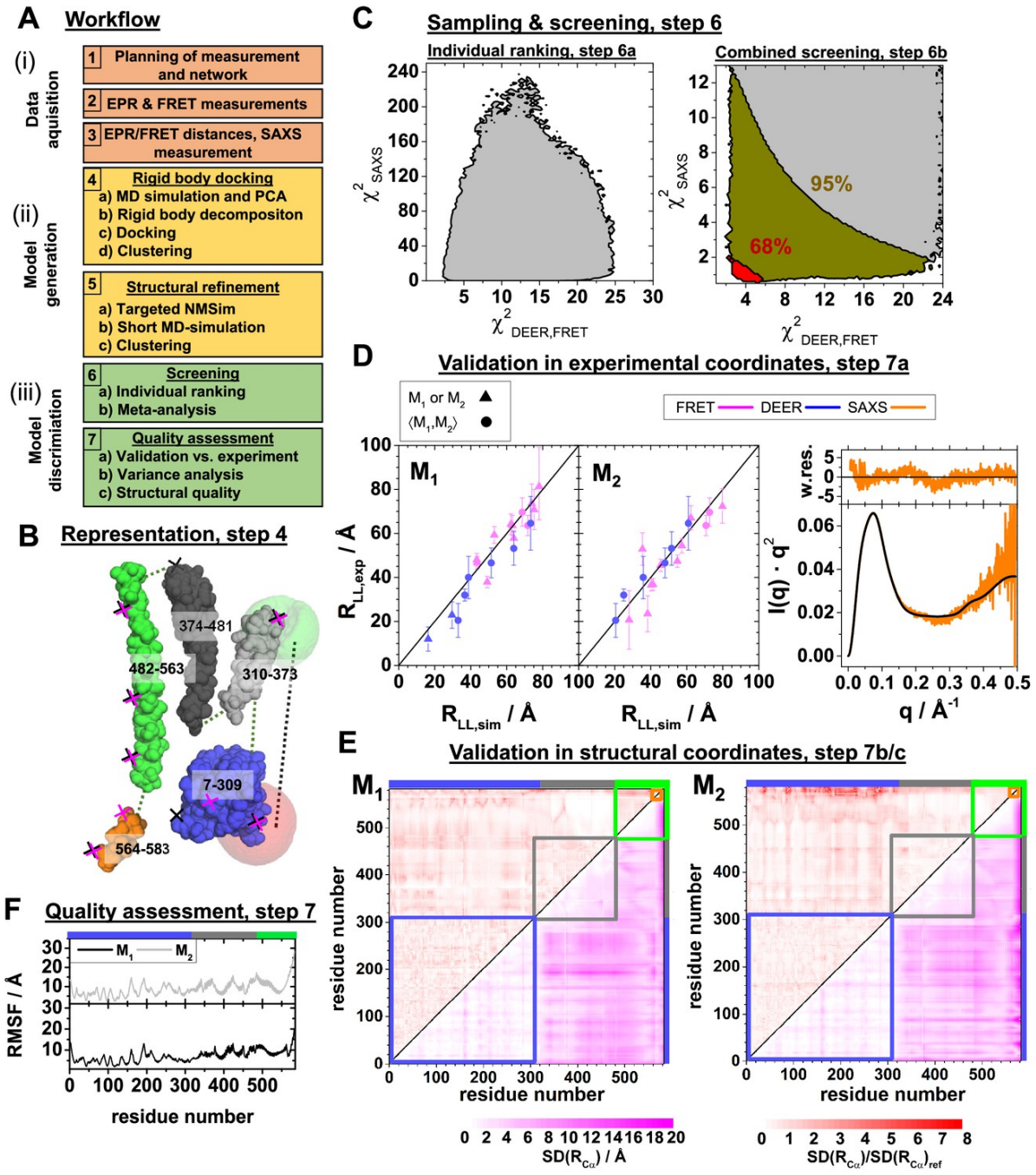

Guanylate binding proteins (GBPs) are soluble dynamin-like proteins that undergo a conformational transition for GTP-controlled oligomerization and disrupt membranes of intracellular parasites to exert their function as part of the innate immune system of mammalian cells. We apply neutron spin echo, X-ray scattering, fluorescence, and EPR spectroscopy as techniques for integrative dynamic structural biology to study the structural basis and mechanism of conformational transitions in the human GBP1 (hGBP1). We mapped hGBP1's essential dynamics from nanoseconds to milliseconds by motional spectra of sub-domains. We find a GTP-independent flexibility of the C-terminal effector domain in the µs-regime and resolve structures of two distinct conformers essential for an

opening of hGBP1 like a pocket knife and for oligomerization. Our results on hGBP1's conformational heterogeneity and dynamics (intrinsic flexibility) deepen our molecular understanding relevant for its reversible oligomerization, GTP-triggered association of the GTPase-domains and assembly-dependent GTP-hydrolysis.