

remodeling complexes as a central region interacting protein complex, and our demonstration that knockdown of this protein attenuates Gro-mediated repression, provides further support for the idea that regulation of chromatin structure is a critical aspect of Gro mediated repression. On the other hand, modulation of chromatin structure is likely not the only mechanism of Gro mediated repression as histone deacetylase inhibitors and Rpd3

knockdown reduce, but do not abolish Gro-mediated repression (16,18) (Figure 3C). Through a combination of proteomic screening, reporter assays, and genome-wide expression profiling, our results suggest a possible new mechanism of Gro mediated repression involving the action of the spliceosome. Future experiments will focus on elucidating the underlying mechanisms by which these interacting partners act in Gro-mediated repression.

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Author contributions: AJC, PNK, and WT-J conceived and planned the study, which was coordinated by AJC. PNK and AJC wrote the manuscript. PNK and WT-J conducted most of the experiments. TYY assisted with the co-immunoprecipitation study. MC carried out the bioinformatics analysis. AAV and JAW carried out the MuDPIT analysis. All authors reviewed and approved the manuscript.

REFERENCES

1. Courey, A. J., and Jia, S. (2001) Transcriptional repression: the long and the short of it. *Genes Dev* **15**, 2786-2796
2. Turki-Judeh, W., and Courey, A. J. (2012) Groucho: a corepressor with instructive roles in development. *Current topics in developmental biology* **98**, 65-96
3. Martinez, C. A., and Arnosti, D. N. (2008) Spreading of a corepressor linked to action of long-range repressor hairy. *Mol Cell Biol* **28**, 2792-2802
4. Chen, G., and Courey, A. J. (2000) Groucho/TLE family proteins and transcriptional repression. *Gene* **249**, 1-16
5. Gasperowicz, M., and Otto, F. (2005) Mammalian Groucho homologs: redundancy or specificity? *J Cell Biochem* **95**, 670-687
6. Nagel, A. C., Krejci, A., Tenin, G., Bravo-Patino, A., Bray, S., Maier, D., and Preiss, A. (2005) Hairless-mediated repression of notch target genes requires the combined activity of Groucho and CtBP corepressors. *Mol Cell Biol* **25**, 10433-10441
7. Blair, S. S. (2007) Wing vein patterning in Drosophila and the analysis of intercellular signaling. *Annual review of cell and developmental biology* **23**, 293-319
8. Hasson, P., and Paroush, Z. (2006) Crosstalk between the EGFR and other signalling pathways at the level of the global transcriptional corepressor Groucho/TLE. *British journal of cancer* **94**, 771-775
9. Allen, T., van Tuyl, M., Iyengar, P., Jothy, S., Post, M., Tsao, M. S., and Lobe, C. G. (2006) Grg1 acts as a lung-specific oncogene in a transgenic mouse model. *Cancer Res* **66**, 1294-1301