The lack of available fusion tags that possess both affinity and visualization properties is a hurdle for biomolecular research. Typically, either a choice is made between an affinity tag and a reporter tag. Both can be employed in tandem if a fusion can be made at both termini of the target protein. However, this often presents a problem of the target protein becoming to cumbersome to work with, depending on the size of the affinity and reporter tag. Our work with DsRed-Monomer, which binds immobilized copper ions, overcomes this challenge. We demonstrate that DsRed-Monomer can be employed as an affinity tag for the purification of conjugated peptides/proteins and that its natural fluorescence can be useful in the detection of the attached proteins/peptides. Further, it can be employed in the isolation of proteins that complex with the protein/peptide fused to DsRed-Monomer. To demonstrate our strategy, we worked with a model bait-ligand pair, namely calmodulin (CaM) and the M13 peptide. CaM is a calcium-binding protein that is involved in the regulation of several cellular responses through its interaction with other proteins. This protein forms a complex with the M13 peptide in the presence of calcium. We constructed two fusion proteins, DsRed-Monomer-CaM and M13-DsRed-Monomer. The DsRed-Monomer-CaM fusion was employed to show the usefulness of DsRed-Monomer in the affinity purification of CaM, followed by the detection of CaM based on the fluorescence of DsRed-Monomer in a gel-blot assay. The M13-DsRed-Monomer fusion protein was employed in the isolation of the protein, CaM, and the purification of the complex based on the affinity of DsRed-Monomer to immobilized copper ions.

**M13 Peptide**

The sequence of M13, a synthetic peptide, is based on the calmodulin-binding domain of skeletal muscle myosin light chain kinase (skMLCK) (residues 577-602).

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