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Bibliography

Bibliography

Adams, V.H., McBryant, S.J., Wade, P.A., Woodcock, C.L., and Hansen, J.C. (2007). Intrinsic disorder and autonomous domain function in the multifunctional nuclear protein, MeCP2. *J. Biol. Chem.* *282*, 15057–15064.

Agarwal, N., Hardt, T., Brero, A., Nowak, D., Rothbauer, U., Becker, A., Leonhardt, H., and Cardoso, M.C. (2007). MeCP2 interacts with HP1 and modulates its heterochromatin association during myogenic differentiation. *Nucleic Acids Res* *35*, 5402–5408.

Akhtar, W., de Jong, J., Pindyurin, A. V, Pagie, L., Meuleman, W., de Ridder, J., Berns, A., Wessels, L.F. a, van Lohuizen, M., and van Steensel, B. (2013). Chromatin position effects assayed by thousands of reporters integrated in parallel. *Cell* *154*, 914–927.

Al-Allaf, F. a., Tolmachov, O.E., Zambetti, L.P., Tchetchelnitski, V., and Mehmet, H. (2012). Remarkable stability of an instability-prone lentiviral vector plasmid in *Escherichia coli* Stbl3. *3 Biotech* 61–70.

Alvarez-Saavedra, M., Antoun, G., Yanagiya, A., Oliva-Hernandez, R., Cornejo-Palma, D., Perez-Iratxeta, C., Sonenberg, N., and Cheng, H.Y.M. (2011). miRNA-132 orchestrates chromatin remodeling and translational control of the circadian clock. *Hum. Mol. Genet.* *20*, 731–751.

Amir, R.E., Van den Veyver, I.B., Wan, M., Tran, C.Q., Francke, U., and Zoghbi, H.Y. (1999). Rett syndrome is caused by mutations in X-linked MECP2, encoding methyl-CpG-binding protein 2. *Nat. Genet.* *23*, 185–188.

Anderson, A., Wong, K., Jacoby, P., Downs, J., and Leonard, H. (2014). Twenty years of surveillance in Rett syndrome: what does this tell us? *Orphanet J. Rare Dis.* *9*, 87.

Babbio, F., Castiglioni, I., Cassina, C., Gariboldi, M., Pistore, C., Magnani, E., Badaracco, G., Monti, E., and Bonapace, I. (2012). Knock-down of methyl CpG-binding protein 2 (MeCP2) causes alterations in cell proliferation and nuclear lamins expression in mammalian cells. *BMC Cell Biol.* *13*, 19.

Baker, S.A., Chen, L., Wilkins, A.D., Yu, P., Lichtarge, O., and Zoghbi, H.Y. (2013). An AT-hook domain in MeCP2 determines the clinical course of Rett syndrome and related disorders. *Cell* *152*, 984–996.

Ballas, N., Liou, D.T., Grunseich, C., and Mandel, G. (2009). Non-cell autonomous influence of MeCP2-deficient glia on neuronal dendritic morphology. *Nat. Neurosci.* *12*, 311–317.

Ballestar, E., Yusufzai, T.M., and Wolffe, A.P. (2000). Effects of Rett syndrome mutations of the methyl-CpG binding domain of the transcriptional repressor MeCP2 on selectivity for association with methylated DNA. *Biochemistry* *39*, 7100–7106.

- Barth, T.K., and Imhof, A. (2010). Fast signals and slow marks: the dynamics of histone modifications. *Trends Biochem. Sci.* *35*, 618–626.
- Battich, N., Stoeger, T., and Pelkmans, L. (2013). Image-based transcriptomics in thousands of single human cells at single-molecule resolution. *Nat. Methods* *10*, 1127–1133.
- Bellini, E., Pavesi, G., Barbiero, I., Bergo, A., Chandola, C., Nawaz, M.S., Rusconi, L., Stefanelli, G., Strollo, M., Valente, M.M., et al. (2014). MeCP2 post-translational modifications: a mechanism to control its involvement in synaptic plasticity and homeostasis? *Front. Cell. Neurosci.* *8*, 1–15.
- Belmont, A.S., Li, G., Sudlow, G., and Robinett, C. (1999). Visualization of large-scale chromatin structure and dynamics using the lac operator/lac repressor reporter system. *Methods Cell Biol* *58*, 203–222.
- Ben-Ari, Y., Brody, Y., Kinor, N., Mor, A., Tsukamoto, T., Spector, D.L., Singer, R.H., and Shav-Tal, Y. (2010). The life of an mRNA in space and time. *J. Cell Sci.* *123*, 1761–1774.
- Ben-Shachar, S., Chahrour, M., Thaller, C., Shaw, C.A., and Zoghbi, H.Y. (2009). Mouse models of MeCP2 disorders share gene expression changes in the cerebellum and hypothalamus. *Hum Mol Genet* *18*, 2431–2442.
- Bergo, A., Strollo, M., Gai, M., Barbiero, I., Stefanelli, G., Gigli, C.C., Cunto, F. Di, and Kilstrup-nielsen, C. (2014). Novel and unexpected centrosome-related functions of MeCP2. *2*.
- Bertrand, E., Chartrand, P., Schaefer, M., Shenoy, S.M., Singer, R.H., and Long, R.M. (1998). Localization of ASH1 mRNA particles in living yeast. *Mol. Cell* *2*, 437–445.
- Bienvenu, T., and Chelly, J. (2006). Molecular genetics of Rett syndrome: when DNA methylation goes unrecognized. *Nat. Rev. Genet.* *7*, 415–426.
- Bodnar, M.S., and Spector, D.L. (2013). Chromatin Meets Its Organizers. *Cell* *153*, 1187–1189.
- Boettcher, M., and McManus, M.T. (2015). Choosing the Right Tool for the Job: RNAi, TALEN, or CRISPR. *Mol. Cell* *58*, 575–585.
- Brero, A., Easwaran, H.P., Nowak, D., Grunewald, I., Cremer, T., Leonhardt, H., and Cardoso, M.C. (2005). Methyl CpG-binding proteins induce large-scale chromatin reorganization during terminal differentiation. *J Cell Biol* *169*, 733–743.

Bibliography

Brink, M.C., Piebes, D.G.E., de Groote, M.L., Luijsterburg, M.S., Casas-Delucchi, C.S., van Driel, R., Rots, M.G., Cardoso, M.C., and Verschure, P.J. (2013). A role for MeCP2 in switching gene activity via chromatin unfolding and HP1 γ displacement. *PLoS One* *8*, e69347.

Brody, Y., and Shav-Tal, Y. (2011). Measuring the kinetics of mRNA transcription in single living cells. *J. Vis. Exp.* 1–6.

Buschdorf, J.P., and Strätling, W.H. (2004). A WW domain binding region in methyl-CpG-binding protein MeCP2: Impact on Rett syndrome. *J. Mol. Med.* *82*, 135–143.

Buyse, I.M., Fang, P., Hoon, K.T., Amir, R.E., Zoghbi, H.Y., and Roa, B.B. (2000). Diagnostic testing for Rett syndrome by DHPLC and direct sequencing analysis of the MECP2 gene: identification of several novel mutations and polymorphisms. *Am. J. Hum. Genet.* *67*, 1428–1436.

Chahrour, M., Jung, S.Y., Shaw, C., Zhou, X., Wong, S.T.C., Qin, J., and Zoghbi, H.Y. (2008). MeCP2, a key contributor to neurological disease, activates and represses transcription. *Science* *320*, 1224–1229.

Chambeyron, S., and Bickmore, W.A. (2004). Chromatin decondensation and nuclear reorganization of the HoxB locus upon induction of transcription. *Genes Dev* *18*, 1119–1130.

Chao, H.-T., and Zoghbi, H.Y. (2009). The yin and yang of MeCP2 phosphorylation. *Proc. Natl. Acad. Sci. U. S. A.* *106*, 4577–4578.

Chen, K.H., Boettiger, A.N., Moffitt, J.R., Wang, S., and Zhuang, X. (2015). Spatially resolved, highly multiplexed RNA profiling in single cells. *Science* *348*, aaa6090.

Cheutin, T., McNairn, A.J., Jenuwein, T., Gilbert, D.M., Singh, P.B., and Misteli, T. (2003). Maintenance of stable heterochromatin domains by dynamic HP1 binding. *Science* (80-.). *299*, 721–725.

Chiang, K., Liu, H., and Rice, A.P. (2013). MiR-132 enhances HIV-1 replication. *Virology* *438*, 1–4.

Christodoulou, J., Grimm, A., Maher, T., and Bennetts, B. (2003). RettBASE: The IRSA MECP2 variation database—a new mutation database in evolution. *Hum. Mutat.* *21*, 466–472.

- Colantuoni, C., Jeon, O.H., Hyder, K., Chenchik, A., Khimani, A.H., Narayanan, V., Hoffman, E.P., Kaufmann, W.E., Naidu, S., and Pevsner, J. (2001). Gene expression profiling in postmortem Rett Syndrome brain: differential gene expression and patient classification. *Neurobiol. Dis.* *8*, 847–865.
- Collins, A.L., Levenson, J.M., Vilaythong, A.P., Richman, R., Armstrong, D.L., Noebels, J.L., Sweatt, J.D., and Zoghbi, H.Y. (2004). Mild overexpression of MeCP2 causes a progressive neurological disorder in mice. *Hum. Mol. Genet.* *13*, 2679–2689.
- Coulon, A., Chow, C.C., Singer, R.H., and Larson, D.R. (2013). Eukaryotic transcriptional dynamics: from single molecules to cell populations. *Nat. Rev. Genet.* *14*, 572–584.
- Cowell, I.G., Aucott, R., Mahadevaiah, S.K., Burgoyne, P.S., Huskisson, N., Bongiorno, S., Prantera, G., Fanti, L., Pimpinelli, S., Wu, R., et al. (2002). Heterochromatin, HP1 and methylation at lysine 9 of histone H3 in animals. *Chromosoma* *111*, 22–36.
- Cutter, A.R., and Hayes, J.J. (2015). A brief review of nucleosome structure. *FEBS Lett.* 1–9.
- Darzacq, X., Shav-Tal, Y., de Turris, V., Brody, Y., Shenoy, S.M., Phair, R.D., and Singer, R.H. (2007). In vivo dynamics of RNA polymerase II transcription. *Nat. Struct. Mol. Biol.* *14*, 796–806.
- Deng, W., and Blobel, G. a. (2014). Manipulating nuclear architecture. *Curr. Opin. Genet. Dev.* *25*, 1–7.
- Dintilhac, A., and Bernués, J. (2002). HMGB1 interacts with many apparently unrelated proteins by recognizing short amino acid sequences. *J. Biol. Chem.* *277*, 7021–7028.
- Dion, M.F., Kaplan, T., Kim, M., Buratowski, S., Friedman, N., and Rando, O.J. (2007). Dynamics of replication-independent histone turnover in budding yeast. *Science* (80-.). *315*, 1405–1408.
- Dobrzynski, M., and Bruggeman, F.J. (2009). Elongation dynamics shape bursty transcription and translation. *Proc. Natl. Acad. Sci. U. S. A.* *106*, 2583–2588.
- Ego, T., Tanaka, Y., and Shimotohno, K. (2005). Interaction of HTLV-1 Tax and methyl-CpG-binding domain 2 positively regulates the gene expression from the hypermethylated LTR. *Oncogene* *24*, 1914–1923.
- Eivazova, E.R., Gavrilov, A., Pirozhkova, I., Petrov, A., Iarovaia, O. V., Razin, S. V., Lipinski, M., and Vassetzky, Y.S. (2009). Interaction in vivo between the two matrix attachment regions flanking a single chromatin loop. *J Mol Biol* *386*, 929–937.

Bibliography

- Ernst, J., and Kellis, M. (2010). Discovery and characterization of chromatin states for systematic annotation of the human genome. *Nat. Biotechnol.* **28**, 817–825.
- Van Esch, H. (2012). MECP2 duplication syndrome. *Mol. Syndromol.* **2**, 128–136.
- Fuks, F., Hurd, P.J., Wolf, D., Nan, X., Bird, A.P., and Kouzarides, T. (2003). The methyl-CpG-binding protein MeCP2 links DNA methylation to histone methylation. *J Biol Chem* **278**, 4035–4040.
- Fyfe, S., Cream, A., de Klerk, N., Christodoulou, J., and Leonard, H. (2003). InterRett and RettBASE: International Rett Syndrome Association databases for Rett syndrome. *J. Child Neurol.* **18**, 709–713.
- Gadalla, K.K.E., Bailey, M.E.S., and Cobb, S.R. (2011). MeCP2 and Rett syndrome: reversibility and potential avenues for therapy. *Biochem. J.* **439**, 1–14.
- Gandhi, S.J., Zenklusen, D., Lionnet, T., and Singer, R.H. (2011). Transcription of functionally related constitutive genes is not coordinated. *Nat. Struct. Mol. Biol.* **18**, 27–34.
- Garg, S.K., Liyo, D.T., Cheval, H., McGann, J.C., Bissonnette, J.M., Murtha, M.J., Foust, K.D., Kaspar, B.K., Bird, A., and Mandel, G. (2013). Systemic delivery of MeCP2 rescues behavioral and cellular deficits in female mouse models of Rett syndrome. *J. Neurosci.* **33**, 13612–13620.
- Georgel, P.T., Horowitz-Scherer, R.A., Adkins, N., Woodcock, C.L., Wade, P.A., and Hansen, J.C. (2003). Chromatin compaction by human MeCP2. Assembly of novel secondary chromatin structures in the absence of DNA methylation. *J Biol Chem* **278**, 32181–32188.
- Ghosh, R.P., Horowitz-Scherer, R.A., Nikitina, T., Shlyakhtenko, L.S., and Woodcock, C.L. (2010a). MeCP2 binds cooperatively to its substrate and competes with histone H1 for chromatin binding sites. *Mol Cell Biol* **30**, 4656–4670.
- Ghosh, R.P., Nikitina, T., Horowitz-Scherer, R. a, Gierasch, L.M., Uversky, V.N., Hite, K., Hansen, J.C., and Woodcock, C.L. (2010b). Unique physical properties and interactions of the domains of methylated DNA binding protein 2. *Biochemistry* **49**, 4395–4410.
- Gibson, D.G., Young, L., Chuang, R.-Y., Venter, J.C., Hutchison, C.A., and Smith, H.O. (2009). Enzymatic assembly of DNA molecules up to several hundred kilobases. *Nat. Methods* **6**, 343–345.

- Gierman, H.J., Indemans, M.H.G., Koster, J., Goetze, S., Seppen, J., Geerts, D., van Driel, R., and Versteeg, R. (2007). Domain-wide regulation of gene expression in the human genome. *Genome Res.* *17*, 1286–1295.
- Gilbert, N., Boyle, S., Fiegler, H., Woodfine, K., Carter, N.P., and Bickmore, W.A. (2004). Chromatin architecture of the human genome: gene-rich domains are enriched in open chromatin fibers. *Cell* *118*, 555–566.
- Goedhart, J., van Weeren, L., Hink, M.A., Vischer, N.O.E., Jalink, K., and Gadella, T.W.J. (2010). Bright cyan fluorescent protein variants identified by fluorescence lifetime screening. *Nat. Methods* *7*, 137–139.
- Gossen, M., and Bujard, H. (1992). Tight control of gene expression in mammalian cells by tetracycline-responsive promoters. *Proc. Natl. Acad. Sci. U. S. A.* *89*, 5547–5551.
- Groner, A.C., Meylan, S., Ciuffi, A., Zangger, N., Ambrosini, G., Denervaud, N., Bucher, P., and Trono, D. (2010). KRAB-zinc finger proteins and KAP1 can mediate long-range transcriptional repression through heterochromatin spreading. *PLoS Genet* *6*, e1000869.
- Guarda, A., Bolognese, F., Bonapace, I.M., and Badaracco, G. (2009). Interaction between the inner nuclear membrane lamin B receptor and the heterochromatic methyl binding protein, MeCP2. *Exp. Cell Res.* *315*, 1895–1903.
- Guo, J.U., Su, Y., Zhong, C., Ming, G.-L., and Song, H. (2011). Hydroxylation of 5-Methylcytosine by TET1 Promotes Active DNA Demethylation in the Adult Brain. *Cell* *145*, 423–434.
- Gurard-Levin, Z. a, and Almouzni, G. (2014). Histone modifications and a choice of variant: a language that helps the genome express itself. *F1000Prime Rep* *6*, 76.
- Guy, J., Hendrich, B., Holmes, M., Martin, J.E., and Bird, A. (2001). A mouse *Mecp2*-null mutation causes neurological symptoms that mimic Rett syndrome. *Nat. Genet.* *27*, 322–326.
- Guy, J., Gan, J., Selfridge, J., Cobb, S., and Bird, A. (2007). Reversal of neurological defects in a mouse model of Rett syndrome. *Science* *315*, 1143–1147.
- Hager, G.L., Fletcher, T.M., Xiao, N., Baumann, C.T., Müller, W.G., and McNally, J.G. (2000). Dynamics of gene targeting and chromatin remodelling by nuclear receptors. *Biochem. Soc. Trans.* *28*, 405–410.
- Hager, G.L., McNally, J.G., and Misteli, T. (2009). Transcription dynamics. *Mol. Cell* *35*, 741–753.

Bibliography

- Hamer, K.M., Sewalt, R.G., den Blaauwen, J.L., Hendrix, T., Satijn, D.P., and Otte, A.P. (2002). A panel of monoclonal antibodies against human polycomb group proteins. *Hybrid Hybridomics* 21, 245–252.
- Harikrishnan, K.N., Chow, M.Z., Baker, E.K., Pal, S., Bassal, S., Brasacchio, D., Wang, L., Craig, J.M., Jones, P.L., Sif, S., et al. (2005). Brahma links the SWI/SNF chromatin-remodeling complex with MeCP2-dependent transcriptional silencing. *Nat Genet* 37, 254–264.
- Harper, C. V, Finkenstädt, B., Woodcock, D.J., Friedrichsen, S., Semprini, S., Ashall, L., Spiller, D.G., Mullins, J.J., Rand, D.A., Davis, J.R.E., et al. (2011). Dynamic analysis of stochastic transcription cycles. *PLoS Biol.* 9, e1000607.
- Hassan, A.H., Prochasson, P., Neely, K.E., Galasinski, S.C., Chandy, M., Carrozza, M.J., and Workman, J.L. (2002). Function and selectivity of bromodomains in anchoring chromatin-modifying complexes to promoter nucleosomes. *Cell* 111, 369–379.
- Hayakawa, T., Haraguchi, T., Masumoto, H., and Hiraoka, Y. (2003). Cell cycle behavior of human HP1 subtypes: distinct molecular domains of HP1 are required for their centromeric localization during interphase and metaphase. *J Cell Sci* 116, 3327–3338.
- Hemmerich, P., Schmiedeberg, L., and Diekmann, S. (2011). Dynamic as well as stable protein interactions contribute to genome function and maintenance. *Chromosom. Res* 19, 131–151.
- Hines, K.A., Cryderman, D.E., Flannery, K.M., Yang, H., Vitalini, M.W., Hazelrigg, T., Mizzen, C.A., and Wallrath, L.L. (2009). Domains of heterochromatin protein 1 required for *Drosophila melanogaster* heterochromatin spreading. *Genetics* 182, 967–977.
- Hocine, S., Raymond, P., Zenklusen, D., Chao, J. a, and Singer, R.H. (2013). Single-molecule analysis of gene expression using two-color RNA labeling in live yeast. *Nat. Methods* 10, 119–121.
- Hoppe, P.S., Coutu, D.L., and Schroeder, T. (2014). Single-cell technologies sharpen up mammalian stem cell research. *Nat. Cell Biol.* 16, 919–927.
- Horike, S., Cai, S., Miyano, M., Cheng, J.F., and Kohwi-Shigematsu, T. (2005). Loss of silent-chromatin looping and impaired imprinting of DLX5 in Rett syndrome. *Nat Genet* 37, 31–40.
- Hsu, P.D., Lander, E.S., and Zhang, F. (2014). Development and Applications of CRISPR-Cas9 for Genome Engineering. *Cell* 157, 1262–1278.

- Hu, K., Nan, X., Bird, A., and Wang, W. (2006). Testing for association between MeCP2 and the brahma-associated SWI/SNF chromatin-remodeling complex. *Nat Genet* *38*, 962–967.
- Huranová, M., Ivani, I., Benda, A., Poser, I., Brody, Y., Hof, M., Shav-Tal, Y., Neugebauer, K.M., and Staněk, D. (2010). The differential interaction of snRNPs with pre-mRNA reveals splicing kinetics in living cells. *J. Cell Biol.* *191*, 75–86.
- Iizuka, M., and Smith, M.M. (2003). Functional consequences of histone modifications. *Curr. Opin. Genet. Dev.* *13*, 154–160.
- Janicki, S.M., Tsukamoto, T., Salghetti, S.E., Tansey, W.P., Sachidanandam, R., Prasanth, K. V, Ried, T., Shav-Tal, Y., Bertrand, E., Singer, R.H., et al. (2004). From silencing to gene expression: real-time analysis in single cells. *Cell* *116*, 683–698.
- Jiang, M., Ash, R.T., Baker, S.A., Suter, B., Ferguson, A., Park, J., Rudy, J., Torsky, S.P., Chao, H.-T., Zoghbi, H.Y., et al. (2013). Dendritic arborization and spine dynamics are abnormal in the mouse model of MECP2 duplication syndrome. *J. Neurosci.* *33*, 19518–19533.
- Johnston, I.G., Gaal, B., das Neves, R.P., Enver, T., Iborra, F.J., and Jones, N.S. (2012). Mitochondrial variability as a source of extrinsic cellular noise. *PLoS Comput. Biol.* *8*.
- Jones, P.L., Veenstra, G.J., Wade, P.A., Vermaak, D., Kass, S.U., Landsberger, N., Strouboulis, J., and Wolffe, A.P. (1998). Methylated DNA and MeCP2 recruit histone deacetylase to repress transcription. *Nat Genet* *19*, 187–191.
- Jost, K.L., Rottach, A., Mildner, M., Bertulat, B., Becker, A., Wolf, P., Sandoval, J., Petazzi, P., Huertas, D., Esteller, M., et al. (2011). Generation and characterization of rat and mouse monoclonal antibodies specific for MeCP2 and their use in X-inactivation studies. *PLoS One* *6*, e26499.
- Kaludov, N.K., and Wolffe, A.P. (2000). MeCP2 driven transcriptional repression in vitro: selectivity for methylated DNA, action at a distance and contacts with the basal transcription machinery. *Nucleic Acids Res* *28*, 1921–1928.
- Van Kampen, N.G. (1992). *Stochastic processes in physics and chemistry*.
- Kang, M., Day, C.A., Kenworthy, A.K., and DiBenedetto, E. (2012). Simplified equation to extract diffusion coefficients from confocal FRAP data. *Traffic* *13*, 1589–1600.
- Kato, M. (2006). A new paradigm for West syndrome based on molecular and cell biology. *Epilepsy Res.* *70*, 87–95.

Bibliography

- Kernohan, K.D., Jiang, Y., Tremblay, D.C., Bonvissuto, A.C., Eubanks, J.H., Mann, M.R.W., Berube, N.G., and Bérubé, N.G. (2010). ATRX partners with cohesin and MeCP2 and contributes to developmental silencing of imprinted genes in the brain. *Dev Cell* *18*, 191–202.
- Kernohan, K.D., Vernimmen, D., Gloor, G.B., and Bérubé, N.G. (2014). Analysis of neonatal brain lacking ATRX or MeCP2 reveals changes in nucleosome density, CTCF binding and chromatin looping. *Nucleic Acids Res.* *42*, 8356–8368.
- Khrapunov, S., Warren, C., Cheng, H., Berko, E.R., Grealley, J.M., and Brenowitz, M. (2014). Unusual characteristics of the DNA binding domain of epigenetic regulatory protein MeCP2 determine its binding specificity. *Biochemistry* *53*, 3379–3391.
- Kimura, H., and Shiota, K. (2003). Methyl-CpG-binding protein, MeCP2, is a target molecule for maintenance DNA methyltransferase, Dnmt1. *J. Biol. Chem.* *278*, 4806–4812.
- Kinde, B., Gabel, H.W., Gilbert, C.S., Griffith, E.C., and Greenberg, M.E. (2015). Reading the unique DNA methylation landscape of the brain: Non-CpG methylation, hydroxymethylation, and MeCP2. *Proc. Natl. Acad. Sci. U. S. A.* 1–7.
- Klose, R.J., Sarraf, S.A., Schmiedeberg, L., McDermott, S.M., Stancheva, I., and Bird, A.P. (2005). DNA binding selectivity of MeCP2 due to a requirement for A/T sequences adjacent to methyl-CpG. *Mol Cell* *19*, 667–678.
- Kouzarides, T. (2007a). SnapShot: Histone-Modifying Enzymes. *Cell* *131*.
- Kouzarides, T. (2007b). Chromatin Modifications and Their Function. *Cell* *128*, 693–705.
- Kriaucionis, S., and Bird, A. (2004). The major form of MeCP2 has a novel N-terminus generated by alternative splicing. *Nucleic Acids Res.* *32*, 1818–1823.
- Kucukkal, T.G., and Alexov, E. (2015). Structural, Dynamical, and Energetical Consequences of Rett Syndrome Mutation R133C in MeCP2. *Comput. Math. Methods Med.* *2015*, 746157.
- Kwak, H., and Lis, J.T. (2013). Control of transcriptional elongation. *Annu. Rev. Genet.* *47*, 483–508.
- Lam, C.W., Yeung, W.L., Ko, C.H., Poon, P.M., Tong, S.F., Chan, K.Y., Lo, I.F., Chan, L.Y., Hui, J., Wong, V., et al. (2000). Spectrum of mutations in the MECP2 gene in patients with infantile autism and Rett syndrome. *J Med Genet* *37*, E41.

- Lange, S., Katayama, Y., Schmid, M., Burkacky, O., Brauchle, C., Lamb D.C., D.C., and Jansen, R.P. (2008). Simultaneous transport of different localized mRNA species revealed by live-cell imaging. *Traffic* 9, 1256–1267.
- Larson, D.R., Singer, R.H., and Zenklusen, D. (2009). A single molecule view of gene expression. *Trends Cell Biol.* 19, 630–637.
- Larson, D.R., Zenklusen, D., Wu, B., Chao, J. a, and Singer, R.H. (2011). Real-time observation of transcription initiation and elongation on an endogenous yeast gene. *Science* 332, 475–478.
- LaSalle, J.M. (2007). The odyssey of MeCP2 and parental imprinting. *Epigenetics* 2, 5–10.
- Lee, J.H., Daugharthy, E.R., Scheiman, J., Kalthor, R., Yang, J.L., Ferrante, T.C., Terry, R., Jeanty, S.S.F., Li, C., Amamoto, R., et al. (2014). Highly Multiplexed Subcellular RNA Sequencing in Situ. *Science* (80-.). 343, 1360–1363.
- de Leeuw, W., Verschure, P.J., and van Liere, R. (2006). Isualization and analysis of large data collections: a case study applied to confocal microscopy data. *IEEE Trans Vis Comput Graph* 12, 1251–1258.
- de Leon-Guerrero, S.D., Pedraza-Alva, G., and Perez-Martinez, L. (2011). In sickness and in health: the role of methyl-CpG binding protein 2 in the central nervous system. *Eur J Neurosci* 33, 1563–1574.
- Leonhardt, H., Rahn, H.P., Weinzierl, P., Sporberr, A., Cremer, T., Zink, D., and Cardoso, M.C. (2000). Dynamics of DNA replication factories in living cells. *J Cell Biol* 149, 271–280.
- Lev Maor, G., Yearim, A., and Ast, G. (2015). The alternative role of DNA methylation in splicing regulation. *Trends Genet.* 31, 274–280.
- Lewis, J.D., Meehan, R.R., Henzel, W.J., Maurer-Fogy, I., Jeppesen, P., Klein, F., and Bird, A. (1992). Purification, sequence, and cellular localization of a novel chromosomal protein that binds to methylated DNA. *Cell* 69, 905–914.
- Li, X. (1998). Generation of Destabilized Green Fluorescent Protein as a Transcription Reporter. *J. Biol. Chem.* 273, 34970–34975.
- Li, G., and Zhu, P. (2015). Structure and organization of chromatin fiber in the nucleus. *FEBS Lett.*
- Li, B., Carey, M., and Workman, J.L. (2007). The Role of Chromatin during Transcription. *Cell* 128, 707–719.

Bibliography

- Linhoff, M.W., Garg, S.K., and Mandel, G. (2015). A High-Resolution Imaging Approach to Investigate Chromatin Architecture in Complex Tissues. *Cell* 163, 246–255.
- Lionnet, T., Czaplinski, K., Darzacq, X., Shav-Tal, Y., Wells, A.L., Chao, J.A., Park, H.Y., de Turris, V., Lopez-Jones, M., and Singer, R.H. (2011). A transgenic mouse for in vivo detection of endogenous labeled mRNA. *Nat. Methods* 8, 165–170.
- Lioy, D.T., Garg, S.K., Monaghan, C.E., Raber, J., Foust, K.D., Kaspar, B.K., Hirrlinger, P.G., Kirchhoff, F., Bissonnette, J.M., Ballas, N., et al. (2011). A role for glia in the progression of Rett's syndrome. *Nature* 475, 497–500.
- Lister, R., Mukamel, E.A., Nery, J.R., Urich, M., Puddifoot, C.A., Johnson, N.D., Lucero, J., Huang, Y., Dwork, A.J., Schultz, M.D., et al. (2013). Global epigenomic reconfiguration during mammalian brain development. *Science* 341, 1237905.
- Liu, B., Xu, H., Miao, J., Zhang, A., Kou, X., Li, W., Zhou, L., Xie, H.-G., Sirois, P., and Li, K. (2015). CRISPR/Cas: A Faster and More Efficient Gene Editing System. *J. Nanosci. Nanotechnol.* 15, 1946–1959.
- Lubs, H., Abidi, F., Bier, J.A.B., Abuelo, D., Ouzts, L., Voeller, K., Fennell, E., Stevenson, R.E., Schwartz, C.E., and Arena, F. (1999). XLMR syndrome characterized by multiple respiratory infections, hypertelorism, severe CNS deterioration and early death localizes to distal Xq28. *Am. J. Med. Genet.* 85, 243–248.
- Luger, K., and Hansen, J.C. (2005). Nucleosome and chromatin fiber dynamics. *Curr. Opin. Struct. Biol.* 15, 188–196.
- Luijsterburg, M.S., Goedhart, J., Moser, J., Kool, H., Geverts, B., Houtsmuller, A.B., Mullenders, L.H., Vermeulen, W., and van Driel, R. (2007). Dynamic in vivo interaction of DDB2 E3 ubiquitin ligase with UV-damaged DNA is independent of damage-recognition protein XPC. *J Cell Sci* 120, 2706–2716.
- Luikenhuis, S., Giacometti, E., Beard, C.F., and Jaenisch, R. (2004). Expression of MeCP2 in postmitotic neurons rescues Rett syndrome in mice. *Proc. Natl. Acad. Sci. U. S. A.* 101, 6033–6038.
- Lunyak, V. V., Burgess, R., Prefontaine, G.G., Nelson, C., Sze, S.-H., Chenoweth, J., Schwartz, P., Pevzner, P.A., Glass, C., Mandel, G., et al. (2002). Corepressor-dependent silencing of chromosomal regions encoding neuronal genes. *Science* 298, 1747–1752.
- Lv, J., Xin, Y., Zhou, W., and Qiu, Z. (2013). The epigenetic switches for neural development and psychiatric disorders. *J. Genet. Genomics* 40, 339–346.
- Lyst, M.J., Ekiert, R., Ebert, D.H., Merusi, C., Nowak, J., Selfridge, J., Guy, J., Kastan, N.R.,

- Robinson, N.D., de Lima Alves, F., et al. (2013). Rett syndrome mutations abolish the interaction of MeCP2 with the NCoR/SMRT co-repressor. *Nat. Neurosci.* *16*, 898–902.
- MacQuarrie, K.L., Fong, A.P., Morse, R.H., and Tapscott, S.J. (2011). Genome-wide transcription factor binding: Beyond direct target regulation. *Trends Genet.* *27*, 141–148.
- Maheshri, N., and O’Shea, E.K. (2007). Living with noisy genes: how cells function reliably with inherent variability in gene expression. *Annu. Rev. Biophys. Biomol. Struct.* *36*, 413–434.
- Mari, F., Azimonti, S., Bertani, I., Bolognese, F., Colombo, E., Caselli, R., Scala, E., Longo, I., Grosso, S., Pescucci, C., et al. (2005). CDKL5 belongs to the same molecular pathway of MeCP2 and it is responsible for the early-onset seizure variant of Rett syndrome. *Hum. Mol. Genet.* *14*, 1935–1946.
- Marti, A., Paz, D., Esteller, M., and Ausio, J. (2014). MeCP2 : the long trip from a chromatin protein to neurological disorders. 1–12.
- Martínez de Paz, A., Vicente Sanchez-Mut, J., Samitier-Martí, M., Petazzi, P., Sáez, M., Szczesna, K., Huertas, D., Esteller, M., and Ausió, J. (2015). Circadian Cycle-Dependent MeCP2 and Brain Chromatin Changes. *PLoS One* *10*, e0123693.
- Martins, S.B., Rino, J., Carvalho, T., Carvalho, C., Yoshida, M., Klose, J.M., de Almeida, S.F., and Carmo-Fonseca, M. (2011). Spliceosome assembly is coupled to RNA polymerase II dynamics at the 3’ end of human genes. *Nat. Struct. Mol. Biol.* *18*, 1115–1123.
- Mason, P.B., and Struhl, K. (2005). Distinction and relationship between elongation rate and processivity of RNA polymerase II in vivo. *Mol. Cell* *17*, 831–840.
- Matsumura, S., Persson, L.M., Wong, L., and Wilson, A.C. (2010). The latency-associated nuclear antigen interacts with MeCP2 and nucleosomes through separate domains. *J Virol* *84*, 2318–2330.
- McBurney, M.W., Staines, W.A., Boekelheide, K., Parry, D., Jardine, K., and Pickavance, L. (1994). Murine PGK-1 promoter drives widespread but not uniform expression in transgenic mice. *Dev. Dyn.* *200*, 278–293.
- McFarland, K.N., Huizenga, M.N., Darnell, S.B., Sangrey, G.R., Berezovska, O., Cha, J.-H.J.H.J., Outeiro, T.F., and Sadri-Vakili, G. (2014). MeCP2: a novel Huntingtin interactor. *Hum. Mol. Genet.* *23*, 1036–1044.
- McNally, J.G., Müller, W.G., Walker, D., Wolford, R., and Hager, G.L. (2000). The glucocorticoid receptor: rapid exchange with regulatory sites in living cells. *Science* *287*, 1262–1265.

Bibliography

Meehan, R.R., Lewis, J.D., and Bird, A.P. (1992). Characterization of MeCP2, a vertebrate DNA binding protein with affinity for methylated DNA. *Nucleic Acids Res.* *20*, 5085–5092.

Meins, M., Lehmann, J., Gerresheim, F., Herchenbach, J., Hagedorn, M., Hameister, K., and Epplen, J.T. (2005). Submicroscopic duplication in Xq28 causes increased expression of the MECP2 gene in a boy with severe mental retardation and features of Rett syndrome. *J. Med. Genet.* *42*, e12.

Mellén, M., Ayata, P., Dewell, S., Kriaucionis, S., and Heintz, N. (2012). MeCP2 binds to 5hmC enriched within active genes and accessible chromatin in the nervous system. *Cell* *151*, 1417–1430.

Mnatzakanian, G.N., Lohi, H., Munteanu, I., Alfred, S.E., Yamada, T., MacLeod, P.J.M., Jones, J.R., Scherer, S.W., Schanen, N.C., Friez, M.J., et al. (2004). A previously unidentified MECP2 open reading frame defines a new protein isoform relevant to Rett syndrome. *Nat. Genet.* *36*, 339–341.

Mor, A., Suliman, S., Ben-Yishay, R., Yunger, S., Brody, Y., and Shav-Tal, Y. (2010). Dynamics of single mRNP nucleocytoplasmic transport and export through the nuclear pore in living cells. *Nat. Cell Biol.* *12*, 543–552.

Muotri, A.R., Marchetto, M.C.N., Coufal, N.G., Oefner, R., Yeo, G., Nakashima, K., and Gage, F.H. (2010). L1 retrotransposition in neurons is modulated by MeCP2. *Nature* *468*, 443–446.

Murtaza, M., Dawson, S.-J., Tsui, D.W.Y., Gale, D., Forshew, T., Piskorz, A.M., Parkinson, C., Chin, S.-F., Kingsbury, Z., Wong, A.S.C., et al. (2013). Non-invasive analysis of acquired resistance to cancer therapy by sequencing of plasma DNA. *Nature* *497*, 108–112.

Na, E.S., Nelson, E.D., Kavalali, E.T., and Monteggia, L.M. (2013). The impact of MeCP2 loss- or gain-of-function on synaptic plasticity. *Neuropsychopharmacology* *38*, 212–219.

Nan, X., Meehan, R.R., and Bird, A. (1993). Dissection of the methyl-CpG binding domain from the chromosomal protein MeCP2. *Nucleic Acids Res.* *21*, 4886–4892.

Nan, X., Campoy, F.J., and Bird, A. (1997). MeCP2 is a transcriptional repressor with abundant binding sites in genomic chromatin. *Cell* *88*, 471–481.

Nan, X., Cross, S., and Bird, A. (1998a). Gene silencing by methyl-CpG-binding proteins. *Novartis Found Symp* *214*, 6–21,46–50.

Nan, X., Ng, H.H., Johnson, C.A., Laherty, C.D., Turner, B.M., Eisenman, R.N., and Bird, A. (1998b). Transcriptional repression by the methyl-CpG-binding protein MeCP2 involves a histone deacetylase complex. *Nature* *393*, 386–389.

- Nan, X., Hou, J., Maclean, A., Nasir, J., Lafuente, M.J., Shu, X., Kriaucionis, S., and Bird, A. (2007). Interaction between chromatin proteins MECP2 and ATRX is disrupted by mutations that cause inherited mental retardation. *Proc Natl Acad Sci U S A* *104*, 2709–2714.
- Navin, N., Kendall, J., Troge, J., Andrews, P., Rodgers, L., McIndoo, J., Cook, K., Stepanisky, A., Levy, D., Esposito, D., et al. (2011). Tumour evolution inferred by single-cell sequencing. *Nature* *472*, 90–94.
- Neul, J.L., and Zoghbi, H.Y. (2004). Rett syndrome: a prototypical neurodevelopmental disorder. *Neuroscientist* *10*, 118–128.
- Nikitina, T., Ghosh, R.P., Horowitz-Scherer, R.A., Hansen, J.C., Grigoryev, S.A., and Woodcock, C.L. (2007a). MeCP2-chromatin interactions include the formation of chromatosome-like structures and are altered in mutations causing Rett syndrome. *J Biol Chem* *282*, 28237–28245.
- Nikitina, T., Shi, X., Ghosh, R.P., Horowitz-Scherer, R.A., Hansen, J.C., and Woodcock, C.L. (2007b). Multiple modes of interaction between the methylated DNA binding protein MeCP2 and chromatin. *Mol Cell Biol* *27*, 864–877.
- Nomura, J., and Takumi, T. (2012). Animal models of psychiatric disorders that reflect human copy number variation. *Neural Plast.* *2012*.
- Noordermeer, D., and Duboule, D. (2013). Chromatin looping and organization at developmentally regulated gene loci. *Wiley Interdiscip. Rev. Dev. Biol.* *2*, 615–630.
- Peccoud, J., and Ycart, B. (1995). Markovian Modeling of Gene-Product Synthesis. *Theor. Popul. Biol.* *48*, 222–234.
- Rafalska-Metcalf, I.U., and Janicki, S.M. (2007). Show and tell: visualizing gene expression in living cells. *J. Cell Sci.* *120*, 2301–2307.
- Rafalska-Metcalf, I.U., Powers, S.L., Joo, L.M., LeRoy, G., and Janicki, S.M. (2010). Single cell analysis of transcriptional activation dynamics. *PLoS One* *5*, e10272.
- Raj, A., Peskin, C.S., Tranchina, D., Vargas, D.Y., and Tyagi, S. (2006). Stochastic mRNA synthesis in mammalian cells. *PLoS Biol.* *4*, e309.
- Raj, A., van den Bogaard, P., Rifkin, S.A., van Oudenaarden, A., and Tyagi, S. (2008). Imaging individual mRNA molecules using multiple singly labeled probes. *Nat. Methods* *5*, 877–879.

Bibliography

- Ramocki, M.B., Tavyev, Y.J., and Peters, S.U. (2010). The MECP2 Duplication Syndrome.
- Ratnakumar, K., and Bernstein, E. (2013). ATRX: The case of a peculiar chromatin remodeler. *Epigenetics* 8, 3–9.
- Reddy, K.L., Zullo, J.M., Bertolino, E., and Singh, H. (2008). Transcriptional repression mediated by repositioning of genes to the nuclear lamina. *Nature* 452, 243–247.
- Reid, G., Gallais, R., and Metivier, R. (2009). Marking time: the dynamic role of chromatin and covalent modification in transcription. *Int. J. Biochem. Cell Biol.* 41, 155–163.
- Rett, A. (1966). [On a unusual brain atrophy syndrome in hyperammonemia in childhood] [article in german]. *Wien Med Wochenschr* 116, 723–726.
- Revenkova, E., Focarelli, M.L., Susani, L., Paulis, M., Bassi, M.T., Mannini, L., Frattini, A., Delia, D., Krantz, I., Vezzoni, P., et al. (2009). Cornelia de Lange syndrome mutations in SMC1A or SMC3 affect binding to DNA. *Hum. Mol. Genet.* 18, 418–427.
- Robinett, C.C., Straight, A., Li, G., Wilhelm, C., Sudlow, G., Murray, A., and Belmont, A.S. (1996). In vivo localization of DNA sequences and visualization of large-scale chromatin organization using lac operator/repressor recognition. *J Cell Biol* 135, 1685–1700.
- Rottach, A., Kremmer, E., Nowak, D., Boisguerin, P., Volkmer, R., Cardoso, M.C., Leonhardt, H., and Rothbauer, U. (2008). Generation and characterization of a rat monoclonal antibody specific for PCNA. *Hybrid.* 27, 91–98.
- van Royen, M.E., Cunha, S.M., Brink, M.C., Mattern, K.A., Nigg, A.L., Dubbink, H.J., Verschure, P.J., Trapman, J., and Houtsmuller, A.B. (2007). Compartmentalization of androgen receptor protein-protein interactions in living cells. *J Cell Biol* 177, 63–72.
- Rybakova, K.N., Bruggeman, F.J., Tomaszewska, A., Mone, M.J., Carlberg, C., and Westerhoff, H. V (2015). Multiplex Eukaryotic Transcription (In)activation: Timing, Bursting and Cycling of a Ratchet Clock Mechanism. *PLoS Comput. Biol.* 11, e1004236.
- Sage, D., Neumann, F.R., Hediger, F., Gasser, S.M., and Unser, M. (2005). Automatic tracking of individual fluorescence particles: Application to the study of chromosome dynamics. *IEEE Trans. Image Process.* 14, 1372–1383.
- Saunders, A., Core, L.J., and Lis, J.T. (2006). Breaking barriers to transcription elongation. *Nat. Rev. Mol. Cell Biol.* 7, 557–567.

- Schmidt, U., Basyuk, E., Robert, M.C., Yoshida, M., Villemin, J.P., Auboeuf, D., Aitken, S., and Bertrand, E. (2011). Real-time imaging of cotranscriptional splicing reveals a kinetic model that reduces noise: Implications for alternative splicing regulation. *J. Cell Biol.* *193*, 819–829.
- Schmiedeberg, L., Weisshart, K., Diekmann, S., Meyer Zu Hoerste, G., and Hemmerich, P. (2004). High- and low-mobility populations of HP1 in heterochromatin of mammalian cells. *Mol Biol Cell* *15*, 2819–2833.
- Schotta, G., Lachner, M., Sarma, K., Ebert, A., Sengupta, R., Reuter, G., Reinberg, D., and Jenuwein, T. (2004). A silencing pathway to induce H3-K9 and H4-K20 trimethylation at constitutive heterochromatin. *Genes Dev.* *18*, 1251–1262.
- Schultz, D.C., Ayyanathan, K., Negorev, D., Maul, G.G., and Rauscher 3rd, F.J. (2002). SETDB1: a novel KAP-1-associated histone H3, lysine 9-specific methyltransferase that contributes to HP1-mediated silencing of euchromatic genes by KRAB zinc-finger proteins. *Genes Dev* *16*, 919–932.
- Schwabe, A., Rybakova, K.N., and Bruggeman, F.J. (2012). Transcription stochasticity of complex gene regulation models. *Biophys. J.* *103*, 1152–1161.
- Shahbazian, M.D., and Grunstein, M. (2007). Functions of site-specific histone acetylation and deacetylation. *Annu. Rev. Biochem.* *76*, 75–100.
- Shahbazian, M.D., Young, J.I., Yuva-Paylor, L.A., Spencer, C.M., Antalffy, B.A., Noebels, J.L., Armstrong, D.L., Paylor, R., and Zoghbi, H.Y. (2002a). Mice with truncated MeCP2 recapitulate many Rett syndrome features and display hyperacetylation of histone H3. *Neuron* *35*, 243–254.
- Shahbazian, M.D., Antalffy, B., Armstrong, D.L., and Zoghbi, H.Y. (2002b). Insight into Rett syndrome: MeCP2 levels display tissue- and cell-specific differences and correlate with neuronal maturation. *Hum Mol Genet* *11*, 115–124.
- Shav-Tal, Y., Darzacq, X., Shenoy, S.M., Fusco, D., Janicki, S.M., Spector, D.L., and Singer, R.H. (2004). Dynamics of single mRNPs in nuclei of living cells. *Science* *304*, 1797–1800.
- Shirai, S., Takahashi, K., Kohsaka, S., Tsukamoto, T., Isogai, H., Kudo, S., Sawa, H., Nagashima, K., and Tanaka, S. (2011). *Original Article* High expression of MeCP2 in JC virus-infected cells of progressive multifocal leukoencephalopathy brains. 38–41.
- Singleton, M.K., Gonzales, M.L., Leung, K.N., Yasui, D.H., Schroeder, D.I., Dunaway, K., and LaSalle, J.M. (2011). MeCP2 is required for global heterochromatic and nucleolar changes during activity-dependent neuronal maturation. *Neurobiol Dis* *43*, 190–200.

Bibliography

Skene, P.J., Illingworth, R.S., Webb, S., Kerr, A.R.W., James, K.D., Turner, D.J., Andrews, R., and Bird, A.P. (2010). Neuronal MeCP2 Is Expressed at Near Histone-Octamer Levels and Globally Alters the Chromatin State. *Mol. Cell* 37, 457–468.

Sokal, R., and Rohlf, F. (2011). *Biometry: The principles and practice of statistics in biological research* (New York: WH Freeman and co).

Song, C., Feodorova, Y., Guy, J., Peichl, L., Jost, K.L., Kimura, H., Cardoso, M.C., Bird, A., Leonhardt, H., Joffe, B., et al. (2014). DNA methylation reader MECP2: cell type- and differentiation stage-specific protein distribution. *Epigenetics Chromatin* 7, 17.

Stafford, G. a, and Morse, R.H. (2001). GCN5 dependence of chromatin remodeling and transcriptional activation by the GAL4 and VP16 activation domains in budding yeast. *Mol. Cell. Biol.* 21, 4568–4578.

van Steensel, B. (2011). Chromatin: constructing the big picture. *EMBO J.* 30, 1885–1895.

Stegle, O., Teichman, S.A., and Marioni, J.C. (2015). Computational and analytical challenges in single-cell transcriptomics. *Nat. Publ. Gr.* 16, 133–145.

Suter, D.M., Molina, N., Gatfield, D., Schneider, K., Schibler, U., and Naef, F. (2011). Mammalian genes are transcribed with widely different bursting kinetics. *Science* 332, 472–474.

Svejstrup, J.Q. (2004). The RNA polymerase II transcription cycle: Cycling through chromatin. *Biochim. Biophys. Acta - Gene Struct. Expr.* 1677, 64–73.

Tao, J., Hu, K., Chang, Q., Wu, H., Sherman, N.E., Martinowich, K., Klose, R.J., Schanen, C., Jaenisch, R., Wang, W., et al. (2009). Phosphorylation of MeCP2 at Serine 80 regulates its chromatin association and neurological function. *Proc. Natl. Acad. Sci. U. S. A.* 106, 4882–4887.

Thatcher, K.N., and Lasalle, J.M. (2006). Dynamic Changes in Histone H3 Lysine 9 Acetylation Localization ND ES SC ABBREVIATIONS. 24–31.

Tsukamoto, T., Hashiguchi, N., Janicki, S.M., Tumber, T., Belmont, a S., and Spector, D.L. (2000). Visualization of gene activity in living cells. *Nat. Cell Biol.* 2, 871–878.

Tudor, M., Akbarian, S., Chen, R.Z., and Jaenisch, R. (2002). Transcriptional profiling of a mouse model for Rett syndrome reveals subtle transcriptional changes in the brain. *Proc. Natl. Acad. Sci. U. S. A.* 99, 15536–15541.

Tumber, T., Sudlow, G., and Belmont, A.S. (1999). Large-scale chromatin unfolding and remodeling induced by VP16 acidic activation domain. *J Cell Biol* 145, 1341–1354.

- Vakoc, C.R., Letting, D.L., Gheldof, N., Sawado, T., Bender, M.A., Groudine, M., Weiss, M.J., Dekker, J., and Blobel, G.A. (2005). Proximity among distant regulatory elements at the beta-globin locus requires GATA-1 and FOG-1. *Mol Cell* *17*, 453–462.
- Valinluck, V., Tsai, H.-H., Rogstad, D.K., Burdzy, A., Bird, A., and Sowers, L.C. (2004). Oxidative damage to methyl-CpG sequences inhibits the binding of the methyl-CpG binding domain (MBD) of methyl-CpG binding protein 2 (MeCP2). *Nucleic Acids Res.* *32*, 4100–4108.
- Venkatesh, S., and Workman, J.L. (2015). Histone exchange, chromatin structure and the regulation of transcription. *Nat. Rev. Mol. Cell Biol.* *16*, 178–189.
- Verschure, P.J., van Der Kraan, I., Manders, E.M., and van Driel, R. (1999). Spatial relationship between transcription sites and chromosome territories. *J Cell Biol* *147*, 13–24.
- Verschure, P.J., Van Der Kraan, I., Enserink, J.M., Mone, M.J., Manders, E.M., and Van Driel, R. (2002). Large-scale chromatin organization and the localization of proteins involved in gene expression in human cells. *J Histochem Cytochem* *50*, 1303–1312.
- Verschure, P.J., van der Kraan, I., de Leeuw, W., van der Vlag, J., Carpenter, A.E., Belmont, A.S., and van Driel, R. (2005). In vivo HP1 targeting causes large-scale chromatin condensation and enhanced histone lysine methylation. *Mol. Cell. Biol.* *25*, 4552–4564.
- Vicent, G.P., Ballare, C., Nacht, A.S., Clausell, J., Subtil-Rodriguez, A., Quiles, I., Jordan, A., and Beato, M. (2008). Convergence on chromatin of non-genomic and genomic pathways of hormone signaling. *J Steroid Biochem Mol Biol* *109*, 344–349.
- Viñuelas, J., Kaneko, G., Coulon, A., Vallin, E., Morin, V., Mejia-pous, C., Kupiec, J., Beslon, G., and Gandrillon, O. (2013). Quantifying the contribution of chromatin dynamics to stochastic gene expression reveals long, locus-dependent periods between transcriptional bursts. *BMC Biol.* *11*, 15.
- Volpi, E. V., Chevret, E., Jones, T., Vatcheva, R., Williamson, J., Beck, S., Campbell, R.D., Goldsworthy, M., Powis, S.H., Ragoussis, J., et al. (2000). Large-scale chromatin organization of the major histocompatibility complex and other regions of human chromosome 6 and its response to interferon in interphase nuclei. *J Cell Sci* *113* (Pt 9), 1565–1576.
- Wang, W. (2003). The SWI/SNF family of ATP-dependent chromatin remodelers: similar mechanisms for diverse functions. *Curr Top Microbiol Immunol* *274*, 143–169.

Bibliography

Wansink, D.G., Schul, W., van der Kraan, I., van Steensel, B., van Driel, R., and de Jong, L. (1993). Fluorescent labeling of nascent RNA reveals transcription by RNA polymerase II in domains scattered throughout the nucleus. *J Cell Biol* 122, 283–293.

Weaving, L.S., Christodoulou, J., Williamson, S.L., Friend, K.L., McKenzie, O.L.D., Archer, H., Evans, J., Clarke, A., Pelka, G.J., Tam, P.P.L., et al. (2004). Mutations of CDKL5 cause a severe neurodevelopmental disorder with infantile spasms and mental retardation. *Am. J. Hum. Genet.* 75, 1079–1093.

Weil, T.T., Parton, R.M., and Davis, I. (2010). Making the message clear: visualizing mRNA localization. *Trends Cell Biol* 20, 380–390.

Weitzel, J.M., Buhrmester, H., and Strätling, W.H. (1997). Chicken MAR-binding protein ARBP is homologous to rat methyl-CpG-binding protein MeCP2. *Mol. Cell. Biol.* 17, 5656–5666.

Wendt, K.S., and Grosveld, F.G. (2014). Transcription in the context of the 3D nucleus. *Curr. Opin. Genet. Dev.* 25, 62–67.

de Wit, E., Greil, F., and van Steensel, B. (2007). High-resolution mapping reveals links of HP1 with active and inactive chromatin components. *PLoS Genet* 3, e38.

Xu, X., Miller, E.C., and Pozzo-Miller, L. (2014). Dendritic spine dysgenesis in Rett syndrome. *Front. Neuroanat.* 8, 1–8.

Yadon, A.N., Singh, B.N., Hampsey, M., and Tsukiyama, T. (2013). DNA looping facilitates targeting of a chromatin remodeling enzyme. *Mol. Cell* 50, 93–103.

Yang, T., Ramocki, M.B., Neul, J.L., Lu, W., Roberts, L., Knight, J., Ward, C.S., Zoghbi, H.Y., Kheradmand, F., and Corry, D.B. (2012). Overexpression of Methyl-CpG Binding Protein 2 Impairs TH1 Responses. *Sci. Transl. Med.* 4, 163ra158.

Yasui, D.H., Peddada, S., Bieda, M.C., Vallero, R.O., Hogart, A., Nagarajan, R.P., Thatcher, K.N., Farnham, P.J., and Lasalle, J.M. (2007). Integrated epigenomic analyses of neuronal MeCP2 reveal a role for long-range interaction with active genes. *Proc Natl Acad Sci U S A* 104, 19416–19421.

Yntema, H.G., Kleefstra, T., Oudakker, A.R., Romein, T., de Vries, B.B.A., Nillesen, W., Sistermans, E.A., Brunner, H.G., Hamel, B.C.J., and van Bokhoven, H. (2002). Low frequency of MECP2 mutations in mentally retarded males. *Eur. J. Hum. Genet.* 10, 487–490.

- Young, J.I., Hong, E.P., Castle, J.C., Crespo-Barreto, J., Bowman, A.B., Rose, M.F., Kang, D., Richman, R., Johnson, J.M., Berget, S., et al. (2005). Regulation of RNA splicing by the methylation-dependent transcriptional repressor methyl-CpG binding protein 2. *Proc. Natl. Acad. Sci. U. S. A.* *102*, 17551–17558.
- Yunger, S., Rosenfeld, L., Garini, Y., and Shav-Tal, Y. (2010). Single-allele analysis of transcription kinetics in living mammalian cells. *Nat. Methods* *7*, 631–633.
- Yusufzai, T.M., and Wolffe, A.P. (2000). Functional consequences of Rett syndrome mutations on human MeCP2. *Nucleic Acids Res* *28*, 4172–4179.
- Zhao, R., Bodnar, M.S., and Spector, D.L. (2009). Nuclear neighborhoods and gene expression. *Curr. Opin. Genet. Dev.* *19*, 172–179.
- Zhao, R., Nakamura, T., Fu, Y., Lazar, Z., and Spector, D.L. (2011). Gene bookmarking accelerates the kinetics of. *13*.
- Zhou, Q., Li, T., and Price, D.H. (2012). RNA polymerase II elongation control. *Annu. Rev. Biochem.* *81*, 119–143.
- Zhou, Z., Hong, E.J., Cohen, S., Zhao, W.N., Ho, H.Y.H., Schmidt, L., Chen, W.G., Lin, Y., Savner, E., Griffith, E.C., et al. (2006). Brain-Specific Phosphorylation of MeCP2 Regulates Activity-Dependent Bdnf Transcription, Dendritic Growth, and Spine Maturation. *Neuron* *52*, 255–269.