

# IQ-motif selectivity in human IQGAP2 and IQGAP3: Binding of calmodulin and myosin essential light chain

Atcheson, E.<sup>a</sup>, Hamilton, E.<sup>ab</sup>, Pathmanathan, S.<sup>ac</sup>, Greer, B.<sup>a</sup>, Harriott, P.<sup>a</sup>, Timson, D.J.<sup>a</sup>

<sup>a</sup> School of Biological Sciences, Queen's University Belfast, Medical Biology Centre, 97 Lisburn Road, United Kingdom

<sup>b</sup> Belfast Metropolitan College, Castlereagh Campus, Montgomery Road, United Kingdom

<sup>c</sup> Department of Botany, University of Jaffna, Sri Lanka

## Abstract

The IQGAP [IQ-motif-containing GAP (GTPase-activating protein)] family members are eukaryotic proteins that act at the interface between cellular signalling and the cytoskeleton. As such they collect numerous inputs from a variety of signalling pathways. A key binding partner is the calcium-sensing protein CaM (calmodulin). This protein binds mainly through a series of IQ-motifs which are located towards the middle of the primary sequence of the IQGAPs. In some IQGAPs, these motifs also provide binding sites for CaM-like proteins such as myosin essential light chain and S100B. Using synthetic peptides and native gel electrophoresis, the binding properties of the IQ-motifs from human IQGAP2 and IQGAP3 have been mapped. The second and third IQ-motifs in IQGAP2 and all four of the IQ-motifs of IQGAP3 interacted with CaM in the presence of calcium ions. However, there were differences in the type of interaction: while some IQ-motifs were able to form complexes with CaM which were stable under the conditions of the experiment, others formed more transient interactions. The first IQ-motifs from IQGAP2 and IQGAP3 formed transient interactions with CaM in the absence of calcium and the first motif from IQGAP3 formed a transient interaction with the myosin essential light chain Mlc1sa. None of these IQ-motifs interacted with S100B. Molecular modelling suggested that all of the IQ-motifs, except the first one from IQGAP2 formed  $\alpha$ -helices in solution. These results extend our knowledge of the selectivity of IQ-motifs for CaM and related proteins.

## Author keywords

$\alpha$ -helical peptide; Calcium-dependent interaction; IQ-motif; IQ-motif-containing gtpase-activating protein (iqgap); Myosin essential light chain; Native gel electrophoresis

## Indexed keywords

**EMTREE drug terms:** calcium ion; calmodulin; enzyme activator; IQ motif containing guanosine triphosphatase activating protein 2; IQ motif containing guanosine triphosphatase activating protein 3; myosin light chain; protein S100B; unclassified drug

**EMTREE medical terms:** alpha helix; article; controlled study; Escherichia coli; gel electrophoresis; molecular model; nonhuman; peptide mapping; protein binding; protein expression; protein motif; protein protein interaction; protein purification; protein stability; structure activity relation; structure analysis

**Species Index:** Eukaryota