SLiM BASICS

In the early days of studying protein behavior, researchers recognized that large, structured protein domains often interacted with each other in a lock-and-key fashion, fitting together almost like puzzle pieces. Toward the end of the 20th century, however, the growing discovery of previously overlooked unstructured regions suggested that there was more to the story. One type of protein interaction mediated by the unstructured proteome involves short linear motifs (SLiMs), abundant stretches of up to 10 amino acids. Their interactions with other proteins are generally transient and weak, but SLiMs are nevertheless significant contributors to protein function and regulatory mechanisms in the cell.

Structured protein domains	SLiMs
Approximately 50–200 amino acids, with several points of contact	Just ~2–10 amino acids, with only 2–3 that act as core binding determinants
Distinct three-dimensional structure	Lack a three-dimensional structure
Strong and often long-lasting interactions, such as in protein complex formation	Weak, transient interactions
Bind domains of other protein partners, interactions that often resemble a lock-and-key mechanism	Typically bind to a conserved pocket on a globular protein domain