In vitro interactions between the β_{1a} subunit of the skeletal muscle DHPR and RyR1

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The β_{1a} subunit of the skeletal muscle dihydropyridine receptor (DHPR) plays two important roles in excitation-contraction (EC) coupling in skeletal muscle. β_{1a} was originally found to target the α_{1S} subunit of the DHPR to sarcolemmal tetrads which oppose skeletal ryanodine receptor (RyR1) channels in the sarcoplasmic reticulum. It was later found to also aid in transmission of EC coupling between the α_{1S} subunit and RyR1, through its C-terminal tail residues. This presumably depends on an interaction between the C-terminal tail of β_{1a} and RyR1 since the β_{1a} subunit binds to RyR1 in affinity chromatography experiments, but direct binding of the C-terminal tail to RyR1 has not been reported. Nor have direct functional interactions between the proteins been demonstrated. We show here, using affinity chromatography, that a peptide corresponding to the native sequence of the C-terminus of β_{1a}, but not a peptide with a scrambled sequence, binds to RyR1 (N=3). In addition the peptide and the full β_{1a} subunit at 0.1 to 1 nM significantly increase both [^{3}H]ryanodine binding (N=7-18) and single RyR1 channel activity, with maximum 3- to 5-fold activation at ~10nM (N=7-10 at each of eight concentrations). The increase in RyR1 channel activity with both full length β_{1a} and the C-terminal peptide was irreversible within the lifetime of the bilayer, indicating high affinity binding. Therefore the C-terminal tail of the β_{1a} subunit is capable of directly binding to and activating RyR1, suggesting that β_{1a} may enhance EC coupling by virtue of its ability to activate RyR1.