A Novel Form of Allosteric Regulation in *Bacillus subtilis* Ribonucleotide Reductase Revealed by SAXS and Cryo-Electron Microscopy

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Abstract: DNA replication and repair are required for all modern life on Earth. *De novo* synthesis of the building blocks of DNA is carried out by the essential enzyme ribonucleotide reductase (RNR), which reduces the precursors of RNA (ribonucleotides) to those of DNA (deoxyribonucleotides) via a conserved and ancient radical mechanism. Due to their central role in nucleotide metabolism, RNRs are typically under strict allosteric control. In recent years, structural studies of the prototypic class Ia RNRs of *Escherichia coli* and humans have revealed that allosteric regulation of overall activity involves the formation of unusual ring-shaped complexes that prevent radical chemistry. By contrast, class Ib RNRs, used by many microbes and common pathogens, were long thought to be simpler than Ia RNRs and devoid of this type of regulation. Contrary to this belief, our studies using a combination of small-angle X-ray scattering, crystallography, and cryo-electron microscopy reveal that the class Ib RNR from *Bacillus subtilis* adopts a wider variety of quaternary structures than any class Ia RNR thus far examined. This surprising discovery entails inhibition via formation of a novel helical fiber.