

# jmb

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*Cover Illustration: LDL cholesterol (yellow spheres) are cleared from the blood by liver LDLRs, which in turn are regulated by circulating PCSK9 (orange ribbon model). The N-terminal region of PCSK9 harbors several missense mutations associated with high or low LDL levels, but has so far eluded structural studies, since it is intrinsically disordered. In this issue, Ultsch et al. report that upon interaction with a Fab ligand, this region becomes structured, featuring a central helix (highlighted with an orange glow). This suggests that the mutations may exert their biological functions within the context of an ordered conformational state. The amino acids depicted with side chains are the three missense mutations and the two posttranslational modification sites. Artistic illustration by Allison Bruce (A. K. Bruce Design).*