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Supplemental material is available online only.

**FIG S1**, TIF file, 1.2 MB.

**FIG S2**, TIF file, 1.9 MB.

**FIG S3**, TIF file, 0.6 MB.

**FIG S4**, TIF file, 0.2 MB.

**FIG S5**, TIF file, 0.2 MB.

**FIG S6**, TIF file, 0.4 MB.

**FIG S7**, TIF file, 0.8 MB.

**FIG S8**, TIF file, 0.7 MB.

**TABLE S1**, TIF file, 1.5 MB.

**TABLE S2**, XLSX file, 0.2 MB.

## ACKNOWLEDGMENTS

H.X. was supported by a fellowship from the China Scholarship Council.

We acknowledge support from the Medical Faculty's core facilities Cell Sorting and Immunomonitoring and Microarray/Next Generation Sequencing. Plasmids pWPXL, psPAX2, and pMD2.G are gifts from Didier Trono. CRISPR reagents and libraries were a gift from Feng Zhang obtained from Addgene. Plasmid NL4-3- $\Delta$ 6-drEGFP was kindly provided by Robert Siliciano.

K.Ü., A. Ensser, B.G., and M.L. designed and supervised the study. H.X. and D.J. performed the experiments. H.X., E.W., M.M., P.K., A.B.O.V.S., A. Ensser, and K.Ü. analyzed the data. H.X. and K.Ü. wrote the manuscript. A. Ensser, B.G., E.W., M.M., P.K., A. Ekici, A.B.O.V.S., M.L., F. F., M.T., and D.J. reviewed the manuscript.

We declare that we have no competing interests.

## REFERENCES

- Jacob AG, Smith CWJ. 2017. Intron retention as a component of regulated gene expression programs. *Hum Genet* 136:1043–1057. <https://doi.org/10.1007/s00439-017-1791-x>.
- Braunschweig U, Barbosa-Morais NL, Pan Q, Nachman EN, Alipanahi B, Gonatopoulos-Pournatzis T, Frey B, Irimia M, Blencowe BJ. 2014. Widespread intron retention in mammals functionally tunes transcriptomes. *Genome Res* 24:1774–1786. <https://doi.org/10.1101/gr.177790.114>.
- Zhang S-J, Wang C, Yan S, Fu A, Luan X, Li Y, Shen QS, Zhong X, Chen J-Y, Wang X, Tan BC-M, He A, Li C-Y. 2017. Isoform evolution in primates through independent combination of alternative RNA processing events. *Mol Biol Evol* 34:2453–2468. <https://doi.org/10.1093/molbev/msx212>.
- Hammarskjöld M-L, Rekosh D. 2017. SR proteins: to shuttle or not to shuttle, that is the question. *J Cell Biol* 216:1875–1877. <https://doi.org/10.1083/jcb.201705009>.
- Galganski L, Urbanek MO, Krzyzosiak WJ. 2017. Nuclear speckles: molecular organization, biological function and role in disease. *Nucleic Acids Res* 45:10350–10368. <https://doi.org/10.1093/nar/gkx759>.
- Cochrane AW, McNally MT, Moulard AJ. 2006. The retrovirus RNA trafficking granule: from birth to maturity. *Retrovirology* 3:18. <https://doi.org/10.1186/1742-4690-3-18>.
- Ahmad N, Maitra RK, Venkatesan S. 1989. Rev-induced modulation of Nef protein underlies temporal regulation of human immunodeficiency virus replication. *Proc Natl Acad Sci U S A* 86:6111–6115. <https://doi.org/10.1073/pnas.86.16.6111>.
- Karn J, Stoltzfus CM. 2012. Transcriptional and posttranscriptional regulation of HIV-1 gene expression. *Cold Spring Harb Perspect Med* 2:a006916. <https://doi.org/10.1101/cshperspect.a006916>.
- Sauter D, Hotter D, Van Driessche B, Stürzel CM, Kluge SF, Wildum S, Yu H, Baumann B, Wirth T, Plantier J-C, Leoz M, Hahn BH, Van Lint C, Kirchhoff F. 2015. Differential regulation of NF- $\kappa$ B-mediated proviral and antiviral host gene expression by primate lentiviral Nef and Vpu proteins. *Cell Rep* 10:586–599. <https://doi.org/10.1016/j.celrep.2014.12.047>.
- Lemieux C, Marguerat S, Lafontaine J, Barbezier N, Bähler J, Bachand F. 2011. A pre-mRNA degradation pathway that selectively targets intron-containing genes requires the nuclear poly(A)-binding protein. *Mol Cell* 44:108–119. <https://doi.org/10.1016/j.molcel.2011.06.035>.
- Sandri-Goldin RM. 2004. Viral regulation of mRNA export. *J Virol* 78:4389–4396. <https://doi.org/10.1128/jvi.78.9.4389-4396.2004>.
- Cullen BR. 2000. Nuclear RNA export pathways. *Mol Cell Biol* 20:4181–4187. <https://doi.org/10.1128/mcb.20.12.4181-4187.2000>.
- Grewe B, Uberla K. 2010. The human immunodeficiency virus type 1 Rev protein: manage a trois during the early phase of the lentiviral replication cycle. *J Gen Virol* 91:1893–1897. <https://doi.org/10.1099/vir.0.022509-0>.
- Mousseau G, Valente ST. 2017. Role of host factors on the regulation of Tat-mediated HIV-1 transcription. *Curr Pharm Des* 23:4079–4090. <https://doi.org/10.2174/1381612823666170622104355>.
- Suhasini M, Reddy TR. 2009. Cellular proteins and HIV-1 Rev function. *Curr HIV Res* 7:91–100. <https://doi.org/10.2174/157016209787048474>.
- Katahira J. 2012. mRNA export and the TREX complex. *Biochim Biophys Acta* 1819:507–513. <https://doi.org/10.1016/j.bbagma.2011.12.001>.
- Bray M, Prasad S, Dubay JW, Hunter E, Jeang KT, Rekosh D, Hammarskjöld ML. 1994. A small element from the Mason-Pfizer monkey virus genome makes human immunodeficiency virus type 1 expression and replication Rev-independent. *Proc Natl Acad Sci U S A* 91:1256–1260. <https://doi.org/10.1073/pnas.91.4.1256>.
- Malim MH, Cullen BR. 1993. Rev and the fate of pre-mRNA in the nucleus: implications for the regulation of RNA processing in eukaryotes. *Mol Cell Biol* 13:6180–6189. <https://doi.org/10.1128/mcb.13.10.6180>.
- Pollard VW, Malim MH. 1998. The HIV-1 Rev protein. *Annu Rev Microbiol* 52:491–532. <https://doi.org/10.1146/annurev.micro.52.1.491>.
- Cochrane AW, Jones KS, Beidas S, Dillon PJ, Skalka AM, Rosen CA. 1991. Identification and characterization of intragenic sequences which repress human immunodeficiency virus structural gene expression. *J Virol* 65:5305–5313. <https://doi.org/10.1128/JVI.65.10.5305-5313.1991>.
- Mikaélian I, Krieg M, Gait MJ, Karn J. 1996. Interactions of INS (CRS) elements and the splicing machinery regulate the production of Rev-responsive mRNAs. *J Mol Biol* 257:246–264. <https://doi.org/10.1006/jmbi.1996.0160>.
- Brightly DW, Rosenberg M, Steitz JA. 1994. A cis-acting repressive sequence that overlaps the Rev-responsive element of human immunodeficiency virus type 1 regulates nuclear retention of env mRNAs independently of known splice signals. *Proc Natl Acad Sci U S A* 91:8314–8318. <https://doi.org/10.1073/pnas.91.18.8314>.

23. Black A, Luo J, Chun S, Bakker A, Fraser J, Rosenblatt J. 1996. Specific binding of polypyrimidine tract binding protein and hnRNP A1 to HIV-1 CRS elements. *Virus Genes* 12:275–285. <https://doi.org/10.1007/BF00284648>.
24. Maldarelli F, Martin MA, Strebel K. 1991. Identification of posttranscriptionally active inhibitory sequences in human immunodeficiency virus type 1 RNA: novel level of gene regulation. *J Virol* 65:5732–5743. <https://doi.org/10.1128/JVI.65.11.5732-5743.1991>.
25. Haas J, Park E-C, Seed B. 1996. Codon usage limitation in the expression of HIV-1 envelope glycoprotein. *Curr Biol* 6:315–324. [https://doi.org/10.1016/s0960-9822\(02\)00482-7](https://doi.org/10.1016/s0960-9822(02)00482-7).
26. Graf M, Bojak A, Deml L, Bieler K, Wolf H, Wagner R. 2000. Concerted action of multiple cis-acting sequences is required for Rev dependence of late human immunodeficiency virus type 1 gene expression. *J Virol* 74:10822–10826. <https://doi.org/10.1128/jvi.74.22.10822-10826.2000>.
27. Wagner R, Graf M, Bieler K, Wolf H, Grunwald T, Foley P, Überla K. 2000. Rev-independent expression of synthetic *gag-pol* genes of human immunodeficiency virus type 1 and simian immunodeficiency virus: implications for the safety of lentiviral vectors. *Hum Gene Ther* 11:2403–2413. <https://doi.org/10.1089/104303400750038507>.
28. Zhang Q, Chen C-Y, Yedavalli VSRK, Jeang K-T. 2013. NEAT1 long noncoding RNA and paraspeckle bodies modulate HIV-1 posttranscriptional expression. *mBio* 4:e00596-12. <https://doi.org/10.1128/mBio.00596-12>.
29. Kula A, Gharu L, Marcello A. 2013. HIV-1 pre-mRNA commitment to Rev mediated export through PSF and Matrin 3. *Virology* 435:329–340. <https://doi.org/10.1016/j.virol.2012.10.032>.
30. Zolotukhin AS, Michalowski D, Bear J, Smulevitch SV, Traish AM, Peng R, Patton J, Shatsky IN, Felber BK. 2003. PSF acts through the human immunodeficiency virus type 1 mRNA instability elements to regulate virus expression. *Mol Cell Biol* 23:6618–6630. <https://doi.org/10.1128/mcb.23.18.6618-6630.2003>.
31. Yedavalli VSRK, Jeang K-T. 2011. Matrin 3 is a co-factor for HIV-1 Rev in regulating post-transcriptional viral gene expression. *Retrovirology* 8:61. <https://doi.org/10.1186/1742-4690-8-61>.
32. Fong K-W, Li Y, Wang W, Ma W, Li K, Qi RZ, Liu D, Songyang Z, Chen J. 2013. Whole-genome screening identifies proteins localized to distinct nuclear bodies. *J Cell Biol* 203:149–164. <https://doi.org/10.1083/jcb.201303145>.
33. Kula A, Guerra J, Knezevich A, Kleva D, Myers MP, Marcello A. 2011. Characterization of the HIV-1 RNA associated proteome identifies Matrin 3 as a nuclear cofactor of Rev function. *Retrovirology* 8:60. <https://doi.org/10.1186/1742-4690-8-60>.
34. Sarracino A, Gharu L, Kula A, Pasternak AO, Avettand-Fenoel V, Rouzioux C, Bardina M, De Wit S, Benkirane M, Berkhout B, Van Lint C, Marcello A. 2018. Posttranscriptional regulation of HIV-1 gene expression during replication and reactivation from latency by nuclear matrix protein MATR3. *mBio* 9:e02158-18. <https://doi.org/10.1128/mBio.02158-18>.
35. Gordon H, Ajamian L, Valiente-Echeverría F, Lévesque K, Rigby WF, Mouland AJ. 2013. Depletion of hnRNP A2/B1 overrides the nuclear retention of the HIV-1 genomic RNA. *RNA Biol* 10:1714–1725. <https://doi.org/10.4161/rna.26542>.
36. Dziembowski A, Ventura A-P, Rutz B, Caspary F, Faux C, Halgand F, Laprêve O, Séraphin B. 2004. Proteomic analysis identifies a new complex required for nuclear pre-mRNA retention and splicing. *EMBO J* 23:4847–4856. <https://doi.org/10.1038/sj.emboj.7600482>.
37. Frankiw L, Majumdar D, Burns C, Vlach L, Moradian A, Sweredoski MJ, Baltimore D. 2019. BUD13 promotes a type I interferon response by countering intron retention in Irf7. *Mol Cell* 73:803–814.e6. <https://doi.org/10.1016/j.molcel.2018.11.038>.
38. Amit M, Donyo M, Hollander D, Goren A, Kim E, Gelfman S, Lev-Maor G, Burstein D, Schwartz S, Postolsky B, Pupko T, Ast G. 2012. Differential GC content between exons and introns establishes distinct strategies of splice-site recognition. *Cell Rep* 1:543–556. <https://doi.org/10.1016/j.celrep.2012.03.013>.
39. Fernandez JP, Moreno-Mateos MA, Gohr A, Miao L, Chan SH, Irimia M, Giraldez AJ. 2018. RES complex is associated with intron definition and required for zebrafish early embryogenesis. *PLoS Genet* 14:e1007473. <https://doi.org/10.1371/journal.pgen.1007473>.
40. Galy V, Gadad O, Fromont-Racine M, Romano A, Jacquier A, Nehrbass U. 2004. Nuclear retention of unspliced mRNAs in yeast is mediated by perinuclear Mlp1. *Cell* 116:63–73. [https://doi.org/10.1016/s0092-8674\(03\)01026-2](https://doi.org/10.1016/s0092-8674(03)01026-2).
41. Coyle JH, Bor Y-C, Rekosh D, Hammarskjöld M-L. 2011. The Tpr protein regulates export of mRNAs with retained introns that traffic through the Nxf1 pathway. *RNA* 17:1344–1356. <https://doi.org/10.1261/rna.2616111>.
42. Bonnet A, Bretes H, Palancade B. 2015. Nuclear pore components affect distinct stages of intron-containing gene expression. *Nucleic Acids Res* 43:4249–4261. <https://doi.org/10.1093/nar/gkv280>.
43. Zander G, Hackmann A, Bender L, Becker D, Lingner T, Salinas G, Krebber H. 2016. mRNA quality control is bypassed for immediate export of stress-responsive transcripts. *Nature* 540:593–596. <https://doi.org/10.1038/nature20572>.
44. Blanco R, Carrasco L, Ventoso I. 2003. Cell killing by HIV-1 protease. *J Biol Chem* 278:1086–1093. <https://doi.org/10.1074/jbc.M205636200>.
45. Malim MH, Emerman M. 2008. HIV-1 accessory proteins—ensuring viral survival in a hostile environment. *Cell Host Microbe* 3:388–398. <https://doi.org/10.1016/j.chom.2008.04.008>.
46. Stewart SA, Poon B, Jowett JB, Xie Y, Chen IS. 1999. Lentiviral delivery of HIV-1 Vpr protein induces apoptosis in transformed cells. *Proc Natl Acad Sci U S A* 96:12039–12043. <https://doi.org/10.1073/pnas.96.21.12039>.
47. Shalem O, Sanjana NE, Hartenian E, Shi X, Scott DA, Mikkelsen T, Heckl D, Ebert BL, Root DE, Doench JG, Zhang F. 2014. Genome-scale CRISPR-Cas9 knockout screening in human cells. *Science* 343:84–87. <https://doi.org/10.1126/science.1247005>.
48. Sanjana NE, Shalem O, Zhang F. 2014. Improved vectors and genome-wide libraries for CRISPR screening. *Nat Methods* 11:783–784. <https://doi.org/10.1038/nmeth.3047>.
49. Li W, Xu H, Xiao T, Cong L, Love MI, Zhang F, Irizarry RA, Liu JS, Brown M, Liu XS. 2014. MAGeCK enables robust identification of essential genes from genome-scale CRISPR/Cas9 knockout screens. *Genome Biol* 15:554. <https://doi.org/10.1186/s13059-014-0554-4>.
50. Shifrut E, Carnevale J, Tobin V, Roth TL, Woo JM, Bui CT, Li PJ, Diolaiti ME, Ashworth A, Marson A. 2018. Genome-wide CRISPR screens in primary human T cells reveal key regulators of immune function. *Cell* 175:1958–1971.e15. <https://doi.org/10.1016/j.cell.2018.10.024>.
51. Takada I, Tsuchiya M, Yanaka K, Hidano S, Takahashi S, Kobayashi T, Ogawa H, Nakagawa S, Makishima M. 2018. Ess2 bridges transcriptional regulators and spliceosomal complexes via distinct interacting domains. *Biochem Biophys Res Commun* 497:597–604. <https://doi.org/10.1016/j.bbrc.2018.02.110>.
52. Schapira M, Tyers M, Torrent M, Arrowsmith CH. 2017. WD40 repeat domain proteins: a novel target class? *Nat Rev Drug Discov* 16:773–786. <https://doi.org/10.1038/nrd.2017.179>.
53. Yan C, Wan R, Bai R, Huang G, Shi Y. 2017. Structure of a yeast step II catalytically activated spliceosome. *Science* 355:149–155. <https://doi.org/10.1126/science.aak9979>.
54. Zhan X, Yan C, Zhang X, Lei J, Shi Y. 2018. Structure of a human catalytic step I spliceosome. *Science* 359:537–545. <https://doi.org/10.1126/science.aar6401>.
55. Hou S, Qu D, Li Y, Zhu B, Liang D, Wei X, Tang W, Zhang Q, Hao J, Guo W, Wang W, Zhao S, Wang Q, Azam S, Khan M, Zhao H, Zhang L, Lei H. 2019. XAB2 depletion induces intron retention in POLR2A to impair global transcription and promote cellular senescence. *Nucleic Acids Res* 47:8239–8254. <https://doi.org/10.1093/nar/gkz532>.
56. Zhang X, Yan C, Hang J, Finci LI, Lei J, Shi Y. 2017. An atomic structure of the human spliceosome. *Cell* 169:918–929.e14. <https://doi.org/10.1016/j.cell.2017.04.033>.
57. Chanarat S, Sträßer K. 2013. Splicing and beyond: the many faces of the Prp19 complex. *Biochim Biophys Acta* 1833:2126–2134. <https://doi.org/10.1016/j.bbamcr.2013.05.023>.
58. Grainger RJ, Beggs JD. 2005. Prp8 protein: at the heart of the spliceosome. *RNA* 11:533–557. <https://doi.org/10.1261/rna.2220705>.
59. Wang T, Birsoy K, Hughes NW, Krupczak KM, Post Y, Wei JJ, Lander ES, Sabatini DM. 2015. Identification and characterization of essential genes in the human genome. *Science* 350:1096–1101. <https://doi.org/10.1126/science.aac7041>.
60. Reed R. 2003. Coupling transcription, splicing and mRNA export. *Curr Opin Cell Biol* 15:326–331. [https://doi.org/10.1016/s0955-0674\(03\)00048-6](https://doi.org/10.1016/s0955-0674(03)00048-6).
61. Valencia P, Dias AP, Reed R. 2008. Splicing promotes rapid and efficient mRNA export in mammalian cells. *Proc Natl Acad Sci U S A* 105:3386–3391. <https://doi.org/10.1073/pnas.08002510105>.
62. Blissenbach M, Grewe B, Hoffmann B, Brandt S, Überla K. 2010. Nuclear RNA export and packaging functions of HIV-1 Rev revisited. *J Virol* 84:6598–6604. <https://doi.org/10.1128/JVI.02264-09>.
63. Grewe B, Hoffmann B, Ohs I, Blissenbach M, Brandt S, Tippler B, Grunwald T, Überla K. 2012. Cytoplasmic utilization of human immunodeficiency virus type 1 genomic RNA is not dependent on a nuclear interaction with Gag. *J Virol* 86:2990–3002. <https://doi.org/10.1128/JVI.06874-11>.
64. Taniguchi I, Mabuchi N, Ohno M. 2014. HIV-1 Rev protein specifies the viral RNA export pathway by suppressing TAP/NXF1 recruitment. *Nucleic Acids Res* 42:6645–6658. <https://doi.org/10.1093/nar/gku304>.

65. Edenfeld G, Volohonsky G, Krukkert K, Naffin E, Lammel U, Grimm A, Engelen D, Reuveny A, Volk T, Klämbt C. 2006. The splicing factor crooked neck associates with the RNA-binding protein HOW to control glial cell maturation in *Drosophila*. *Neuron* 52:969–980. <https://doi.org/10.1016/j.neuron.2006.10.029>.
66. Hammani K, Cook WB, Barkan A. 2012. RNA binding and RNA remodeling activities of the half-a-tetratricopeptide (HAT) protein HCF107 underlie its effects on gene expression. *Proc Natl Acad Sci U S A* 109:5651–5656. <https://doi.org/10.1073/pnas.1200318109>.
67. Chung S, Zhou Z, Huddleston KA, Harrison DA, Reed R, Coleman TA, Rymond BC. 2002. Crooked neck is a component of the human spliceosome and implicated in the splicing process. *Biochim Biophys Acta* 1576:287–297. [https://doi.org/10.1016/S0167-4781\(02\)00368-8](https://doi.org/10.1016/S0167-4781(02)00368-8).
68. Fica SM, Oubridge C, Wilkinson ME, Newman AJ, Nagai K. 2019. A human postcatalytic spliceosome structure reveals essential roles of metazoan factors for exon ligation. *Science* 363:710–714. <https://doi.org/10.1126/science.aaw5569>.
69. Liu M, Lu Y, Yang B, Chen Y, Radda JSD, Hu M, Katz SG, Wang S. 2020. Multiplexed imaging of nucleosome architectures in single cells of mammalian tissue. *Nat Commun* 11:2907. <https://doi.org/10.1038/s41467-020-16732-5>.
70. Sithole N, Williams CA, Vaughan AM, Kenyon JC, Lever AML. 2018. DDX17 specifically, and independently of DDX5, controls use of the HIV A4/5 splice acceptor cluster and is essential for efficient replication of HIV. *J Mol Biol* 430:3111–3128. <https://doi.org/10.1016/j.jmb.2018.06.052>.
71. Alamancos GP, Pagès A, Trincado JL, Bellora N, Eyras E. 2015. Leveraging transcript quantification for fast computation of alternative splicing profiles. *RNA* 21:1521–1531. <https://doi.org/10.1261/rna.051557.115>.
72. Ren L, McLean JR, Hazbun TR, Fields S, Vander Kooi C, Ohi MD, Gould KL. 2011. Systematic two-hybrid and comparative proteomic analyses reveal novel yeast pre-mRNA splicing factors connected to Prp19. *PLoS One* 6:e16719. <https://doi.org/10.1371/journal.pone.0016719>.
73. Katahira J, Yoneda Y. 2009. Roles of the TREX complex in nuclear export of mRNA. *RNA Biol* 6:149–152. <https://doi.org/10.4161/ma.6.2.8046>.
74. Takemura R, Takeiwa T, Taniguchi I, McCloskey A, Ohno M. 2011. Multiple factors in the early splicing complex are involved in the nuclear retention of pre-mRNAs in mammalian cells. *Genes Cells* 16:1035–1049. <https://doi.org/10.1111/j.1365-2443.2011.01548.x>.
75. Wyszczanski P, Zweckstetter M. 2016. Retention and splicing complex (RES)—the importance of cooperativity. *RNA Biol* 13:128–133. <https://doi.org/10.1080/15476286.2015.1096484>.
76. Karamysheva Z, Diaz-Martinez LA, Warrington R, Yu H. 2015. Graded requirement for the spliceosome in cell cycle progression. *Cell Cycle* 14:1873–1883. <https://doi.org/10.1080/15384101.2015.1039209>.
77. Zhang K, Smouse D, Perrimon N. 1991. The crooked neck gene of *Drosophila* contains a motif found in a family of yeast cell cycle genes. *Genes Dev* 5:1080–1091. <https://doi.org/10.1101/gad.5.6.1080>.
78. Chanarat S, Seizl M, Strässer K. 2011. The Prp19 complex is a novel transcription elongation factor required for TREX occupancy at transcribed genes. *Genes Dev* 25:1147–1158. <https://doi.org/10.1101/gad.623411>.
79. Lei H, Zhai B, Yin S, Gygi S, Reed R. 2013. Evidence that a consensus element found in naturally intronless mRNAs promotes mRNA export. *Nucleic Acids Res* 41:2517–2525. <https://doi.org/10.1093/nar/gks1314>.
80. Biswas P, Jiang X, Pacchia AL, Dougherty JP, Peltz SW. 2004. The human immunodeficiency virus type 1 ribosomal frameshifting site is an invariant sequence determinant and an important target for antiviral therapy. *J Virol* 78:2082–2087. <https://doi.org/10.1128/jvi.78.4.2082-2087.2004>.
81. Yang H-C, Xing S, Shan L, O'Connell K, Dinoso J, Shen A, Zhou Y, Shrum CK, Han Y, Liu JO, Zhang H, Margolick JB, Siliciano RF. 2009. Small-molecule screening using a human primary cell model of HIV latency identifies compounds that reverse latency without cellular activation. *J Clin Invest* 119:3473–3486. <https://doi.org/10.1172/JCI39199>.
82. Platt EJ, Wehrly K, Kuhmann SE, Chesebro B, Kabat D. 1998. Effects of CCR5 and CD4 cell surface concentrations on infections by macrophage-tropic isolates of human immunodeficiency virus type 1. *J Virol* 72:2855–2864. <https://doi.org/10.1128/JVI.72.4.2855-2864.1998>.
83. de Jong SJ, Albrecht J-C, Schmidt M, Müller-Fleckenstein I, Biesinger B. 2010. Activation of noncanonical NF-kappaB signaling by the oncoprotein Tio. *J Biol Chem* 285:16495–16503. <https://doi.org/10.1074/jbc.M110.102848>.
84. Malim MH, Hauber J, Fenrick R, Cullen BR. 1988. Immunodeficiency virus rev trans-activator modulates the expression of the viral regulatory genes. *Nature* 335:181–183. <https://doi.org/10.1038/335181a0>.
85. Fouchier RA, Meyer BE, Simon JH, Fischer U, Malim MH. 1997. HIV-1 infection of non-dividing cells: evidence that the amino-terminal basic region of the viral matrix protein is important for Gag processing but not for post-entry nuclear import. *EMBO J* 16:4531–4539. <https://doi.org/10.1093/emboj/16.15.4531>.
86. Naldini L, Trono D, Verma IM. 2016. Lentiviral vectors, two decades later. *Science* 353:1101–1102. <https://doi.org/10.1126/science.aah6192>.
87. Thomas M, Sonntag E, Müller R, Schmidt S, Zielke B, Fossen T, Stamminger T. 2015. pUL69 of human cytomegalovirus recruits the cellular protein arginine methyltransferase 6 via a domain that is crucial for mRNA export and efficient viral replication. *J Virol* 89:9601–9615. <https://doi.org/10.1128/JVI.01399-15>.
88. Rio DC, Ares M, Hannon GJ, Nilsen TW. 2010. Purification of RNA using TRIzol (TRI reagent). *Cold Spring Harb Protoc* 2010:pdb.prot5439. <https://doi.org/10.1101/pdb.prot5439>.
89. Brandt S, Blissenbach M, Grewe B, Konietzny R, Grunwald T, Uberla K. 2007. Rev proteins of human and simian immunodeficiency virus enhance RNA encapsidation. *PLoS Pathog* 3:e54. <https://doi.org/10.1371/journal.ppat.0030054>.
90. Kim D, Paggi JM, Park C, Bennett C, Salzberg SL. 2019. Graph-based genome alignment and genotyping with HISAT2 and HISAT-genotype. *Nat Biotechnol* 37:907–915. <https://doi.org/10.1038/s41587-019-0201-4>.
91. Li H. 2011. A statistical framework for SNP calling, mutation discovery, association mapping and population genetical parameter estimation from sequencing data. *Bioinformatics* 27:2987–2993. <https://doi.org/10.1093/bioinformatics/btr509>.
92. Feng Y-Y, Ramu A, Cotto KC, Skidmore ZL, Kunisaki J, Conrad DF, Lin Y, Chapman WC, Uppaluri R, Govindan R, Griffith OL, Griffith M. 2018. RegTools: integrated analysis of genomic and transcriptomic data for discovery of splicing variants in cancer. *bioRxiv* <https://doi.org/10.1101/436634>.
93. Li B, Dewey CN. 2011. RSEM: accurate transcript quantification from RNA-Seq data with or without a reference genome. *BMC Bioinformatics* 12:323. <https://doi.org/10.1186/1471-2105-12-323>.
94. Robinson JT, Thorvaldsdóttir H, Winckler W, Guttman M, Lander ES, Getz G, Mesirov JP. 2011. Integrative genomics viewer. *Nat Biotechnol* 29:24–26. <https://doi.org/10.1038/nbt.1754>.
95. Corvelo A, Hallegger M, Smith CWJ, Eyras E. 2010. Genome-wide association between branch point properties and alternative splicing. *PLoS Comput Biol* 6:e1001016. <https://doi.org/10.1371/journal.pcbi.1001016>.
96. Yeo G, Burge CB. 2004. Maximum entropy modeling of short sequence motifs with applications to RNA splicing signals. *J Comput Biol* 11:377–394. <https://doi.org/10.1089/1066527041410418>.
97. Schafer S, Miao K, Benson CC, Heinig M, Cook SA, Hubner N. 2015. Alternative splicing signatures in RNA-seq data: percent spliced in (PSI). *Curr Protoc Hum Genet* 87:11.16.1–11.16.14. <https://doi.org/10.1002/0471142905.hg1116s87>.
98. Budhiraja S, Liu H, Couturier J, Malovannaya A, Qin J, Lewis DE, Rice AP. 2015. Mining the human complexome database identifies RBM14 as an XPO1-associated protein involved in HIV-1 Rev function. *J Virol* 89:3557–3567. <https://doi.org/10.1128/JVI.03232-14>.