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Disorder is a critical component of lipoprotein sorting in Gram-negative bacteria

Jessica El Rayes, Joanna Szewczyk, Michaël Deghelt, Naemi Csoma, André Matagne, Bogdan I. Iorga, Seung-Hyun Cho & Jean-François Collet

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Abstract

Gram-negative bacteria express structurally diverse lipoproteins in their cell envelope. Here, we find that approximately half of lipoproteins destined to the *Escherichia coli* outer membrane display an intrinsically disordered linker at their N terminus. Intrinsically disordered regions are common in proteins, but establishing their importance in vivo has remained challenging. As we sought to unravel how lipoproteins mature, we discovered that unstructured linkers are required for optimal trafficking by the Lol lipoprotein sorting system, whereby linker deletion re-routes three unrelated lipoproteins to the inner membrane. Focusing on the stress sensor RcsF, we found that replacing the linker with an artificial peptide restored normal outer-membrane targeting only when the peptide was of similar length and disordered. Overall, this study reveals the role played by intrinsic disorder in lipoprotein sorting, providing mechanistic insight into the biogenesis of these proteins and suggesting that evolution can select for intrinsic disorder that supports

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