A nuclear isoform of the focal adhesion LIM-domain protein Trip6 integrates activating and repressing signals at AP-1- and NF-kappaB-regulated promoters.

Glucocorticoid receptor (GR)-mediated transrepression of the transcription factors AP-1 and NF-kappaB, responsible for most of the anti-inflammatory effects of glucocorticoids, is initiated by the tethering of GR to the promoters of target genes. We report that this tethering is mediated by a nuclear isoform of the focal adhesion LIM domain protein Trip6. Trip6 functions as a coactivator for both AP-1 and NF-kappaB. As shown by chromatin immunoprecipitation, Trip6 is recruited to the promoters of target genes together with AP-1 or NF-kappaB. In the presence of glucocorticoids, GR joins the Trip6 complex. Reducing the level of Trip6 by RNA interference or abolishing its interaction with GR by dominant-negative mutation eliminates transrepression. We propose that GR tethering to the target promoter through Trip6 forms the basis of transrepression, and that Trip6 exerts its nuclear functions by acting as a molecular platform, enabling target promoters to integrate activating or repressing signals.

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