

ity to bind CD47 (40). It is possible that SHPS-1 functions with different activities in innervated muscles and denervated muscles.

SHP-2 has been reported to interact with the tyrosine-phosphorylated cytoplasmic domain of SHPS-1 (9, 10), and to regulate EGF, insulin, and the IGF-I signaling pathway (10, 20). In our experiments, since the expression and localization of SHP-2 did not change after denervation, SHP-2 appears to be independent of the intracellular changes caused by denervation. We also demonstrated that SHP-2 does not concentrate at NMJs. Tanowitz *et al.* reported that SHP-2 is concentrated at NMJs in mouse diaphragm (41). But Mei *et al.* showed that SHP-2 localizes in the cytoplasm of muscle fibers in rat hindlimbs (42). We also examined SHP-2 in rat hindlimb muscles and our results are consistent with the latter results. Additionally, we performed co-immunoprecipitation experiments but could not detect any interaction between SHPS-1 and SHP-2 in either innervated or denervated muscles (data not shown). Our results suggest that SHPS-1 interacts with novel proteins other than SHP-2, and regulates intracellular signaling in response to changes caused by denervation in skeletal muscle.

Little is known about SHPS-1 except for its interactions with SHP-1 and SHP-2, and its participation in cell adhesion. Most previous studies utilized cultured cells; therefore, how SHPS-1 functions *in vivo* has remained unclear, even in brain where it is highly expressed. Our results contribute new information about the function of SHPS-1 *in vivo*, and suggest that SHPS-1 plays an important role in denervated and undifferentiated skeletal muscle.

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