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Insights into the Structure, Mechanism and Regulation of Scavenger Mrna Decapping Activity.

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Complete removal of residual N-7 guanine cap from degraded messenger RNA is necessary to prevent accumulation of intermediates that might interfere with RNA processing, export, and translation. The human scavenger decapping enzyme, DcpS, catalyzes residual cap hydrolysis following mRNA degradation, releasing N-7 methyl guanosine monophosphate and 5'-diphosphate terminated cap or mRNA products. DcpS structures bound to m⁷GpppG or m⁷GpppA reveal an asymmetric DcpS dimer that simultaneously creates an open nonproductive DcpS-cap complex and a closed productive DcpS-cap complex that alternate via 30 Å domain movements. Structural and biochemical analysis suggests an autoregulatory mechanism whereby premature decapping of mature RNA is prevented by blocking the conformational changes that are required to form a closed productive active site capable of cap hydrolysis.