Flightin and cardiac Myosin Binding Protein C: functional convergence of two distinct myosin rod binding proteins

Flightin is a 20kDa protein that in *Drosophila melanogaster* is expressed only in the indirect flight muscles (IFM) where it has been shown to be essential for flight and for the structural integrity of the sarcomere. In vitro binding assays demonstrated that flightin binds to the myosin rod and that a single amino acid mutation in zone 27 of the myosin rod (E1554L) abolished flightin binding. *Drosophila* deficient for flightin (fln^o) are flightless and display a characteristic fiber hypercontraction phenotype. There are no vertebrate homologs of flightin but previous studies have shown that cardiac Myosin Binding Protein C (cMyBPC), a ~130 kDa modular protein implicated in familial hypertrophic cardiomyopathy, binds to the same region of the myosin rod as flightin. Previous studies demonstrated that thick filaments from mouse cardiac muscle deficient in cMyBP-C and *Drosophila* IFM deficient in flightin show parallel reductions in flexural rigidity suggesting that cMyBP-C and flightin contribute to filament stiffness. To determine if cMyBPC and flightin are functionally homologous, we generated transgenics flies that express the human cMyBPC gene in the IFM via the the actin 88F promoter. Expression of cMyBP-C in wild-type (fln+) *Drosophila* does not affect flight ability demonstrating that expression of this protein is not detrimental to the flight muscle. Examination of IFM fibers by polarized light microscopy shows that expression of cMyBP-C partially rescues the hypercontraction phenotype engendered by fln^o.