

REFERENCES

- Adamson, C.S. and Freed, E.O. (2008) Recent progress in antiretrovirals--lessons from resistance. *Drug Discov Today* 13, 424-32.
- Agosto, L.M., Yu, J.J., Dai, J., Kaletsky, R., Monie, D. and O'Doherty, U. (2007) HIV-1 integrates into resting CD4+ T cells even at low inoculum as demonstrated with an improved assay for HIV-1 integration. *Virology* 368, 60-72.
- Aldrovandi, G.M. and Zack, J.A. (1996) Replication and pathogenicity of human immunodeficiency virus type 1 accessory gene mutants in SCID-hu mice. *J Virol* 70, 1505-11.
- Amado, R.G. and Chen, I.S. (1999) Lentiviral vectors--the promise of gene therapy within reach? *Science* 285, 674-6.
- Balakrishnan, M. and Jonsson, C.B. (1997) Functional identification of nucleotides conferring substrate specificity to retroviral integrase reactions. *J Virol* 71, 1025-35.
- Baltimore, D. (1970) RNA-dependent DNA polymerase in virions of RNA tumour viruses. *Nature* 226, 1209-11.
- Barbosa, P., Charneau, P., Dumey, N. and Clavel, F. (1994) Kinetic analysis of HIV-1 early replicative steps in a coculture system. *AIDS Res Hum Retroviruses* 10, 53-9.
- Bartsevich, V.V., Miller, J.C., Case, C.C. and Pabo, C.O. (2003) Engineered zinc finger proteins for controlling stem cell fate. *Stem Cells* 21, 632-7.

- Beerli, R.R., Segal, D.J., Dreier, B. and Barbas, C.F., 3rd. (1998) Toward controlling gene expression at will: specific regulation of the erbB-2/HER-2 promoter by using polydactyl zinc finger proteins constructed from modular building blocks. *Proc Natl Acad Sci U S A* 95, 14628-33.
- Blancafort, P., Segal, D.J. and Barbas, C.F., 3rd. (2004) Designing transcription factor architectures for drug discovery. *Mol Pharmacol* 66, 1361-71.
- Bohjanen, P.R., Colvin, R.A., Puttaraju, M., Been, M.D. and Garcia-Blanco, M.A. (1996) A small circular TAR RNA decoy specifically inhibits Tat-activated HIV-1 transcription. *Nucleic Acids Res* 24, 3733-8.
- BouHamdan, M., Duan, L.X., Pomerantz, R.J. and Strayer, D.S. (1999) Inhibition of HIV-1 by an anti-integrase single-chain variable fragment (SFv): delivery by SV40 provides durable protection against HIV-1 and does not require selection. *Gene Ther* 6, 660-6.
- Brown, P.O. (1990) Integration of retroviral DNA. *Curr Top Microbiol Immunol* 157, 19-48.
- Brown, R.S. (2005) Zinc finger proteins: getting a grip on RNA. *Curr Opin Struct Biol* 15, 94-8.
- Bugreev, D.V., Baranova, S., Zakharova, O.D., Parissi, V., Desjobert, C., Sotofattori, E., Balbi, A., Litvak, S., Tarrago-Litvak, L. and Nevinsky, G.A. (2003) Dynamic, thermodynamic, and kinetic basis for recognition and transformation of DNA by human immunodeficiency virus type 1 integrase. *Biochemistry* 42, 9235-47.

- Bukrinsky, M.I., Haggerty, S., Dempsey, M.P., Sharova, N., Adzhubel, A., Spitz, L., Lewis, P., Goldfarb, D., Emerman, M. and Stevenson, M. (1993) A nuclear localization signal within HIV-1 matrix protein that governs infection of non-dividing cells. *Nature* 365, 666-9.
- Bushman, F.D. and Craigie, R. (1991) Activities of human immunodeficiency virus (HIV) integration protein in vitro: specific cleavage and integration of HIV DNA. *Proc Natl Acad Sci U S A* 88, 1339-43.
- Bushman, F.D., Engelman, A., Palmer, I., Wingfield, P. and Craigie, R. (1993) Domains of the integrase protein of human immunodeficiency virus type 1 responsible for polynucleotidyl transfer and zinc binding. *Proc Natl Acad Sci U S A* 90, 3428-32.
- Butler, S.L., Hansen, M.S. and Bushman, F.D. (2001) A quantitative assay for HIV DNA integration in vivo. *Nat Med* 7, 631-4.
- Butler, S.L., Johnson, E.P. and Bushman, F.D. (2002) Human immunodeficiency virus cDNA metabolism: notable stability of two-long terminal repeat circles. *J Virol* 76, 3739-47.
- Cai, M., Zheng, R., Caffrey, M., Craigie, R., Clore, G.M. and Gronenborn, A.M. (1997) Solution structure of the N-terminal zinc binding domain of HIV-1 integrase. *Nat Struct Biol* 4, 567-77.
- Cavert, W., Notermans, D.W., Staskus, K., Wietgrefe, S.W., Zupancic, M., Gebhard, K., Henry, K., Zhang, Z.Q., Mills, R., McDade, H., Schuwirth, C.M., Goudsmit, J., Danner, S.A. and Haase, A.T. (1997) Kinetics of response in lymphoid tissues to antiretroviral therapy of HIV-1 infection. *Science* 276, 960-4.

- Chan, D.C., Fass, D., Berger, J.M. and Kim, P.S. (1997) Core structure of gp41 from the HIV envelope glycoprotein. *Cell* 89, 263-73.
- Charpentier, C., Karmochkine, M., Laureillard, D., Tisserand, P., Belec, L., Weiss, L., Si-Mohamed, A. and Piketty, C. (2008) Drug resistance profiles for the HIV integrase gene in patients failing raltegravir salvage therapy. *HIV Med* 9, 765-70.
- Chen, L.F., Hoy, J. and Lewin, S.R. (2007) Ten years of highly active antiretroviral therapy for HIV infection. *Med J Aust* 186, 146-51.
- Chiu, T.K. and Davies, D.R. (2004) Structure and function of HIV-1 integrase. *Curr Top Med Chem* 4, 965-77.
- Choo, Y. and Klug, A. (1994) Toward a code for the interactions of zinc fingers with DNA: selection of randomized fingers displayed on phage. *Proc Natl Acad Sci U S A* 91, 11163-7.
- Choo, Y., Sanchez-Garcia, I. and Klug, A. (1994) In vivo repression by a site-specific DNA-binding protein designed against an oncogenic sequence. *Nature* 372, 642-5.
- Christy, B. and Nathans, D. (1989) DNA binding site of the growth factor-inducible protein Zif268. *Proc Natl Acad Sci U S A* 86, 8737-41.
- Chun, T.W., Carruth, L., Finzi, D., Shen, X., DiGiuseppe, J.A., Taylor, H., Hermankova, M., Chadwick, K., Margolick, J., Quinn, T.C., Kuo, Y.H., Brookmeyer, R., Zeiger, M.A., Barditch-Crovo, P. and Siliciano, R.F. (1997) Quantification of latent tissue reservoirs and total body viral load in HIV-1 infection. *Nature* 387, 183-8.

- Chun, T.W., Finzi, D., Margolick, J., Chadwick, K., Schwartz, D. and Siliciano, R.F. (1995) In vivo fate of HIV-1-infected T cells: quantitative analysis of the transition to stable latency. *Nat Med* 1, 1284-90.
- Cimarelli, A. and Darlix, J.L. (2002) Assembling the human immunodeficiency virus type 1. *Cell Mol Life Sci* 59, 1166-84.
- Clapham, P.R. and McKnight, A. (2002) Cell surface receptors, virus entry and tropism of primate lentiviruses. *J Gen Virol* 83, 1809-29.
- Coffin, J.M. (1995) HIV population dynamics in vivo: implications for genetic variation, pathogenesis, and therapy. *Science* 267, 483-9.
- Coffin JM, Hughes SH, Varmus HE, (1997) Retroviruses [online].
Cold Spring Harbor Laboratory Press. Available:
<http://www.ncbi.nlm.nih.gov/books/NBK19418/>.(2011, March 9).
- Cohli, H., Fan, B., Joshi, R.L., Ramezani, A., Li, X. and Joshi, S. (1994) Inhibition of HIV-1 multiplication in a human CD4+ lymphocytic cell line expressing antisense and sense RNA molecules containing HIV-1 packaging signal and Rev response element(s). *Antisense Res Dev* 4, 19-26.
- De Clercq, E. (2001) New developments in anti-HIV chemotherapy. *Curr Med Chem* 8, 1543-72.
- Deeks, S.G. (2011) HIV infection, inflammation, immunosenescence, and aging. *Annu Rev Med* 62, 141-55.
- Delelis, O., Malet, I., Na, L., Tchertanov, L., Calvez, V., Marcelin, A.G., Subra, F., Deprez, E. and Mouscadet, J.F. (2009) The G140S mutation in HIV integrases from raltegravir-resistant patients rescues catalytic defect due to the resistance Q148H mutation. *Nucleic Acids Res* 37, 1193-201.

- Demirov, D.G. and Freed, E.O. (2004) Retrovirus budding. *Virus Res* 106, 87-102.
- Deprez, E., Barbe, S., Kolaski, M., Leh, H., Zouhiri, F., Auclair, C., Brochon, J.C., Le Bret, M. and Mouscadet, J.F. (2004) Mechanism of HIV-1 integrase inhibition by styrylquinoline derivatives in vitro. *Mol Pharmacol* 65, 85-98.
- Dimauro, S., Mancuso, M. and Naini, A. (2004) Mitochondrial encephalomyopathies: therapeutic approach. *Ann N Y Acad Sci* 1011, 232-45.
- Donehower, L.A. and Varmus, H.E. (1984) A mutant murine leukemia virus with a single missense codon in pol is defective in a function affecting integration. *Proc Natl Acad Sci U S A* 81, 6461-5.
- Dreier, B., Beerli, R.R., Segal, D.J., Flippin, J.D. and Barbas, C.F., 3rd. (2001) Development of zinc finger domains for recognition of the 5'-ANN-3' family of DNA sequences and their use in the construction of artificial transcription factors. *J Biol Chem* 276, 29466-78.
- Dreier, B., Fuller, R.P., Segal, D.J., Lund, C.V., Blancafort, P., Huber, A., Koksch, B. and Barbas, C.F., 3rd. (2005) Development of zinc finger domains for recognition of the 5'-CNN-3' family DNA sequences and their use in the construction of artificial transcription factors. *J Biol Chem* 280, 35588-97.
- Dreier, B., Segal, D.J. and Barbas, C.F., 3rd. (2000) Insights into the molecular recognition of the 5'-GNN-3' family of DNA sequences by zinc finger domains. *J Mol Biol* 303, 489-502.
- Drellich, M., Wilhelm, R. and Mous, J. (1992) Identification of amino acid residues critical for endonuclease and integration activities of HIV-1 IN protein in vitro. *Virology* 188, 459-68.

- Dull, T., Zufferey, R., Kelly, M., Mandel, R.J., Nguyen, M., Trono, D. and Naldini, L. (1998) A third-generation lentivirus vector with a conditional packaging system. *J Virol* 72, 8463-71.
- Eckert, D.M. and Kim, P.S. (2001) Mechanisms of viral membrane fusion and its inhibition. *Annu Rev Biochem* 70, 777-810.
- Engelman, A., Bushman, F.D. and Craigie, R. (1993) Identification of discrete functional domains of HIV-1 integrase and their organization within an active multimeric complex. *EMBO J* 12, 3269-75.
- Esposito, D. and Craigie, R. (1999) HIV integrase structure and function. *Adv Virus Res* 52, 319-33.
- Evering, T.H. and Markowitz, M. (2008) Raltegravir: an integrase inhibitor for HIV-1. *Expert Opin Investig Drugs* 17, 413-22.
- Faure, A., Calmels, C., Desjobert, C., Castroviejo, M., Caumont-Sarcos, A., Tarrago-Litvak, L., Litvak, S. and Parissi, V. (2005) HIV-1 integrase crosslinked oligomers are active in vitro. *Nucleic Acids Res* 33, 977-86.
- Flexner, C. (2007) HIV drug development: the next 25 years. *Nat Rev Drug Discov* 6, 959-66.
- Frankel, A.D. and Young, J.A. (1998) HIV-1: fifteen proteins and an RNA. *Annu Rev Biochem* 67, 1-25.
- Freed, E.O. (2001) HIV-1 replication. *Somat Cell Mol Genet* 26, 13-33.
- Gallay, P., Hope, T., Chin, D. and Trono, D. (1997) HIV-1 infection of nondividing cells through the recognition of integrase by the importin/karyopherin pathway. *Proc Natl Acad Sci U S A* 94, 9825-30.

- Ganser-Pornillos, B.K., Yeager, M. and Sundquist, W.I. (2008) The structural biology of HIV assembly. *Curr Opin Struct Biol* 18, 203-17.
- Goncalves, J., Silva, F., Freitas-Vieira, A., Santa-Marta, M., Malho, R., Yang, X., Gabuzda, D. and Barbas, C., 3rd. (2002) Functional neutralization of HIV-1 Vif protein by intracellular immunization inhibits reverse transcription and viral replication. *J Biol Chem* 277, 32036-45.
- Gonzalez, B., Schwimmer, L.J., Fuller, R.P., Ye, Y., Asawapornmongkol, L. and Barbas, C.F., 3rd. (2010) Modular system for the construction of zinc-finger libraries and proteins. *Nat Protoc* 5, 791-810.
- Gotte, M., Li, X. and Wainberg, M.A. (1999) HIV-1 reverse transcription: a brief overview focused on structure-function relationships among molecules involved in initiation of the reaction. *Arch Biochem Biophys* 365, 199-210.
- Grant, P. and Zolopa, A. (2008) Integrase inhibitors: a clinical review of raltegravir and elvitegravir. *J HIV Ther* 13, 36-9.
- Greenberg, K.P., Lee, E.S., Schaffer, D.V. and Flannery, J.G. (2006) Gene delivery to the retina using lentiviral vectors. *Adv Exp Med Biol* 572, 255-66.
- Greisman, H.A. and Pabo, C.O. (1997) A general strategy for selecting high-affinity zinc finger proteins for diverse DNA target sites. *Science* 275, 657-61.
- Grote, A., Hiller, K., Scheer, M., Munch, R., Nortemann, B., Hempel, D.C. and Jahn, D. (2005) JCat: a novel tool to adapt codon usage of a target gene to its potential expression host. *Nucleic Acids Res* 33, W526-31.
- Gupta, R.K. and Pillay, D. (2007) HIV resistance and the developing world. *Int J Antimicrob Agents* 29, 510-7.

- Hahn, B.H., Shaw, G.M., Arya, S.K., Popovic, M., Gallo, R.C. and Wong-Staal, F. (1984) Molecular cloning and characterization of the HTLV-III virus associated with AIDS. *Nature* 312, 166-9.
- Han, Y., Lassen, K., Monie, D., Sedaghat, A.R., Shimoji, S., Liu, X., Pierson, T.C., Margolick, J.B., Siliciano, R.F. and Siliciano, J.D. (2004) Resting CD4+ T cells from human immunodeficiency virus type 1 (HIV-1)-infected individuals carry integrated HIV-1 genomes within actively transcribed host genes. *J Virol* 78, 6122-33.
- Haynes, B.F., Pantaleo, G. and Fauci, A.S. (1996) Toward an understanding of the correlates of protective immunity to HIV infection. *Science* 271, 324-8.
- Hazuda, D.J. (2010) Resistance to inhibitors of the human immunodeficiency virus type 1 integration. *Braz J Infect Dis* 14, 513-8.
- Hazuda, D.J., Felock, P., Witmer, M., Wolfe, A., Stillmock, K., Grobler, J.A., Espeseth, A., Gabryelski, L., Schleif, W., Blau, C. and Miller, M.D. (2000) Inhibitors of strand transfer that prevent integration and inhibit HIV-1 replication in cells. *Science* 287, 646-50.
- Hicks, C., Gulick, R.M., Roquebert, B., Blum, L., Collin, G., Damond, F., Peytavin, G., Leleu, J., Matheron, S., Chene, G., Brun-Vezinet, F. and Descamps, D. (2009) Raltegravir: the first HIV type 1 integrase inhibitor Selection of the Q148R integrase inhibitor resistance mutation in a failing raltegravir containing regimen. *Clin Infect Dis* 48, 931-9.
- Isalan, M., Klug, A. and Choo, Y. (2001) A rapid, generally applicable method to engineer zinc fingers illustrated by targeting the HIV-1 promoter. *Nat Biotechnol* 19, 656-60.

- Jamieson, A.C., Kim, S.H. and Wells, J.A. (1994) In vitro selection of zinc fingers with altered DNA-binding specificity. *Biochemistry* 33, 5689-95.
- Jelinek, W.R. and Schmid, C.W. (1982) Repetitive sequences in eukaryotic DNA and their expression. *Annu Rev Biochem* 51, 813-44.
- Jenkins, T.M., Engelman, A., Ghirlando, R. and Craigie, R. (1996) A soluble active mutant of HIV-1 integrase: involvement of both the core and carboxyl-terminal domains in multimerization. *J Biol Chem* 271, 7712-8.
- Jonsson, C.B., Donzella, G.A., Gaucan, E., Smith, C.M. and Roth, M.J. (1996) Functional domains of Moloney murine leukemia virus integrase defined by mutation and complementation analysis. *J Virol* 70, 4585-97.
- Jurriaans, S., de Ronde, A., Dekker, J., Goudsmit, J. and Cornelissen, M. (1992) Analysis of human immunodeficiency virus type 1 LTR-LTR junctions in peripheral blood mononuclear cells of infected individuals. *J Gen Virol* 73 (Pt 6), 1537-41.
- Kafri, T., Blomer, U., Peterson, D.A., Gage, F.H. and Verma, I.M. (1997) Sustained expression of genes delivered directly into liver and muscle by lentiviral vectors. *Nat Genet* 17, 314-7.
- Katz, R.A. and Skalka, A.M. (1994) The retroviral enzymes. *Annu Rev Biochem* 63, 133-73.
- Katzman, M. and Sudol, M. (1996) Influence of subterminal viral DNA nucleotides on differential susceptibility to cleavage by human immunodeficiency virus type 1 and visna virus integrases. *J Virol* 70, 9069-73.

- Kelly, J., Beddall, M.H., Yu, D., Iyer, S.R., Marsh, J.W. and Wu, Y. (2008) Human macrophages support persistent transcription from unintegrated HIV-1 DNA. *Virology* 372, 300-12.
- Killebrew, D.A., Troelstrup, D. and Shiramizu, B. (2004) Preferential HIV-1 integration sites in macrophages and HIV-associated malignancies. *Cell Mol Biol* (Noisy-le-grand) 50 Online Pub, OL581-9.
- Kim, S.Y., Byrn, R., Groopman, J. and Baltimore, D. (1989) Temporal aspects of DNA and RNA synthesis during human immunodeficiency virus infection: evidence for differential gene expression. *J Virol* 63, 3708-13.
- Koelsch, K.K., Liu, L., Haubrich, R., May, S., Havlir, D., Gunthard, H.F., Ignacio, C.C., Campos-Soto, P., Little, S.J., Shafer, R., Robbins, G.K., D'Aquila, R.T., Kawano, Y., Young, K., Dao, P., Spina, C.A., Richman, D.D. and Wong, J.K. (2008) Dynamics of total, linear nonintegrated, and integrated HIV-1 DNA in vivo and in vitro. *J Infect Dis* 197, 411-9.
- LaFemina, R.L., Callahan, P.L. and Cordingley, M.G. (1991) Substrate specificity of recombinant human immunodeficiency virus integrase protein. *J Virol* 65, 5624-30.
- Lanao, J.M., Briones, E. and Colino, C.I. (2007) Recent advances in delivery systems for anti-HIV1 therapy. *J Drug Target* 15, 21-36.
- Le Rouzic, E. and Benichou, S. (2005) The Vpr protein from HIV-1: distinct roles along the viral life cycle. *Retrovirology* 2, 11.
- Lee, M.S., Gippert, G.P., Soman, K.V., Case, D.A. and Wright, P.E. (1989) Three-dimensional solution structure of a single zinc finger DNA-binding domain. *Science* 245, 635-7.

- Lee, N.S., Dohjima, T., Bauer, G., Li, H., Li, M.J., Ehsani, A., Salvaterra, P. and Rossi, J. (2002) Expression of small interfering RNAs targeted against HIV-1 rev transcripts in human cells. *Nat Biotechnol* 20, 500-5.
- Lehrman, G., Hogue, I.B., Palmer, S., Jennings, C., Spina, C.A., Wiegand, A., Landay, A.L., Coombs, R.W., Richman, D.D., Mellors, J.W., Coffin, J.M., Bosch, R.J. and Margolis, D.M. (2005) Depletion of latent HIV-1 infection in vivo: a proof-of-concept study. *Lancet* 366, 549-55.
- Levy-Mintz, P., Duan, L., Zhang, H., Hu, B., Dornadula, G., Zhu, M., Kulkosky, J., Bizub-Bender, D., Skalka, A.M. and Pomerantz, R.J. (1996) Intracellular expression of single-chain variable fragments to inhibit early stages of the viral life cycle by targeting human immunodeficiency virus type 1 integrase. *J Virol* 70, 8821-32.
- Levy, J.A. (2007) HIV and the pathogenesis of AIDS. [Online] Available: http://books.google.co.th/books?id=ii-pri5nWAkC&pg=PA77&lpg=PA77&dq=non-covalent+circular+HIV+DNA+pathogenesis&source=bl&ots=ao1M013cz-&sig=tcxHPTp5Zq4wOAjM1INYxvJnW4s&hl=th&ei=GkEPTrawK4XKrAfjlqmIBA&sa=X&oi=book_result&ct=result&resnum=1&ved=0CB4Q6AEwAA#v=onepage&q&f=false (2011, May 9).
- Li, Z., Dullmann, J., Schiedlmeier, B., Schmidt, M., von Kalle, C., Meyer, J., Forster, M., Stocking, C., Wahlers, A., Frank, O., Ostertag, W., Kuhlcke, K., Eckert, H.G., Fehse, B. and Baum, C. (2002) Murine leukemia induced by retroviral gene marking. *Science* 296, 497.

- Liem, S.E., Ramezani, A., Li, X. and Joshi, S. (1993) The development and testing of retroviral vectors expressing trans-dominant mutants of HIV-1 proteins to confer anti-HIV-1 resistance. *Hum Gene Ther* 4, 625-34.
- Liszewski, M.K., Yu, J.J. and O'Doherty, U. (2009) Detecting HIV-1 integration by repetitive-sampling Alu-gag PCR. *Methods* 47, 254-60.
- Liu, Q., Segal, D.J., Ghiara, J.B. and Barbas, C.F., 3rd. (1997) Design of polydactyl zinc-finger proteins for unique addressing within complex genomes. *Proc Natl Acad Sci U S A* 94, 5525-30.
- Lu, X., Yu, Q., Binder, G.K., Chen, Z., Slepushkina, T., Rossi, J. and Dropulic, B. (2004) Antisense-mediated inhibition of human immunodeficiency virus (HIV) replication by use of an HIV type 1-based vector results in severely attenuated mutants incapable of developing resistance. *J Virol* 78, 7079-88.
- Mandell, J.G. and Barbas, C.F., 3rd. (2006) Zinc Finger Tools: custom DNA-binding domains for transcription factors and nucleases. *Nucleic Acids Res* 34, W516-23.
- Mann, J.M., Chin, J., Piot, P. and Quinn, T. (1988) The international epidemiology of AIDS. *Sci Am* 259, 82-9.
- Marasco, W.A., Haseltine, W.A. and Chen, S.Y. (1993) Design, intracellular expression, and activity of a human anti-human immunodeficiency virus type 1 gp120 single-chain antibody. *Proc Natl Acad Sci U S A* 90, 7889-93.
- Marchetti, A., Buttitta, F., Miyazaki, S., Gallahan, D., Smith, G.H. and Callahan, R. (1995) Int-6, a highly conserved, widely expressed gene, is mutated by mouse mammary tumor virus in mammary preneoplasia. *J Virol* 69, 1932-8.

- Mazumder, A., Engelman, A., Craigie, R., Fesen, M. and Pommier, Y. (1994) Intermolecular disintegration and intramolecular strand transfer activities of wild-type and mutant HIV-1 integrase. *Nucleic Acids Res* 22, 1037-43.
- McGraw-Hill. (2006) HIV replication. [online] Available <http://highered.mcgraw-hill.com/olc/dl/120088/micro41.swf>. (2011, January 29).
- Mighell, A.J., Markham, A.F. and Robinson, P.A. (1997) Alu sequences. *FEBS Lett* 417, 1-5.
- Miller, J., McLachlan, A.D. and Klug, A. (1985) Repetitive zinc-binding domains in the protein transcription factor IIIA from Xenopus oocytes. *EMBO J* 4, 1609-14.
- Muesing, M.A., Smith, D.H., Cabradilla, C.D., Benton, C.V., Lasky, L.A. and Capon, D.J. (1985) Nucleic acid structure and expression of the human AIDS/lymphadenopathy retrovirus. *Nature* 313, 450-8.
- Nair, R. and Rost, B. (2005) Mimicking cellular sorting improves prediction of subcellular localization. *J Mol Biol* 348, 85-100.
- Naldini, L., Blomer, U., Gage, F.H., Trono, D. and Verma, I.M. (1996a) Efficient transfer, integration, and sustained long-term expression of the transgene in adult rat brains injected with a lentiviral vector. *Proc Natl Acad Sci U S A* 93, 11382-8.
- Naldini, L., Blomer, U., Gallay, P., Ory, D., Mulligan, R., Gage, F.H., Verma, I.M. and Trono, D. (1996b) In vivo gene delivery and stable transduction of nondividing cells by a lentiviral vector. *Science* 272, 263-7.

- Neala, K. (1999) HIV as a lentiviral vector in gene therapy. [online] Avialable: <http://biology.kenyon.edu/slonec/gene-web/Lentiviral/index.htm> (2011, April 19).
- O'Doherty, U., Swiggard, W.J., Jeyakumar, D., McGain, D. and Malim, M.H. (2002) A sensitive, quantitative assay for human immunodeficiency virus type 1 integration. *J Virol* 76, 10942-50.
- Ofotokun, I. and Weitzmann, M.N. (2010) HIV-1 infection and antiretroviral therapies: risk factors for osteoporosis and bone fracture. *Curr Opin Endocrinol Diabetes Obes* 17, 523-9.
- Palella, F.J., Jr., Delaney, K.M., Moorman, A.C., Loveless, M.O., Fuhrer, J., Satten, G.A., Aschman, D.J. and Holmberg, S.D. (1998) Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. HIV Outpatient Study Investigators. *N Engl J Med* 338, 853-60.
- Pan, T. and Coleman, J.E. (1990) GAL4 transcription factor is not a "zinc finger" but forms a Zn(II)2Cys6 binuclear cluster. *Proc Natl Acad Sci U S A* 87, 2077-81.
- Papworth, M., Kolasinska, P. and Minczuk, M. (2006) Designer zinc-finger proteins and their applications. *Gene* 366, 27-38.
- Patel, S.D., Isalan, M., Gavory, G., Ladame, S., Choo, Y. and Balasubramanian, S. (2004) Inhibition of human telomerase activity by an engineered zinc finger protein that binds G-quadruplexes. *Biochemistry* 43, 13452-8.
- Pauza, C.D. (1990) Two bases are deleted from the termini of HIV-1 linear DNA during integrative recombination. *Virology* 179, 886-9.

- Pauza, C.D., Trivedi, P., McKechnie, T.S., Richman, D.D. and Graziano, F.M. (1994) 2-LTR circular viral DNA as a marker for human immunodeficiency virus type 1 infection in vivo. *Virology* 205, 470-8.
- Pavletich, N.P. and Pabo, C.O. (1991) Zinc finger-DNA recognition: crystal structure of a Zif268-DNA complex at 2.1 Å. *Science* 252, 809-17.
- Pollock, R., Giel, M., Linher, K. and Clackson, T. (2002) Regulation of endogenous gene expression with a small-molecule dimerizer. *Nat Biotechnol* 20, 729-33.
- Ramezani, A., Ma, X.Z., Nazari, R. and Joshi, S. (2002) Development and testing of retroviral vectors expressing multimeric hammerhead ribozymes targeted against all major clades of HIV-1. *Front Biosci* 7, a29-36.
- Ratner, L., Haseltine, W., Patarca, R., Livak, K.J., Starcich, B., Josephs, S.F., Doran, E.R., Rafalski, J.A., Whitehorn, E.A., Baumeister, K., et al., Muesing, M.A., Smith, D.H., Cabradilla, C.D., Benton, C.V., Lasky, L.A. and Capon, D.J. (1985) Complete nucleotide sequence of the AIDS virus, HTLV-III Nucleic acid structure and expression of the human AIDS/lymphadenopathy retrovirus. *Nature* 313, 277-84.
- Rebar, E.J., Huang, Y., Hickey, R., Nath, A.K., Meoli, D., Nath, S., Chen, B., Xu, L., Liang, Y., Jamieson, A.C., Zhang, L., Spratt, S.K., Case, C.C., Wolffe, A. and Giordano, F.J. (2002) Induction of angiogenesis in a mouse model using engineered transcription factors. *Nat Med* 8, 1427-32.
- Rebar, E.J. and Pabo, C.O. (1994) Zinc finger phage: affinity selection of fingers with new DNA-binding specificities. *Science* 263, 671-3.

- Reisman, D. and Sugden, B. (1986) trans activation of an Epstein-Barr viral transcriptional enhancer by the Epstein-Barr viral nuclear antigen 1. *Mol Cell Biol* 6, 3838-46.
- Reynolds, L., Ullman, C., Moore, M., Isalan, M., West, M.J., Clapham, P., Klug, A. and Choo, Y. (2003) Repression of the HIV-1 5'LTR promoter and inhibition of HIV-1 replication by using engineered zinc-finger transcription factors. *Proc Natl Acad Sci U S A* 100, 1615-20.
- Sabin, C.A., Worm, S.W., Weber, R., Reiss, P., El-Sadr, W., Dabis, F., De Wit, S., Law, M., D'Arminio Monforte, A., Friis-Moller, N., Kirk, O., Pradier, C., Weller, I., Phillips, A.N. and Lundgren, J.D. (2008) Use of nucleoside reverse transcriptase inhibitors and risk of myocardial infarction in HIV-infected patients enrolled in the D:A:D study: a multi-cohort collaboration. *Lancet* 371, 1417-26.
- Sakkhachornphop, S., Jiranusornkul, S., Kodchakorn, K., Nangola, S., Sirisanthana, T. and Tayapiwatana, C. (2009) Designed zinc finger protein interacting with the HIV-1 integrase recognition sequence at 2-LTR-circle junctions. *Protein Sci* 18, 2219-30.
- Schon, E.A. (2000) Mitochondrial genetics and disease. *Trends Biochem Sci* 25, 555-60.
- Schrager, L.K. and D'Souza, M.P. (1998) Cellular and anatomical reservoirs of HIV-1 in patients receiving potent antiretroviral combination therapy. *JAMA* 280, 67-71.

- Segal, D.J., Dreier, B., Beerli, R.R. and Barbas, C.F., 3rd. (1999) Toward controlling gene expression at will: selection and design of zinc finger domains recognizing each of the 5'-GNN-3' DNA target sequences. *Proc Natl Acad Sci U S A* 96, 2758-63.
- Segal, D.J., Goncalves, J., Eberhardy, S., Swan, C.H., Torbett, B.E., Li, X. and Barbas, C.F., 3rd. (2004) Attenuation of HIV-1 replication in primary human cells with a designed zinc finger transcription factor. *J Biol Chem* 279, 14509-19.
- Shaheen, F., Duan, L., Zhu, M., Bagasra, O. and Pomerantz, R.J. (1996) Targeting human immunodeficiency virus type 1 reverse transcriptase by intracellular expression of single-chain variable fragments to inhibit early stages of the viral life cycle. *J Virol* 70, 3392-400.
- Sherman, P.A. and Fyfe, J.A. (1990) Human immunodeficiency virus integration protein expressed in Escherichia coli possesses selective DNA cleaving activity. *Proc Natl Acad Sci U S A* 87, 5119-23.
- Simons, K. and Gerl, M.J. (2010) Revitalizing membrane rafts: new tools and insights. *Nat Rev Mol Cell Biol* 11, 688-99.
- Skalka, A.M. (2011) Determination of the solution structure of full-length retroviral integrase monomers and dimers, using data from small angle X-ray scattering, crystallography, and biochemical studies analyses. [online] Available: <http://www.fccc.edu/research/pid/skalka/research.html>. (2011, April 19).
- Staunstrup, N.H., Moldt, B., Mates, L., Villesen, P., Jakobsen, M., Ivics, Z., Izsvak, Z. and Mikkelsen, J.G. (2009) Hybrid lentivirus-transposon vectors with a random integration profile in human cells. *Mol Ther* 17, 1205-14.

- Stege, J.T., Guan, X., Ho, T., Beachy, R.N. and Barbas, C.F., 3rd. (2002) Controlling gene expression in plants using synthetic zinc finger transcription factors. *Plant J* 32, 1077-86.
- Stevenson, M., Stanwick, T.L., Dempsey, M.P. and Lamonica, C.A. (1990) HIV-1 replication is controlled at the level of T cell activation and proviral integration. *EMBO J* 9, 1551-60.
- Strayer, D.S., Akkina, R., Bunnell, B.A., Dropulic, B., Planelles, V., Pomerantz, R.J., Rossi, J.J. and Zaia, J.A. (2005) Current status of gene therapy strategies to treat HIV/AIDS. *Mol Ther* 11, 823-42.
- Strayer, D.S., Branco, F., Landre, J., BouHamdan, M., Shaheen, F. and Pomerantz, R.J. (2002) Combination genetic therapy to inhibit HIV-1. *Mol Ther* 5, 33-41.
- Su, K., Wang, D., Ye, J., Kim, Y.C. and Chow, S.A. (2009) Site-specific integration of retroviral DNA in human cells using fusion proteins consisting of human immunodeficiency virus type 1 integrase and the designed polydactyl zinc-finger protein E2C. *Methods* 47, 269-76.
- Tamhane, M. and Akkina, R. (2008) Stable gene transfer of CCR5 and CXCR4 siRNAs by sleeping beauty transposon system to confer HIV-1 resistance. *AIDS Res Ther* 5, 16.
- Tan, W., Zhu, K., Segal, D.J., Barbas, C.F., 3rd and Chow, S.A. (2004) Fusion proteins consisting of human immunodeficiency virus type 1 integrase and the designed polydactyl zinc finger protein E2C direct integration of viral DNA into specific sites. *J Virol* 78, 1301-13.
- Temin, H.M. and Mizutani, S. (1970) RNA-dependent DNA polymerase in virions of Rous sarcoma virus. *Nature* 226, 1211-3.

- Tesio, M., Gammaitoni, L., Gunetti, M., Leuci, V., Pignochino, Y., Jordaney, N., Capellero, S., Cammarata, C., Caione, L., Migliaretti, G., Fagioli, F., Tabilio, A., Aglietta, M. and Piacibello, W. (2008) Sustained long-term engraftment and transgene expression of peripheral blood CD34+ cells transduced with third-generation lentiviral vectors. *Stem Cells* 26, 1620-7.
- Tewari, D., Notkins, A.L. and Zhou, P. (2003) Inhibition of HIV-1 replication in primary human T cells transduced with an intracellular anti-HIV-1 p17 antibody gene. *J Gene Med* 5, 182-9.
- Thiesen, H.J., Bellefroid, E., Revelant, O. and Martial, J.A. (1991) Conserved KRAB protein domain identified upstream from the zinc finger region of Kox 8. *Nucleic Acids Res* 19, 3996.
- Turner, B.G. and Summers, M.F. (1999) Structural biology of HIV. *J Mol Biol* 285, 1-32.
- UNAIDS/WHO. (2010) AIDS epidemic update. [online] Available: http://www.unaids.org/en/media/unaidsonline/documents/unaidspublication/2010/20101123_globalreport_en.pdf (2011, September 1).
- van den Ent, F.M., Vink, C. and Plasterk, R.H. (1994) DNA substrate requirements for different activities of the human immunodeficiency virus type 1 integrase protein. *J Virol* 68, 7825-32.
- Van Maele, B. and Debyser, Z. (2005) HIV-1 integration: an interplay between HIV-1 integrase, cellular and viral proteins. *AIDS Rev* 7, 26-43.

- Vandegraaff, N., Kumar, R., Burrell, C.J. and Li, P. (2001) Kinetics of human immunodeficiency virus type 1 (HIV) DNA integration in acutely infected cells as determined using a novel assay for detection of integrated HIV DNA. *J Virol* 75, 11253-60.
- Vercruyse, T., Pardon, E., Vanstreels, E., Steyaert, J. and Daelemans, D. (2010) An intrabody based on a llama single-domain antibody targeting the N-terminal alpha-helical multimerization domain of HIV-1 rev prevents viral production. *J Biol Chem* 285, 21768-80.
- Vink, C. and Plasterk, R.H. (1993) The human immunodeficiency virus integrase protein. *Trends Genet* 9, 433-8.
- Vink, C., van Gent, D.C., Elgersma, Y. and Plasterk, R.H. (1991) Human immunodeficiency virus integrase protein requires a subterminal position of its viral DNA recognition sequence for efficient cleavage. *J Virol* 65, 4636-44.
- Walther, W. and Stein, U. (2000) Viral vectors for gene transfer: a review of their use in the treatment of human diseases. *Drugs* 60, 249-71.
- Weissenhorn, W., Dessen, A., Harrison, S.C., Skehel, J.J. and Wiley, D.C. (1997) Atomic structure of the ectodomain from HIV-1 gp41. *Nature* 387, 426-30.
- Whitcomb, J.M., Kumar, R. and Hughes, S.H. (1990) Sequence of the circle junction of human immunodeficiency virus type 1: implications for reverse transcription and integration. *J Virol* 64, 4903-6.
- Wilkins, M.R., Gasteiger, E., Bairoch, A., Sanchez, J.C., Williams, K.L., Appel, R.D. and Hochstrasser, D.F. (1999) Protein identification and analysis tools in the ExPASy server. *Methods Mol Biol* 112, 531-52.

- Wu, H., Yang, W.P. and Barbas, C.F., 3rd. (1995) Building zinc fingers by selection: toward a therapeutic application. *Proc Natl Acad Sci U S A* 92, 344-8.
- Wu, Y. and Marsh, J.W. (2001) Selective transcription and modulation of resting T cell activity by preintegrated HIV DNA. *Science* 293, 1503-6.
- Yaghmai, R. and Cutting, G.R. (2002) Optimized regulation of gene expression using artificial transcription factors. *Mol Ther* 5, 685-94.
- Yates, J.L., Warren, N. and Sugden, B. (1985) Stable replication of plasmids derived from Epstein-Barr virus in various mammalian cells. *Nature* 313, 812-5.
- Yoder, K.E. and Bushman, F.D. (2000) Repair of gaps in retroviral DNA integration intermediates. *J Virol* 74, 11191-200.
- Yoshinaga, T. and Fujiwara, T. (1995) Different roles of bases within the integration signal sequence of human immunodeficiency virus type 1 in vitro. *J Virol* 69, 3233-6.
- Zahm, J.A., Bera, S., Pandey, K.K., Vora, A., Stillmock, K., Hazuda, D. and Grandgenett, D.P. (2008) Mechanisms of human immunodeficiency virus type 1 concerted integration related to strand transfer inhibition and drug resistance. *Antimicrob Agents Chemother* 52, 3358-68.
- Zhou, Y., Zhang, H., Siliciano, J.D. and Siliciano, R.F. (2005) Kinetics of human immunodeficiency virus type 1 decay following entry into resting CD4+ T cells. *J Virol* 79, 2199-210.
- Zimmerman, K.A., Fischer, K.P., Joyce, M.A. and Tyrrell, D.L. (2008) Zinc finger proteins designed to specifically target duck hepatitis B virus covalently closed circular DNA inhibit viral transcription in tissue culture. *J Virol* 82, 8013-21.

- Zufferey, R., Dull, T., Mandel, R.J., Bukovsky, A., Quiroz, D., Naldini, L. and Trono, D. (1998) Self-inactivating lentivirus vector for safe and efficient in vivo gene delivery. *J Virol* 72, 9873-80.
- Zufferey, R., Nagy, D., Mandel, R.J., Naldini, L. and Trono, D. (1997) Multiply attenuated lentiviral vector achieves efficient gene delivery in vivo. *Nat Biotechnol* 15, 871-5.