

**EFFECTES DE LA INFECCIÓ PEL VIH I DELS FÀRMACS
ANTIRETROVIRALS ENVERS EL MITOCONDRI: LES
CÈL·LULES MONONUCLEARS DE SANG PERIFÈRICA
COM A MODEL D'ESTUDI**

SÒNIA LÓPEZ MORENO

Tesi Doctoral

8. BIBLIOGRAFIA

A

- Aboulafia DM. Acute pancreatitis. A fatal complication of AIDS therapy. *J Clin Gastroenterol.* 1997 Dec;25(4):640-5.
- Aldeen T et al Lipodystrophy associated with nevirapine-containing antiretroviral therapies. *AIDS* 1999, 13: 865 –867
- Alimonti JB et al. Mechanisms of CD4+ T lymphocyte cell death in human immunodeficiency virus infection and AIDS. *J Gen Virol* 2003 Jul; 84 (Pt 7): 1649-1661.
- Alonso JR et al. Carbon monoxide specifically inhibits cytochrome c oxidase of human mitochondrial respiratory chain. *Pharmacol Toxicol* 2003 Sep;93(3):142-6.
- Anderson S et al. Sequence and organization of the human mitochondrial genome. *Nature* 1981 Apr 9; 290(5806):457-465.
- Andreu AL, Gonzalo-Sanz R. Mitochondrial disorders: a classification for the 21st century. *Neurologia.* 2004 Jan-Feb;19(1):15-22.
- Andreu AL, DiMauro S. Current classification of mitochondrial disorders. *J Neurol.* 2003 Dec;250(12):1403-6.
- Andrews HE et al. Mitochondrial dysfunction plays a key role in progressive axonal loss in Multiple Sclerosis. *Med Hypotheses* 2005;64(4):669-77.
- Arnaudo E et al. Depletion of muscle mitochondrial DNA in AIDS patients with zidovudine-induced myopathy. *Lancet.* 1991 Mar 2;337(8740):508-10.
- Atilano SR et al. Accumulation of mitochondrial DNA damage in keratoconus corneas. *Invest Ophthalmol Vis Sci* 2005 Apr;46(4):1256-63.
- Ault A. FDA warns of potential protease-inhibitor link to hyperglycaemia. *Lancet.* 1997 Jun 21;349(9068):1819.

B

- Badley AD et al. Mitochondrion-mediated apoptosis. *Trends Pharmacol Sci* 2003; 24:298-305.
- Badley AD. In vitro and in vivo effects of HIV protease inhibitors on apoptosis. *Cell Death Differentiation* 2005, in press.

- Baltimore D. Viral RNA dependent DNA polymerase. *Nature* 1970 Jun 27; 226:1211-3.
- Barditch-Crovo P et al. Phase I/II trial of the pharmacokinetics, safety, and antiretroviral activity of tenofovir disoproxil fumarate in human immunodeficiency virus-infected adults. *Antimicrob Agents Chemother.* 2001 Oct; 45(10):2733-2739.
- Barile M et al. 3'azido-3'deoxythymidine uptake into isolated rat liver mitochondria and impairment of ADP/ATP translocator. *Biochem Pharmacol* 1997; 53:913-920.
- Barre-Sinoussi F et al. Isolation of a T-lymphotropic retrovirus from a patient at risk for acquired immune deficiency syndrome (AIDS). *Science* 1983 May 20;220(4599):868-71.
- Barrientos A. In vivo and in organello assessment of OXPHOS activities. *Methods* 2002;26(4):307-16.
- Barrientos A et al. Reduced steady-state levels of mitochondrial RNA and increased mitochondrial DNA amount in human brain with aging. *Brain Res Mol Brain Res.* 1997 Dec 15;52(2):284-9.
- Barrientos A et al. Qualitative and quantitative changes in skeletal muscle mtDNA and expression of mitochondrial-encoded genes in the human aging process. *Biochem Mol Med.* 1997 Dec;62(2):165-71.
- Barrientos A et al. Autosomal recessive Wolfram syndrome associated with an 8.5-kb mtDNA single deletion. *Am J Hum Genet.* 1996 May;58(5):963-70.
- Barrios A et al. Paradoxical CD4+ T-cell decline in HIV-infected patients with complete virus suppression taking tenofovir and didanosine. *AIDS* 2005; 19(6):569-575.
- Barrios A et al. Tenofovir-related nephrotoxicity in HIV-infected patients. *AIDS* 2004; 18(6):960-962.
- Bartz SR and Emerman M. Human immunodeficiency virus type 1 Tat induces apoptosis and increases sensitivity to apoptotic signals by up-regulating FLICE/caspase-8. *J Virol* 1999 Mar;73(3):1956-63.
- Behrens GM et al. Lipodystrophy syndrome in HIV infection: what is it, what causes it and how can it be managed?. *Drug Saf* 2000 Jul;23(1):57-76. Review.
- Ben-Shachar D et al. Mitochondria, synaptic plasticity, and schizophrenia. *Int Rev Neurobiol* 2004;59:273-96. Review.) (Ben-Shachar D. Mitochondrial dysfunction in

- schizophrenia: a possible linkage to dopamine. *J Neurochem* 2002 Dec;83(6):1241-51. Review.
- Berkovic SF et al. Mitochondrial dysfunction in multiple symmetrical lipomatosis. *Ann Neurol*. 1991 May;29(5):566-9.
- Biesecker G et al. Evaluation of mitochondrial DNA content and enzyme levels in tenofovir DF-treated rats, rhesus monkeys and woodchucks. *Antiviral Res*. 2003 May; 58(3):217-225.
- Birkus G et al. Assessment of mitochondrial toxicity in human cells treated with tenofovir: comparison with other nucleoside reverse transcriptase inhibitors. *Antimicrobial Agents and Chemotherapy* 2002; 46(3):716-723.
- Bodnar AG et al. Nuclear complementation restores mtDNA levels in cultured cells from a patient with mtDNA depletion. *Am J Hum Genet* 1993 Sep;53(3):663-9.
- Boyer PD. The ATP synthase: a splendid molecular machine. *Annu rev Biochem* 1997;66:717-49.
- Bradford M. A rapid and sensitive method for quantification of microgram quantities of protein utilizing the principle of protein-dye binding. *Anal Biochem* 1976; 72:248-254.
- Brinkman K et al. Mitochondrial toxicity induced by nucleoside-analogue reverse-transcriptase inhibitors is a key factor in the pathogenesis of antiretroviral-therapy-related lipodystrophy. *Lancet* 1999; 354: 1112-1115.
- Brinkman K et al. Adverse effects of reverse transcriptase inhibitors: mitochondrial toxicity as common pathway. *AIDS* 1998; 12: 1735-1744.
- Brivet FG et al. Fatal lactic acidosis and liver steatosis associated with didanosine and stavudine treatment: a respiratory chain dysfunction? *J Hepatol* 2000; 32:364-365.
- Brodthorn HR et al. Changing incidence of AIDS-defining illnesses in the era of antiretroviral combination therapy. *AIDS* 1997, 11:1731-8.
- Buemi M et al. Renal failure from mitochondrial cytopathies. *Nephron*. 1997; 76(3):249-53.
- Burgeois M et al. Deficiency in complex II of the respiratory chain, presenting as a leukodystrophy in two sisters with Leigh syndrome. *Brain Dev*. 1992 Nov;14(6):404-8.

C

Cadenas E et al. Production of superoxide radicals and hydrogen peroxide by NADH-ubiquinone reductase and ubiquinol-cytochrome c reductase from beef heart mitochondria. *Arch Biochem Biophys* 1977; 180: 248-257.

Cadenas E. Mitochondrial free radical production and cell signaling. *Mol Aspects Med* 2004 Feb-Apr;25(1-2):17-26.

Cameron DW et al. Randomised placebo-controlled trial of ritonavir in advanced HIV-1 disease. *Lancet* 1998, 351:543-9.

Capkova M et al. Activities of cytochrome c oxidase and citrate synthase in lymphocytes of obese and normal-weight subjects. *Int J Obes Relat Metab Disord* 2002 Aug; 26(8):1110-1117.

Cardellach F et al. Effect of smoking cessation on mitochondrial respiratory chain function. *J Toxicol Clin Toxicol* 2003;41(3):223-8.

Cardellach F et al. Mitochondrial respiratory chain activity in skeletal muscle from patients with Parkinson's disease. *Neurology*. 1993 Nov;43(11):2258-62.

Cardellach F et al. Hyperbaric oxygen for acute carbon monoxide poisoning. *N Engl J Med*. 2003 Feb 6;348(6):557-60.

Caron M et al. The HIV-1 nucleoside reverse transcriptase inhibitors stavudine and zidovudine alter adipocyte functions in vitro. *AIDS* 2004; 18:2127-2136.

Carr A and Cooper DA. Adverse effects of antiretroviral therapy. *Lancet*. 2000; 356:1423-30.

Carr A et al. A syndrome of peripheral lipodystrophy, hyperlipidaemia and insulin resistance in patients receiving HIV protease inhibitors. *AIDS* 1998 May 7;12(7):F51-8.

Carr A et al. Abnormal fat distribution and use of protease inhibitors. *Lancet*. 1998 Jun 6;351(9117):1736.

Carr A et al. An objective case definition of lipodystrophy in HIV-infected adults. *Lancet* 2003;361:726-735.

Carr A et al. Pathogenesis of HIV-1-protease inhibitor-associated peripheral lipodystrophy, hyperlipidaemia, and insulin resistance. *Lancet* 1998 Jun 20;351(9119):1881-3. Review.

- Carr A et al. Fatal portal hypertension, liver failure, and mitochondrial dysfunction after HIV-1 nucleoside analogue-induced hepatitis and lactic acidaemia. *Lancet* 2001; 357:1412-1414.
- Carr A et al. Diagnosis, prediction and natural course of HIV-1 protease-inhibitor-associated lipodystrophy, hyperlipidaemia and diabetes mellitus: a cohort study. *Lancet* 1999; 353:2093-2099.
- Carr A. HIV protease inhibitor-related lipodystrophy syndrome. *Clin Infect Dis*. 2000 Jun;30 Suppl 2:S135-42.
- Casademont J et al. Enzymatic diagnosis of oxidative phosphorylation defects on muscle biopsy: better on the homogenate or on a mitochondria-enriched suspension?. *Med Sci Monit* 2004 Sep;10(9):CS49-53.
- Casademont J et al. The effect of zidovudine on skeletal muscle mtDNA in HIV-1 infected patients with mild or no muscle dysfunction. *Brain* 1996; 119:1357-1364.
- Casademont J et al. Mitochondrial DNA and nucleoside toxicity. *N Engl J Med* 2002, 347: 216-218.
- Casademont J et al. Multiple deletions of mtDNA in two brothers with sideroblastic anemia and mitochondrial myopathy and in their asymptomatic mother. *Hum Mol Genet*. 1994 Nov;3(11):1945-9.
- Casademont J et al. Mitochondrial respiratory chain in brain homogenates: activities in different brain areas in patients with Alzheimer's disease. *Aging Clin Exp Res*. 2005 Feb;17(1):1-7.
- Casademont J et al. Cholinesterase inhibitor rivastigmine enhance the mitochondrial electron transport chain in lymphocytes of patients with Alzheimer's disease. *J Neurol Sci*. 2003 Jan 15;206(1):23-6.
- Castro L and Freeman BA. Reactive oxygen species in human health and disease. *Nutrition* 2001 Feb;17(2):161, 163-5.
- Centers for Disease Control (CDC). Kaposi's sarcoma and Pneumocystis pneumonia among homosexual men--New York City and California. *MMWR Morb Mortal Wkly Rep* 1981 Jul 3;30(25):305-8.
- ChapmanTM et al. Tenofovir Disoproxil Fumarate. *Drugs*. 2003; 63(15):1597-1608.

- Chaplain JM et al. Mitochondrial abnormalities in HIV-infected lipotrophic patients treated with antiretroviral agents. *J Acquir Immune Defic Syndr* 2004; 37:1477-1488.
- Chariot P et al. Zidovudine-induced mitochondrial disorder with massive liver steatosis, myopathy, lactic acidosis, and mitochondrial DNA depletion. *J Hepatol* 1999; 30:156-160.1-4.
- Chavan SJ et al. Reduction in T cell apoptosis in patients with HIV disease following antiretroviral therapy. *Clin Immunol* 1999 Oct; 93 (1): 24-33.
- Chen CH et al. Delayed cytotoxicity and selective loss of mitochondrial DNA in cells treated with the anti-human immunodeficiency virus compound 2',3'-dideoxycytidine. *J Biol Chem* 1989, 264:11934-7.
- Chen CH et al. Effect of anti-human immunodeficiency virus nucleoside analogs on mitochondrial DNA and its implication for delayed toxicity. *Mol Pharmacol* 1991, 39:625-628.
- Chen D et al. HIV-1 Tat targets microtubules to induce apoptosis, a process promoted by the pro-apoptotic Bcl-2 relative Bim. *EMBO J* 2002 Dec 16; 21 (24): 6801-6810.
- Chen X et al. Rearranged mitochondrial genomes are present in human oocytes. *Am J Hum Genet.* 1995 Aug;57(2):239-47.
- Cherrington JM et al. Kinetic interaction of the diphosphates of 9-(2-phosphonylmethoxyethyl)adenine and other anti-HIV active purine congeners with HIV reverse transcriptase and human DNA polymerases alpha, beta, and gamma. *Antivir Chem Chemother* 1995, 6:217-221.
- Cherry CL and Wesselingh SL. Nucleoside analogues and HIV: the combined cost to mitochondria. *J Antimicrob Chemother.* 2003; 51:1091-1093.
- Cherry CL et al. Exposure to dideoxynucleosides is reflected in lowered mitochondrial DNA in subcutaneous fat. *J Acquir Immune Defic Syndr* 2002; 30:271-277.
- Cherry CL et al. Nucleoside analogues and neuropathy in the era of HAART. *J Clin Virol* 2003;26:195-207.
- Chiappini F et al. Prospective evaluation of blood concentration of mitochondrial DNA as a marker of toxicity in 157 consecutively recruited untreated or HAART-treated HIV-positive patients. *Lab Invest* 2004; 84:908-914.

- Christensen ER et al. Mitochondrial DNA levels in fat and blood cells from patients with lipodystrophy or peripheral neuropathy and the effect of 90 days of high-dose coenzyme Q treatment: a randomized, double-blind, placebo-controlled pilot study. *CID* 2004, 39:1371-1379.
- Chun TW and Fauci AS. Latent reservoirs of HIV: obstacles to the eradication of virus. *Proc Natl Acad Sci U S A* 1999 Sep 28;96(20):10958-61.
- Church JA et al. Mitochondrial DNA depletion, near-fatal metabolic acidosis, and liver failure in an HIV-infected child treated with combination antiretroviral therapy. *J Pediatr* 2001; 138:748-751.
- Cihlar T et al. Incorporation of selected nucleoside phosphonates and anti-human immunodeficiency virus nucleotide analogs into DNA by human DNA polymerase alpha, beta, and gamma. *Antivir Chem Chemother* 1997, 8:187-195.
- Cihlar T et al. Tenofovir exhibits low cytotoxicity in various human cell types: comparison with other nucleoside reverse transcriptase inhibitors. *Antivir Res* 2002. In press.
- Clayton DA. Transcription and replication of mitochondrial DNA. *Human Reprod* 2000;15:Suppl 2:11-7.
- Cocchi F et al. Identification of RANTES, MIP-1 alpha, and MIP-1 beta as the major HIV-suppressive factors produced by CD8+ T cells. *Science* 1995 Dec 15;270(5243):1811-5.
- Cohen J. Searching for the epidemic's origins. *Science* 2000 Jun 23;288(5474):2164-5.
- Colucci WS. Apoptosis in the heart. *N Engl J Med* 1996 Oct 17; 335 (16): 1224-1226.
- Colvin R. Protease inhibitors and diabetes: a growing problem. *Common Factor*. 1997 Nov;(No 11):8.
- Connor RI et al. Change in coreceptor use coreceptor use correlates with disease progression in HIV-1--infected individuals. *J Exp Med* 1997 Feb 17;185(4):621-8.
- Cossarizza A et al. Increased mitochondrial DNA content in peripheral blood lymphocytes from HIV-infected patients with lipodystrophy. *Antiviral Therapy* 2003, 8:315-321.
- Cossarizza A et al. Mitochondrial functionality and mitochondrial DNA content in lymphocytes of vertically infected human immunodeficiency virus-positive children with highly active antiretroviral therapy-related lipodystrophy. *J Inf Diseases* 2002 Feb 1, 185(3):299-305

Cossarizza A and Moyle G. Antiretroviral nucleoside and nucleotide analogues and mitochondria. *AIDS* 2004; 18:137-151.

Cossarizza A et al. Mitochondrial alterations and dramatic tendency to undergo apoptosis in peripheral blood lymphocytes during acute HIV syndrome. *AIDS* 1997; 11:19-26.

Cossarizza A et al. Mitochondria in the pathogenesis of lipodystrophy induced by anti-HIV antiretroviral drugs: actors or bystanders? *Bioessays*. 2001 Nov; 23 (11):1070-1080.

Côté H et al. Antiretroviral regimen-dependent mitochondrial DNA depletion in clinical samples from the SWATCH trial. In Program and abstracts of the 9th Conference on Retroviruses and Opportunistic Infections, Seattle, February 2002. Abstract 707.

Côté HC et al. Changes in mitochondrial DNA as a marker of nucleoside toxicity in HIV-infected patients. *N Engl J Med* 2002; 346:811-20.

Creaven M et al. Control of the histone-acetyltransferase activity of Tip60 by the HIV-1 transactivator protein, Tat. *Biochemistry* 1999 Jul 6; 38 (27):8826-8830.

Cummins JM et al. Fate of microinjected spermatid mitochondria in the mouse oocyte and embryo. *Zygote* 1998;6:213-22.

D

Dalakas MC et al. Mitochondrial myopathy caused by long-term zidovudine therapy. *N Engl J Med* 1990 Apr 19;322(16):1098-105.

Dalglish AG et al. The CD4 (T4) antigen is an essential component of the receptor for the AIDS retrovirus. *Nature*.1984 Dec 20-1985 Jan 2;312(5996):763-7.

De Luca A et al. "Buffalo hump" in HIV-1 infection. *Lancet*. 1998 Jul 25;352(9124):320.

De Mendoza C et al. Changes in mitochondrial DNA copy number in blood cells from HIV-infected patients undergoing antiretroviral therapy. *AIDS Res Hum Retroviruses* 2004; 20:271-273.

Dean M et al. Genetic restriction of HIV-1 infection and progression to AIDS by a deletion allele of the *CCR5* structural gene. *Science* 1996 Sep 27;273(5283):1856-62.

Deeks SG et al. Safety, pharmacokinetics, and antiretroviral activity of intravenous 9-[2-(R)-(phosphonomethoxy)propyl]adenine, a novel anti-human immunodeficiency virus (HIV) therapy, in HIV-infected adults. *Antimicrobial Agents and Chemotherapy*, 1998 42(9):2380-2384.

Delta: a randomised double-blind controlled trial comparing combinations of zidovudine plus didanosine or zalcitabine with zidovudine alone in HIV-infected individuals. *Lancet* 1996, 348: 283-91.

Deng H et al. Identification of a major co-receptor for primary isolates of HIV-1. *Nature* 1996 Jun 20;381(6584):661-6.

Diehl S et al. Mitochondrial DNA and sperm quality in patients under antiretroviral therapy. *AIDS* 2003, 17:450-451.

DiMauro S. Introduction: mitochondrial encephalomyopathies. *Brain Pathol* 2000 Jul; 10(3):431-41.

Divi RL et al. Mitochondrial damage and DNA depletion in cord blood and umbilical cord from infants exposed in utero to Combivir. *AIDS* 2004; 18:1013-1021.

Domingo P et al. Subcutaneous adipocyte apoptosis in HIV-1 protease inhibitor-associated lipodystrophy. *AIDS* 1999 Nov 12;13(16):2261-2267.

Domingo P et al. Switching to nevirapine decreases insulin levels but does not improve subcutaneous adipocyte apoptosis in patients with highly active antiretroviral therapy-associated lipodystrophy. *J Infect Dis* 2001 Nov 1; 184 (9): 1197-1201.

Donald RJ. Mitochondrial DNA and Disease. *N Engl J Med* 1995;333(10):638-644.

Doranz BJ et al. A dual-tropic primary HIV-1 isolate that uses fusin and the beta-chemokine receptors CKR-5, CKR-3, and CKR-2b as fusion cofactors. *Cell* 1996 Jun 28;85(7):1149-58.

Dowell P et al. Suppression of preadipocyte differentiation and promotion of adipocyte death by HIV protease inhibitors. *J Biol Chem* 2000 Dec 29;275(52):41325-32.

Dube MP and Sattler FR. Metabolic complications of antiretroviral therapies. *AIDS Clin Care* 1998 Jun;10(6):41-4.

E

Elson JL et al. Analysis of European mtDNAs for recombination. *Am J Hum Genet.* 2001 Jan;68(1):145-153.

Ephrussi B et al. Action de l'acriflavine sur les levures. II. Etude génétique du mutant 'petite colonie'. *Ann Inst Pasteur* 1949;76:351-367.

Erol A. Retrograde regulation due to mitochondrial dysfunction may be an important mechanism for carcinogenesis. *Med Hypotheses* 2005 May 16.

Eyre-Walker A and Awadalla P. Does human mtDNA recombine? *J Mol Evol* 2001 Oct-Nov;53(4-5):430-5. Review.

F

Fain JN et al. Comparison of the release of adipokines by adipose tissue, adipose tissue matrix, and adipocytes from visceral and subcutaneous abdominal adipose tissues of obese humans. *Endocrinology* 2004 May;145(5):2273-82.

Falco V et al. Lactic acidosis related to nucleoside therapy in HIV-infected patients. *Expert Opin Pharmacother*. 2003 Aug;4(8):1321-9. Review.

Falco V et al. Severe nucleoside-associated lactic acidosis in human immunodeficiency virus-infected patients: report of 12 cases and review of the literature. *Clin Infect Dis*. 2002 Mar 15;34(6):838-46.

Fauci AS. Multifactorial nature of human immunodeficiency virus disease: implications for therapy. *Science* 1993 Nov 12;262(5136):1011-8. Review.

Feng Y et al. HIV-1 entry cofactor: functional cDNA cloning of a seven-transmembrane, G protein-coupled receptor. *Science* 1996 May 10;272(5263):872-7.

Fernández-Solà J et al. Evidence of apoptosis in chronic alcoholic skeletal myopathy. *Hum Pathol* 2003 Dec; 34 (12): 1247-1252.

Ferri KF et al. Mitochondrial control of cell death induced by HIV-1-encoded proteins. *Ann N Y Acad Sci* 2000;926:149-64. Review.

Fiamingo FG et al. Structural perturbation of the a3-CuB site in mitochondrial cytochrome c oxidase by alcohol solvents. *Biochemistry* 1990 May 15;29(19):4627-33.

Finkel T.H and Banda N.K. Indirect mechanisms of HIV pathogenesis: how does HIV kill T cells? *Curr Opin Immunol* 1994;6:605-15. 20.

Francis DP et al. Epidemic acquired immune deficiency syndrome: epidemiologic evidence for a transmissible agent. *J Natl Cancer Inst* 1983 Jul;71(1):1-4.

Freeman BA and Crapo JD. Biology of disease: free radicals and tissue injury. *Lab Invest* 1982 Nov;47(5):412-26. Review.

G

- Gallant JE and Deresinski S. Tenofovir Disoproxil Fumarate. Clin Infect Dis. 2003; 37:944-50.
- Galli M et al. Body habitus changes and metabolic alterations in protease inhibitor-naive HIV-1-infected patients treated with two nucleoside reverse transcriptase inhibitors. Defic Syndr. 2002 Jan 1;29(1):21-31.
- Galli M et al. Incidence of adipose tissue alterations in first-line antiretroviral therapy. The LipolCoNa Study. Arch Intern Med 2002; 162:2621-2628.
- Gallo RC and Montagnier L. Historical essay. Prospects for the future. Science 2002 Nov 29;298(5599):1730-31.
- Gallo RC. Historical essay. The early years of HIV/AIDS. Science 2002 Nov 29;298(5599):1728-30.
- Gamaley IA and Klyubin IV. Roles of reactive oxygen species: signaling and regulation of cellular functions. Int Rev Cytol 1999;188:203-55. Review.
- Gao F et al. Origin of HIV-1 in the chimpanzee Pan troglodytes troglodytes. Nature 1999 Feb 4;397(6718):436-41.
- Garcia F et al. Cerebrospinal fluid HIV-1 RNA levels in asymptomatic patients with early stage chronic HIV-1 infection: support for the hypothesis of local virus replication. AIDS 1999 Aug 20;13(12):1491-6.
- Gérard Y et al. Symptomatic hyperlactataemia: an emerging complication of antiretroviral therapy. AIDS 2000; 14:2723-2730.
- Gerschenson M. Mitochondria and lipodystrophy: where are we now?. Antivir Ther. 2003 Aug; 8(4):261-3.
- Gherardi RK. Skeletal muscle involvement in HIV-infected patients. Neuropathol Appl Neurobiol 1994;20:232-237.
- Gilead Sciences Inc. Viread (tenofovir disoproxil fumarate) tablets: US package insert [online]. Available from URL: http://www.gilead.com/pdf/viread_pi.pdf.
- Gómez-Zaera M et al. Mitochondrial involvement in antiretroviral therapy-related lipodystrophy. AIDS 2001; 15:1643-1651.

Gottlieb MS et al. Pneumocystis carinii pneumonia and mucosal candidiasis in previously healthy homosexual men: evidence of a new acquired cellular immunodeficiency. N Engl J Med 1981 Dec 10;305(24):1425-31.

Gougeon M.L and Montagnier L. Apoptosis in AIDS. Science 1993;260:1269-70. 19.

Gourlain K et al. Quantitative analysis of human mitochondrial DNA using a real-time PCR assay. HIV Medicine 2003, 4:287-292.

Grabel Birkus et al. Assessment of Mitochondrial Toxicity in Human Cells Treated with Tenofovir: Comparison with other Nucleoside Reverse Transcriptase Inhibitors. Antimicrob. Agents Chemother. 2002 Mar; 46(3): 716-723.

Grau JM et al. Human immunodeficiency virus type 1 infection and myopathy: clinical relevance of zidovudine treatment. Ann Neurol 1993;34:206-211.

Grau JM, Bosch X, Salgado AC, Urbano-Marquez A. Human immunodeficiency virus (HIV) and aplastic anemia. Ann Intern Med. 1989 Apr 1;110(7):576-7.

Green A et al. Tumor necrosis factor increases the rate of lipolysis in primary cultures of adipocytes without altering levels of hormone-sensitive lipase. Endocrinology 1994;134:2581–2588.

Green DR and Reed JC. Mitochondria and apoptosis. Science 1998 Aug 28;281(5381):1309-12. Review.

Grunfeld C and Feingold KR. Metabolic disturbances and wasting in the acquired immunodeficiency syndrome. N Engl J Med 1992, 327:329–337.

H

Hajnoczky G et al. Alcohol and mitochondria in cardiac apoptosis: mechanisms and visualization. Alcohol Clin Exp Res 2005 May;29(5):693-701.

Hall ET et al. 3'-azido-3'-deoxythymidine potently inhibits protein glycosylation. J Biol Chem 1994; 269:14255-14358.

Hamilton JD et al. A controlled trial of early versus late treatment with zidovudine in symptomatic human immunodeficiency virus infection. N Engl J Med 1992 Feb 13;326(7):437-43.

- Hammer SM et al. A trial comparing nucleoside monotherapy with combination therapy in HIV-infected adults with CD4 cell counts from 200 to 500 per cubic millimeter. *N Engl J Med* 1996, 335:1081-90.
- Hammond E et al. Reduction of mitochondrial DNA and respiratory chain activity occurs in adipocytes within 6-12 months of commencing nucleoside reverse transcriptase inhibitor therapy. *AIDS* 2004; 18:815-817.
- Hammond EL et al. Assessment of precision and concordance of quantitative mitochondrial DNA assays: a collaborative international quality assurance study. *J Clin Virol* 2003 May;27(1):97-110.
- Hedley D and Chow S. Flow cytometric measurement of lipid peroxidation in vital cells using parinaric acid. *Cytometry* 1992; 13 (7): 686-692.
- Henry K et al. Lymphocyte mitochondrial biomarkers in asymptomatic HIV-1-infected individuals treated with nucleoside reverse transcriptase inhibitors. *AIDS* 2002, 18(18):2485-2487.
- Herrmann PC et al. Mitochondrial proteome: altered cytochrome c oxidase subunit levels in prostate cancer. *Proteomics* 2003 Sep;3(9):1801-10.
- Herzberg NH et al. Major growth reduction and minor decrease in mitochondrial enzyme activity in cultured human muscle cells after exposure to zidovudine. *Muscle Nerve* 1992 Jun;15(6):706-10.
- Hirano M et al. Defects of intergenomic communication: where do we stand? *Brain Pathol* 2000 Jul;10(3):451-61. Review.
- Ho TT et al. Abnormal fat distribution and use of protease inhibitors. *Lancet*. 1998 Jun 6;351(9117):1736-7.
- Hoek JB et al. Alcohol and mitochondria: a dysfunctional relationship. *Gastroenterology* 2002 Jun;122(7):2049-63. Review.
- Holt IJ et al. Coupled leading-and lagging-strand synthesis of mammalian mitochondrial DNA. *Cell* 2000; 100:515-524.
- Honkoop P et al. Effect of lamivudine on morphology and function of mitochondria in patients with chronic hepatitis B. *Hepatology* 1997; 26:211-215.
- Hoobs GA et al. Cellular targets of 3'azido-3'deoxythymidine: an early (non-delayed) effect on oxidative phosphorylation. *Biochem Pharmacol* 1995; 50:381-390.

Hooper E. Search for the origin of HIV and AIDS. *Science* 2000 Aug 18;289(5482):1140-1.

Hoy JF et al. Changes in mitochondrial DNA in peripheral blood mononuclear cells from HIV-infected patients with lipoatrophy randomized to receive abacavir. *JID* 2004, 190:688-692.

Huff A. Protease inhibitor side effects take people by surprise. *GMHC Treat Issues*. 1997-98 Winter;12(1):25-7.

I-J

Jacotot E et al. The HIV-1 viral protein R induces apoptosis via a direct effect on the mitochondrial permeability transition pore. *J Exp Med* 2000 Jan 3; 191 (1): 33-46.

John M et al. Antiretroviral therapy and the lipodystrophy syndrome. *Antivir Ther* 2001 Mar;6(1):9-20. Review.

John M et al. Randomized, controlled, 48-week study of switching stavudine and/or protease inhibitors to combivir/abacavir to prevent or reverse lipoatrophy in HIV-infected patients. *Journal of Acquired Immune Deficiency Syndromes* 2003, 33:29-33.

K

Kakuda T. Pharmacology of nucleoside and nucleotide reverse transcriptase inhibitor-induced mitochondrial toxicity. *Clin Ther* 2000, 22:685-708.

Kakuda TN et al. Nucleoside reverse transcriptase inhibitor-induced mitochondrial toxicity as an etiology fo lipodystrophy. *AIDS* 1999; 13(16):2311-2312.

Kearney B et al. A multiple-dose, randomized, crossover drug interaction study between Tenofovir DF and Lamivudine or Didanosine. Presented at: The 1st IAS Conference on HIV Pathogenesis and Treatment; The International AIDS Society (IAS); Buenos Aires, Argentina. 8-11 July 2001. Abstract 337.

Kearney BP et al. Tenofovir DF (TDF) and didanosine EC (ddl EC): investigation of pharmacokinetic (PK) drug-drug and drug-food interactions. Presented at: The 6th International Congress on Drug Therapy in HIV Infection; Glasgow, UK. 17-21 November 2002. Abstract 186.

Kelley DE et al. Dysfunction of mitochondria in human skeletal muscle in type 2 diabetes. *Diabetes* 2002 Oct; 51(10):2944-2950.

Kinter A et al. Chemokines, cytokines and HIV: a complex network of interactions that influence HIV pathogenesis. *Immunol Rev* 2000 Oct;177:88-98. Review.

Klopstock T et al. Multiple symmetric lipomatosis: Abnormalities in complex IV and multiple deletions in mitochondrial DNA. *Neurology* 1994; 44:862-866.

L

Lang BF et al. Mitochondrial genome evolution and the origin of eukaryotes. *Annu Rev Genet*;1999:33:351-397.

Large V and Arner P. Regulation of lipolysis in humans. Pathophysiological modulation in obesity, diabetes, and hyperlipidaemia. *Diabetes Metab* 1998 Nov;24(5):409-18. Review.

Larsson NG and Clayton DA. Molecular genetic aspects of human mitochondrial disorders. *Annu Rev Genet* 1995; 29:151–178.

Ledru E et al. Alteration of tumor necrosis factor-alpha T-cell homeostasis following potent antiretroviral therapy: contribution of the development of human immunodeficiency virus-associated lipodystrophy syndrome. *Blood* 2000; 95:3191-3198.

Leitz G et al. The development of lipodystrophy on a protease inhibitor-sparing highly active antiretroviral therapy regimen. *AIDS*. 2000 Mar 10;14(4):468-9.

Levy JA et al. Isolation of lymphocytopathic retroviruses from San Francisco patients with AIDS. *Science* 1984 Aug 24;225(4664):840-2.

Lewis W and Dalakas MC. Mitochondrial toxicity of antiviral drugs. *Nat Med*. 1995; 1:417-422.

Lewis W et al. Mitochondrial toxicity of NRTI antiviral drugs: an integrated cellular perspective. *Nature Rev Drug Discov*. 2003 Oct; 2(10):812-822. Review.

Li CJ et al. Induction of apoptosis in uninfected lymphocytes by HIV-1 Tat protein. *Science*. 1995 Apr 21;268(5209):429-31.

Libera CD and Vescovo G: Muscle wastage in chronic heart failure, between apoptosis, catabolism and altered metabolism: A chimeric view of inflammation? *Curr Opin Clin Nutr Care* 2004; 7:435-441.

- Lim SE and Copeland WC. Differential incorporation and removal of antiviral deoxynucleotides by human DNA polymerase- γ . *Journal of Biological Chemistry* 2001; 276(23):616-623.
- Liu R et al. Homozygous defect in HIV-1 coreceptor accounts for resistance of some multiply-exposed individuals to HIV-1 infection. *Cell* 1996 Aug 9;86(3):367-77.
- Li-Weber M et al. T cell activation-induced and HIV tat-enhanced CD95(APO-1/Fas) ligand transcription involves NF-kappaB. *Eur J Immunol.* 2000 Feb;30(2):661-70.
- Lo JC et al. "Buffalo hump" in men with HIV-1 infection. *Lancet.* 1998 Mar 21;351(9106):867-70.
- López S et al. Mitochondrial effects of antiretroviral therapies in asymptomatic patients. *Antivir Ther.* 2004; 9:47-55.
- Lowell BB et al. Mitochondrial dysfunction and type 2 diabetes. *Science* 2005 Jan 21;307(5708):384-7.
- Luciani F et al. CD95/phosphorylated ezrin association underlies HIV-1 GP120/IL-2-induced susceptibility to CD95(APO-1/Fas)-mediated apoptosis of human resting CD4(+)T lymphocytes. *Cell Death Differ* 2004 May;11(5):574-82.
- Luft R. A case of severe hypermetabolism of nonthyroid origin with a defect in the maintenance of mitochondrial respiratory control: a correlated clinical, biochemical and morphological study. *J Clin Invest* 1962;41:1776-804.
- Lyseng-Williamson KA et al. Tenofovir disoproxil fumarate: A review of its use in the management of HIV infection. *Drugs* 2005; 65(3):413-32.

M

- Macho A et al. Susceptibility of HIV-1-TAT transfected cells to undergo apoptosis. Biochemical mechanisms. *Oncogene* 1999; 18:7543-7551.
- Madge S et al. Lipodystrophy in patients naive to HIV protease inhibitors. *AIDS* 1999 Apr 16;13(6):735-7.
- Maitland D et al. Early virologic failure in HIV-1 infected subjects on didanosine/tenofovir/efavirenz: 12-week results from a randomized trial. *AIDS* 2005; 19(11):1183-1188.

- Mallal SA et al. Contribution of nucleoside reverse transcriptase inhibitors to subcutaneous fat wasting in patients with HIV infection. *AIDS* 2000, 14:1309-1316.
- Mallery SR et al. Implications for oxidative and nitrative stress in the pathogenesis of AIDS-related Kaposi's sarcoma. *Carcinogenesis* 2004 Apr;25(4):597-603.
- Mallolas J et al. Comparison of two HAART sequences in naive HIV-infected patients: a randomized, multicenter, open label, long term follow up clinical trial. In Program and abstracts of the XIV International AIDS Conference 2002, July 7-12, 2002, Barcelona, Spain. Abstract TuOrB1186.
- Maneiro E et al. Effect of nitric oxide on mitochondrial respiratory activity of human articular chondrocytes. *Ann Rheum Dis* 2005 Mar;64(3):388-95.
- Marchington DR et al. Evidence from human oocytes for a genetic bottleneck in an mtDNA disease. *Am J Hum Genet.* 1998 Sep;63(3):769-75.
- Mariotti C et al. Early-onset encephalomyopathy associated with tissue-specific mitochondrial DNA depletion: a morphological, biochemical and molecular-genetic study. *J Neurol* 1995, 242:547-556.
- Martin A et al. Mitochondrial Toxicity Study Group. Reversibility of lipoatrophy in HIV-infected patients 2 years after switching from a thymidine analogue to abacavir: the MITOX Extension Study. *AIDS* 2004; 18:1029-1036.
- Martin AM et al. Accumulation of mitochondrial DNA mutations in human immunodeficiency virus-infected patients treated with nucleoside-analogue reverse-transcriptase inhibitors. *Am J Hum Genet* 2003, 72:549-560.
- Martin JL et al. Effects of antiviral nucleoside analogues on human DNA polymerases and mitochondrial DNA synthesis. *Antimicrob Agents Chemother* 1994; 38: 2743-2749.
- Martinez E and Gatell J. Metabolic abnormalities and use of HIV-1 protease inhibitors. *Lancet* 1998 Sep 5;352(9130):821-2.
- Martínez E et al. Pancreatic toxic effects associated with co-administration of didanosine and tenofovir in HIV-infected adults. *Lancet* 2004; 364(9428):65-67.
- Masanés F et al. Clinical, histological and molecular reversibility of zidovudine myopathy. *J Neurol Sci* 1998;159:226-228.

- Masur H et al. An outbreak of community-acquired *Pneumocystis carinii* pneumonia: initial manifestation of cellular immune dysfunction. *N Engl J Med* 1981 Dec 10;305(24):1431-8.
- Matarrese P et al. Antiapoptotic Activity by HIV Protease Inhibitors either Alone or Boosted. *JAIDS* 2002;31(5) 15:545-546.
- Matarrese P et al. Mitochondrial membrane hyperpolarization hijacks activated T lymphocytes toward the apoptotic-prone phenotype: homeostatic mechanisms of HIV protease inhibitors. *J Immunol* 2003 Jun 15;170(12):6006-15.
- McComsey G and Loneragan JT. Mitochondrial Dysfunction: Patient Monitoring and Toxicity Management. *J Acquir Immune Defic Syndr* 2004; 37:S30-S35.
- McComsey G et al. Analysis of the mitochondrial DNA genome in the peripheral blood leukocytes of HIV-infected patients with or without lipodystrophy. *AIDS* 2002; 16:513-518.
- McComsey GA et al. Improvements in lipodystrophy, mitochondrial DNA levels and fat apoptosis after replacing stavudine with abacavir or zidovudine. *AIDS* 2005; 19:15-23.
- McKenzie R et al. Hepatic failure and lactic acidosis due to fialuridine (FIAU), an investigational nucleoside analogue for chronic hepatitis B. *N Engl J Med* 1995; 333:1099-1105.
- Meyaard L et al. Programmed death of T cells in HIV-1 infection. *Science* 1992;257:217-9. 18.
- Michael NL et al. The role of viral phenotype and CCR-5 gene defects in HIV-1 transmission and disease progression. *Nat Med* 1997 Mar;3(3):338-40.
- Miró Ò et al. Ex vivo analysis of mitochondrial function in patients attended in an emergency department due to carbon monoxide poisoning. *Med Clin (Barc)* 2004 Mar 27;122(11):401-6. Spanish.
- Miró Ò et al. Mitochondrial cytochrome c oxidase inhibition during acute carbon monoxide poisoning. *Pharmacol Toxicol* 1998 Apr;82(4):199-202.
- Miró Ò et al. Oxidative damage on lymphocyte membranes is increased in patients suffering from acute carbon monoxide poisoning. *Toxicol Lett* 1999 Nov 22;110(3):219-23.
- Miró Ò et al. Smoking disturbs mitochondrial respiratory chain function and enhances lipid peroxidation in human circulating lymphocytes. *Carcinogenesis* 1999; 20:1331-1336.

- Miro O et al. Skeletal muscle studies in patients with HIV-related wasting syndrome. *J Neurol Sci.* 1997 Sep 10;150(2):153-9.
- Miró Ò et al. Effects of general anesthetic procedures on mitochondrial function of human skeletal muscle. *Eur J Clin Pharmacol* 1999; 55:35-41.
- Miró Ò et al. Cytochrome c oxidase assay in minute amount of human skeletal muscle using single wavelength spectrophotometers. *J Neurosci Methods.* 1998; 80(1):107-111.
- Miró Ò et al. Respiratory chain dysfunction associated with multiple mitochondrial DNA deletions in antiretroviral therapy-related lipodystrophy. *AIDS* 2000; 14:1855-1857.
- Miró Ò et al. Increased apoptosis in skeletal muscle, highly active antiretroviral therapy and lipodystrophy. Presented at: The 5th International Workshop on Adverse Drug Reactions and Lipodystrophy in HIV; 8-11 July 2003; Paris, France. Abstract 57. *Antivir Ther.* 2003; 8:L42.
- Miró Ò et al. Mitochondrial effects of HIV infection on the peripheral blood mononuclear cells of HIV-infected patients who were never treated with antiretrovirals. *Clin Infect Dis* 2004; 39:710-716.
- Miró Ò et al. Short communication: reversible mitochondrial respiratory chain impairment during symptomatic hyperlactatemia associated with antiretroviral therapy. *AIDS Res Hum Retroviruses* 2003; 19:1027-1032.
- Miró Ò et al. Mitochondrial DNA depletion and respiratory chain enzyme deficiencies are associated with lipodystrophy in HIV-infected patients on HAART. *Antivir Ther.* 2003; 8:333-338.
- Miró Ò et al. Upregulatory Mechanisms Compensate for Mitochondrial DNA Depletion in Asymptomatic Individuals Receiving Stavudine Plus Didanosine. *J Acquir Immune Defic Syndr* 2004; 37:1550-1555.
- Miró Ò et al. Skeletal muscle studies in patients with HIV-related wasting syndrome. *J Neurol Sci* 1997 Sep 10; 150 (2): 153-159.
- Mishriki YY. A baffling case of bulging belly. Protease paunch. *Postgrad Med* 1998 Sep;104(3):45-6.
- Mital et al. Mitochondrial DNA and sperm quality in patients on antiretroviral therapy-response. *AIDS* 2004, 18:963.

- Mitchell W. Neurological and developmental effects of HIV and AIDS in children and adolescents. *Ment Retard Dev Disabil Res Rev* 2001; 7 (3): 211-216.
- Mitsuya H et al. 3'-Azido-3'-deoxythymidine (BW A509U): an antiviral agent that inhibits the infectivity and cytopathic effect of human T-lymphotropic virus type III/lymphadenopathy-associated virus in vitro. *Proc Natl Acad Sci U S A* 1985 Oct;82(20):7096-100.
- Miura T et al. Depletion of mitochondrial DNA in HIV-1-infected patients and its amelioration by antiretroviral therapy. *J Med Virol* 2003; 70:497-505.
- Montagnier L. Historical essay. A history of HIV discovery. *Science* 2002 Nov 29;298(5599):1727-8.
- Montaner JS et al. Nucleoside-related mitochondrial toxicity among HIV-infected patients receiving antiretroviral therapy: insights from the evaluation of venous lactic acid and peripheral blood mitochondrial DNA. *Clin Infect Dis* 2004;38:S73-S79.
- Moraes CT et al. Mitochondrial DNA deletions in progressive external ophthalmoplegia and Kearns-Sayre syndrome. *N Engl J Med*. 1989 May 18;320(20):1293-9.
- Morris AA et al. Liver failure associated with mitochondrial DNA depletion. *J Hepatol* 1998 Apr;28(4):556-63.
- Morrison TB et al. Quantification of low-copy transcripts by continuous SYBR Green I monitoring during amplification. *Biotechniques* 1998; 24: 954-958, 960, 962.
- Moyle G et al. Early virological failure in persons with viral loads >100,000 cps/ml and CD4 counts <200 cells/mm³ receiving ddI/tenofovir/efavirenz as initial therapy: results from a randomized comparative trial. Program and abstracts of the 44th Annual ICAAC Meeting; October 30-November 2, 2004; Washington, DC. Abstract H-566.
- Moyle G. Mitochondrial toxicity hypothesis for lipodystrophy: a refutation. *AIDS* 2001; 15: 413-415.
- Moyle GJ et al. Hyperlactataemia and lactic acidosis during antiretroviral therapy: relevance, reproducibility and possible risk factors. *AIDS* 2002;16: 1341-1349.
- Muller-Hocker J et al. Depletion of mitochondrial DNA in the liver of an infant with neonatal giant cell hepatitis. *Hum Pathol* 2002 Feb; 33(2):247-253.
- Munk B. Protease paunch?. *Posit Aware* 1997 Nov-Dec;8(6):20-1.

Muro-Cacho C.A et al. Analysis of apoptosis in lymph nodes of HIV-infected persons. Intensity of apoptosis correlates with the general state of activation of the lymphoid tissue and not with stage of disease or viral burden. *J Immunol* 1995;154:5555-66.

Muthumani K et al. HIV-1 Vpr induces apoptosis through caspase 9 in T cells and peripheral blood mononuclear cells. *J Biol Chem* 2002;277:37820-37831.

N

N Israel et al. Tumor necrosis factor stimulates transcription of HIV-1 in human T lymphocytes, independently and synergistically with mitogens. *The Journal of Immunology* 1989;143 (12):3956-3960.

Narula J et al. Apoptosis in myocytes in end-stage heart failure. *N Engl J Med* 1996 Oct 17; 335 (16): 1182-1189.

Nass MMK et al. Intramitochondrial fibers with DNA characteristics. *J Cell Biol* 1963;19:593-629.

Negredo E et al. Unexpected CD4+ cell count decline in patients receiving didanosine and tenofovir-based regimens despite undetectable viral load. *AIDS* 2004 Feb; 18(3):459-463.

Negredo E et al. Lopinavir/Ritonavir plus Nevirapine as a nucleoside-sparing approach in antiretroviral-experienced patients (NEKA Study). *J Acquir Immune Defic Syndr* 2005; 38:47-52.

Negredo E et al. Safety and efficacy of once-daily dose didanosine, tenofovir and nevirapine as a simplification antiretroviral approach. *Antivir Ther.* 2004 Jun; 9(3):335-42.

Negredo F et al. Muscle biopsies to identify mitochondrial toxicity (MT) in HIV-1-infected patients. *Libro de Abstracts de la 8th Conference on Retroviruses and Opportunistic Infections.* Chicago, EE.UU., 2001; 244.

Nerurkar PV et al. Highly active antiretroviral therapy (HAART)-associated lactic acidosis: in vitro effects of combination of nucleoside analogues and protease inhibitors on mitochondrial function and lactic acid production. *Cell Mol Biol* 2003; 49:1205-1211.

Nie Z et al. HIV-1 protease processes procaspase 8 to cause mitochondrial release of cytochrome c, caspase cleavage and nuclear fragmentation. *Cell Death Differ* 2002 Nov;9(11):1172-84.

Nolan D et al. Contribution of nucleoside-analogue reverse transcriptase inhibitor therapy to lipotrophy from the population to the cellular level. *Antiviral Therapy* 2003, 8:617-626.

Nolan D et al. Mitochondrial DNA depletion and morphologic changes in adipocytes associated with nucleoside reverse transcriptase inhibitor therapy. *AIDS* 2003, 17:1329-1338.

Nolan D et al. Tumour necrosis factor-alpha gene -238G/A promoter polymorphism associated with a more rapid onset of lipodystrophy. *AIDS* 2003 Jan 3;17(1):121-3.

Nolan D and Mallal S. Complications associated with NRTI therapy: Update on clinical features and possible pathogenic mechanisms. *Antivir Ther* 2004; 9:849-863.

Nolan D. Metabolic complications associated with HIV protease inhibitor therapy. *Drugs* 2003; 63(23):2555-2574.

O

Odoardi F et al. Pathogenic role of mtDNA duplications in mitochondrial diseases associated with mtDNA deletions. *Am J Med Genet A*. 2003 Apr 30;118(3):247-54.

Osmanov S et al. Estimated global distribution and regional spread of HIV-1 genetic subtypes in the year 2000. *J Acquir Immune Defic Syndr* 2002 Feb 1;29(2):184-90.

Otake K et al. The carboxyl-terminal region of HIV-1 Nef protein is a cell surface domain that can interact with CD4+ T cells. *J Immunol*. 1994 Dec 15;153(12):5826-37.

P

Pace CS et al. Mitochondrial proliferation, DNA depletion and adipocyte differentiation in subcutaneous adipose tissue of HIV-positive HAART recipients. *Antivir Ther* 2003; 8:323-331.

Pallotti F and Lenaz G. Isolation and Subfractionation of Mitochondria from Animal Cells and Tissue Culture Lines. In: *Methods in Cell Biology*. Pon LA and Schon EA (editors). San Diego: Academic Press, 2001; Mitochondria (65): pp. 1-35.

Pan-Zhou XR et al. Differential effects of antiretroviral nucleoside analogs on mitochondrial function in HepG2 cells. *Antimicrob Agent Chemother* 2000; 44:496-503.

- Paredes R i col. Tratamiento de la lipodistrofia en pacientes con infección por el virus de la inmunodeficiencia humana. *Med Clin (Barc)* 2001; 116:469-475.
- Patki AH et al. CD4+-T-cell counts, spontaneous apoptosis, and Fas expression in peripheral blood mononuclear cells obtained from human immunodeficiency virus type 1-infected subjects. *Clin Diagn Lab Immunol* 1997 Nov;4 (6):736-41.
- Pecora Fulco P and Kirian MA. Effect of tenofovir on didanosine absorption in patients with HIV. *Ann Pharmacother.* 2003 Sep; 37(9):1325-8.
- Pedrol E et al. Lack of muscle toxicity with didanosine (ddI). Clinical and experimental studies. *J Neurol Sci* 1996; 138:42-48.
- Petit C et al. Quantitation of blood lymphocyte mitochondrial DNA for the monitoring of antiretroviral drug-induced mitochondrial DNA depletion. *J Acquir Immune Defic Syndr* 2003; 33:461-469.
- Petit F et al. Mitochondria are sensors for HIV drugs. *Trends Pharmacol Sci* 2005 May;26(5):258-64. Review.
- Phenix BN et al. Antiapoptotic mechanism of HIV protease inhibitors: preventing mitochondrial transmembrane potential loss. *Blood* 2001; 15:1078-85.
- Phenix BN et al. Decreased HIV-associated T cell apoptosis by HIV protease inhibitors. *AIDS Res Hum Retroviruses* 2000 Apr 10; 16 (6): 559-567.
- Phenix BNet al. Decreased HIV-associated T cell apoptosis by HIV protease inhibitors. *AIDS Res Hum Retrov* 2000; 16:559-67.
- Piganeau Get al. A broad survey of recombination in animal mitochondria. *Mol Biol Evol* 2004 Dec;21(12):2319-25.
- Piketti C et al. Long-term clinical outcome of human immunodeficiency virus-infected patients with discordant immunologic and virologic responses to a protease-inhibitor containing regimen. *J Infect Dis* 2001; 183:1328-1335.
- Pilon AA et al. Induction of apoptosis by a nonnucleoside human immunodeficiency virus type 1 reverse transcriptase inhibitor. *Antimicrob Agents Chemother* 2002; 46:2687-2691.
- Plymale DR et al. Both necrosis and apoptosis contribute to HIV-1-induced killing of CD4 cells. *AIDS* 1999; 13:1827-1839.

Podzamczar D et al. Early virological failure and occurrence of resistance in naive patients receiving tenofovir, didanosine and efavirenz. *Antivir Ther* 2004; 9:S172.

Podzamczar D et al. A randomized clinical trial comparing nelfinavir or nevirapine associated to zidovudine/lamivudine in HIV-infected naive patients: the COMBINE study. *Antiviral Therapy* 2002; 7: 81-90.

Poirier MC et al. Long-term mitochondrial toxicity in HIV-uninfected infants born to HIV-infected mothers. *J Acquir Immune Defic Syndr* 2003;33:175-183.

Polo R et al. Factors associated with mitochondrial dysfunction in circulating peripheral blood lymphocytes from HIV-infected people. *J Acquir Immune Defic Syndr* 2003; 34:32-36.

Pozniak AL et al. Comparison of the efficacy and safety of tenofovir disoproxil fumarate versus stavudine when used in combination with lamivudine and efavirenz in HIV-1 infected patients naive to antiretroviral therapy after 48 weeks of treatment: Study 903. In: Program and abstracts of the Sixth International Congress on Drug Therapy in HIV Infection, Glasgow, UK, November 17-21 2002.

Prins JB et al. Tumor necrosis factor-alpha induces apoptosis of human adipose cells. *Diabetes* 1997 Dec;46(12):1939-44.

Q-R

Ray AS et al. Role of purine nucleoside phosphorylase in interactions between 2',3'-dideoxyinosine and allopurinol, ganciclovir, or tenofovir. *Antimicrob Agents Chemother* 2004; 48(4):1089-95.

Recasens M et al. Obesity and inflammation. *Rev Med Univ Navarra*. 2004 Apr-Jun;48(2):49-54.

Reiss P et al. Greater and more rapid depletion of mitochondrial DNA in blood of patients treated with dual (zidovudine+didanosine or zidovudine+zalcitabine) vs. single (zidovudine) nucleoside reverse transcriptase inhibitors. *HIV Med* 2004; 5:11-14.

Reus S et al. Lipodystrophy and hyperglycemia produced by protease inhibitors. *An Med Interna*. 2000 Mar;17(3):123-6.

Ririe KM et al. Product differentiation by analysis of DNA melting curves during the polymerase chain reaction. *Anal Biochem* 1997; 245: 154-160.

- Rodriguez-Santiago B et al. Is mitochondrial DNA depletion involved in Alzheimer's disease? *Eur J Hum Genet* 2001; 9:279-285.
- Rodriguez Santiago B et al. Is there a relation between Alzheimer's disease and defects of mitochondrial DNA? *Rev Neurol*. 2001 Aug 16-31;33(4):301-5. Spanish.
- Roge BT et al. Skeletal muscle mitochondrial function and exercise capacity in HIV-infected patients with lipodystrophy and elevated p-lactate levels. *AIDS* 2002; 16:973-982.
- Roggero R et al. Binding of human immunodeficiency virus type 1 gp120 to CXCR4 induces mitochondrial transmembrane depolarization and cytochrome c-mediated apoptosis independently of Fas signaling. *J Virol* 2001 Aug;75(16):7637-50.
- Roshal M et al. Apoptosis in AIDS. *Apoptosis* 2001 Feb-Apr; 6 (1-2): 103-116.
- Rossignol R et al. Mitochondrial threshold effects. *Biochem J* 2003;370:751-762.
- Rotig A et al. Deletion of mitochondrial DNA in a case of early-onset diabetes mellitus, optic atrophy, and deafness (Wolfram syndrome, MIM 222300). *J Clin Invest*. 1993 Mar;91(3):1095-8.
- Rotig A et al. Maternally inherited duplication of the mitochondrial genome in a syndrome of proximal tubulopathy, diabetes mellitus, and cerebellar ataxia. *Am J Hum Genet*. 1992 Feb;50(2):364-70.
- Rotig A et al. Pearson's marrow-pancreas syndrome. A multisystem mitochondrial disorder in infancy. *J Clin Invest*. 1990 Nov;86(5):1601-8.
- Ruan H et al. Profiling gene transcription in vivo reveals adipose tissue as an immediate target of tumor necrosis factor-alpha: implications for insulin resistance. *Diabetes* 2002 Nov;51(11):3176-88. Erratum in: *Diabetes*. 2002 Feb;52(2):578.
- Ruiz-Pesini E et al. Human mtDNA haplogroups associated with high or reduced spermatozoa motility. *Am J Hum Genet*. 2000 Sep;67(3):682-96.
- Rustin P et al. Biochemical and molecular investigations in respiratory chain deficiencies. *Clin Chim Acta* 1994; 228: 35-51.

S

- Safai B et al. Seroepidemiological studies of human T-lymphotropic retrovirus type III in acquired immunodeficiency syndrome. *Lancet* 1984 Jun 30;1(8392):1438-40.

- Saint-Marc T et al. A syndrome of peripheral fat wasting (lipodystrophy) in patients receiving long-term nucleoside analogue therapy. *AIDS*. 1999 Sep 10;13(13):1659-67.
- Saint-Marc T et al. The effects of discontinuing stavudine therapy on clinical and metabolic abnormalities in patients suffering from lipodystrophy. *AIDS* 1999; 13:2188-2189.
- Saint-Marc T and Touraine JL. "Buffalo hump" in HIV-1 infection. *Lancet*. 1998 Jul 25;352(9124):319-20.
- Sandri M et al. Apoptosis, DNA damage and ubiquitin expression in normal and mdx muscle fibers after exercise. *FEBS Lett* 1995 Oct 16; 373 (3): 291-295.
- Sarngadharan MG et al. Antibodies reactive with human T-lymphotropic retroviruses (HTLV-III) in the serum of patients with AIDS. *Science*. 1984 May 4;224(4648):506-8.
- Schapira AH. Primary and secondary defects of the mitochondrial respiratory chain. *J Inherit Metab Dis*. 2002 May;25(3):207-14. Review.
- Schwartz M et al. Paternal inheritance of mitochondrial DNA. *N Engl J Med* 2002;347(8):576-580.
- Shen CC et al. Repair of mitochondrial DNA damage induced by bleomycin in human cells. *Mutat Res* 1995.
- Shikuma C et al. Subcutaneous adipose tissue mitochondrial DNA analysis from individuals with HAART-associated lipodystrophy. *Libro de Abstracts de la 8th Conference on Retroviruses and Opportunistic Infections*. Chicago, EE.UU., 2001; 244.
- Shikuma CM et al. Mitochondrial DNA decrease in subcutaneous adipose tissue of HIV-infected individuals with peripheral lipoatrophy. *AIDS* 2001; 15:1801-1809.
- Shiramizu B et al. Brief Report: Placenta and Cord Blood Mitochondrial DNA Toxicity in HIV-Infected Women Receiving Nucleoside Reverse Transcriptase Inhibitors During Pregnancy. *J Acquir Immune Defic Syndr* 2003;32:370-374.
- Shitara H et al. Selective and continuous elimination of mitochondria microinjected into mouse eggs from spermatids, but not from liver cells, occurs throughout embryogenesis. *Genetics* 2000;156:1277-84.
- Simmons G et al. Potent inhibition of HIV-1 infectivity in macrophages and lymphocytes by a novel CCR5 antagonist. *Science* 1997 Apr 11;276(5310):276-9.

- Singh KK. Mitochondrial dysfunction is a common phenotype in aging and cancer. *Ann N Y Acad Sci* 2004 Jun;1019:260-4. Review.
- Sloand EM et al. Protease inhibitors stimulate hematopoiesis and decrease apoptosis and ICE expression in CD34(+) cells. *Blood* 2000 Oct 15; 96 (8): 2735-2739.
- Smith DE et al. Thymidine analogue withdrawal for lipoatrophic patients on protease-sparing therapy improves lipoatrophy but compromises antiviral control: the PIILR extension study. *AIDS* 2002, 16(18):2489-2401.
- Stierum RH et al. Single-nucleotide patch base excision repair of uracil in DNA by mitochondrial protein extracts. *Nucleic Acids Res* 1999 Sep 15; 27(18):3712-9.
- Strack PR et al. Apoptosis mediated by HIV protease is preceded by cleavage of Bcl-2. *Proc Natl Acad Sci* 1996; 93:9571-9576.
- Stricker RB and Goldberg B. Fat accumulation and HIV-1 protease inhibitors. *Lancet* 1998 Oct 24;352(9137):1392.
- Sullivan AK and Nelson MR. Marked hyperlipidaemia on ritonavir therapy. *AIDS*. 1997 Jun;11(7):938-9.
- Sutovsky P et al. Ubiquitinated sperm mitochondria, selective proteolysis, and the regulation of mitochondrial inheritance in mammalian embryos. *Biol Reprod* 2000 Aug;63(2):582-90.

T

- Taanman JW et al. Molecular mechanisms in mitochondrial DNA depletion syndrome. *Hum Mol Genet* 1997 Jun;6(6):935-42.
- Temin HM and Mizutani S. RNA-dependent DNA polymerase in virions of Rous sarcoma virus. *Nature* 1970 Jun 27;226(5252):1211-3.
- Tews DS. Apoptosis and muscle fiber loss in neuromuscular disorders. *Neuromusc Dis* 2002; 12:613-622.
- Torre D and Pugliese. Pathogenic mechanisms of mitochondrial DNA depletion in HIV-1 infection. *Clin Infect Dis* 2005; 40:905-906.
- Torre D et al. Role of nitric oxide in HIV-infection: friend or foe? *Lancet Infect Dis* 2002; 2:273-280.

Tritschler HJ et al. Mitochondrial myopathy of childhood associated with depletion of mitochondrial DNA. *Neurology* 1992 Jan;42(1):209-17.

Tung MY et al. The durability of virological success of tenofovir and didanosine dosed at either 400 or 250 mg once daily. *HIV Med* 2005; 6(3):151-154.

Turrens JF and Boveris A. Generation of superoxide anion by the NADH dehydrogenase of bovine heart mitochondria. *Biochem.J.* 1980; 191: 421-427.

Turrens JF et al. Ubisemiquinone is the electron donor for superoxide formation by complex III of heart mitochondria. *Arch Biochem Biophys* 1985; 237: 408-414.

Twu C et al. Cardiomyocytes undergo apoptosis in human immunodeficiency virus cardiomyopathy through mitochondrion- and death receptor-controlled pathways. *Proc Natl Acad Sci USA* 2002 Oct 29; 99 (22): 14386-14391.

U-V

Valenti D et al. AZT inhibition of the ADP/ATP antiport in isolated rat heart mitochondria. *Int J Mol Med* 2000; 6:93-96.

Van der Valk M et al. Prevalence of lipodystrophy and mitochondrial DNA content of blood and subcutaneous fat in HIV-1-infected patients randomly allocated to zidovudine- or stavudine-based therapy. *Antiviral Therapy* 2004, 9(3):385-393.

Venkatraman A et al. Modification of the mitochondrial proteome in response to the stress of ethanol-dependent hepatotoxicity. *J Biol Chem* 2004 May 21;279(21):22092-101. Epub 2004 Mar 18.

Vigano A et al. HAART-associated lipodystrophy is not correlated to mitochondrial abnormalities in PBLs from HIV-infected children. *Libro de Abstracts de la 8th Conference on Retroviruses and Opportunistic Infections*. Chicago, EE.UU., 2001; 239.

Vijayvergiya C et al. Mutant superoxide dismutase 1 forms aggregates in the brain mitochondrial matrix of amyotrophic lateral sclerosis mice. *J Neurosci* 2005 Mar 9;25(10):2463-70.

Villaroya F et al. Lipodystrophy associated with highly active anti-retroviral therapy for HIV infection: adipocyte as a target of anti-retroviral-induced mitochondrial toxicity. *Trends Pharmacol Sci* 2005; 26:88-93.

Viora M et al. Interference with cell cycle progression and induction of apoptosis by dideoxynucleoside analogs. *Int J Immunopharmacol* 1997 Jun; 19 (6): 311-321.

Vittecoq D et al. Mitochondrial damage associated with long-term antiretroviral treatment: associated alteration or causal disorder? *J Acquir Immune Defic Syndr* 2002; 31:299-308.

Volberding PA et al. A comparison of immediate with deferred zidovudine therapy for asymptomatic HIV-infected adults with CD4 cell counts of 500 or more per cubic millimeter. AIDS Clinical Trials Group. *N Engl J Med* 1995 Aug 17;333(7):401-7.

W

Walker UA et al. Increased long-term mitochondrial toxicity in combinations of nucleoside analogue reverse-transcriptase inhibitors. *AIDS* 2002, 16:2165-2173.

Walker UA et al. Antiretroviral therapy with didanosine, stavudine, and zalcitabine is associated with depletion of mtDNA in the liver. *Antivir Ther* 2003;8:L15-L16.

Walker UA et al. Depletion of mitochondrial DNA in liver under antiretroviral therapy with didanosine, stavudine or zalcitabine. *Hepathol* 2004; 39:311-317.

Walker UA et al. Decrease of mitochondrial content in adipose tissue of HIV-1-infected patients treated with NRTIs. 2nd International Workshop on Adverse Drug Reactions and Lipodystrophy in HIV. *Antiviral Therapy* 2000; 5 (Supl): 5.

Walker UA et al. Evidence of Nucleoside Analogue Reverse Transcriptase Inhibitor-Associated Genetic and Structural Defects of Mitochondria in Adipose Tissue of HIV-Infected Patients. *J Acquir Immune Defic Syndr.* 2002; 29:117-121.

Wallace DC. Diseases of mitochondrial DNA. *Annu Rev Biochem* 1992;61:1175-212. Di Mauro 2000.

Walli R et al. Treatment with protease inhibitors associated with peripheral insulin resistance and impaired oral glucose tolerance in HIV-1-infected patients. *AIDS* 1998 Oct 22;12(15):F167-73.

Walter Neupert. Protein import into mitochondria. *Annu Rev Biochem* 1997;66:863-917.

Weiss SH et al. Screening test for HTLV-III (AIDS agent) antibodies. Specificity, sensitivity, and applications. *JAMA* 1985 Jan 11;253(2):221-5.

- Wenchich L et al. Mitochondrial energy metabolism in very premature neonates. *Biol Neonate* 2002; 81(4):229-235.
- Westendorp MO et al. HIV-1 Tat potentiates TNF-induced NF-kappa B activation and cytotoxicity by altering the cellular redox state. *EMBO J* 1995 Feb 1;14(3):546-54.
- White AJ. Mitochondrial toxicity and HIV therapy. *Sex Transm Infect* 2001; 77:158-173.
- White DJ et al. Sperm mitochondrial DNA deletions as a consequence of long term highly active antiretroviral therapy. *AIDS* 2001, 15:1061-1062.
- Wig N et al. Tumor necrosis factor-alpha levels in patients with HIV with wasting in South Asia. *AIDS Patient Care STDS*. 2005 Apr;19(4):212-5.
- Williams MD et al. Increased oxidative damage is correlated to altered mitochondrial function in heterozygous manganese superoxide dismutase knockout mice. *J Biol Chem* 1998; 273:28510-28515.
- Wood E et al. "Discordant" increased in CD4 cell count relative to plasma viral load in a closely followed cohort of patients initiating antiretroviral therapy. *J Acquir Immune Def Syndr* 2002; 30:159-166.
- Wurtz R. Abnormal fat distribution and use of protease inhibitors. *Lancet* 1998 Jun 6;351(9117):1735-6.

X

- Xing H et al. TNF alpha-mediated inhibition and reversal of adipocyte differentiation is accompanied by suppressed expression of PPARgamma without effects on Pref-1 expression. *Endocrinology*. 1997 Jul;138(7):2776-83.
- Xu W et al. Nitric oxide: orchestrating hypoxia regulation through mitochondrial respiration and the endoplasmic reticulum stress response. *Cell Res* 2005 Jan;15(1):63-5.
- Xu Y et al. Impaired development of mitochondria plays a role in the central nervous system defects of fetal alcohol syndrome. *Birth Defects Res A Clin Mol Teratol* 2005 Feb;73(2):83-91.
- Xu Z et al. Mitochondrial degeneration in amyotrophic lateral sclerosis. *J Bioenerg Biomembr* 2004 Aug;36(4):395-9. Review.

Y

Yerroum M et al. Cytochrome c oxidase deficiency in the muscle of patients with zidovudine myopathy is segmental and affects both mitochondrial DNA- and nuclear DNA-encoded subunits. *Acta Neuropathol (Berl)*. 2000 Jul; 100(1):82-6.

Z

Zauli G et al. Human immunodeficiency virus type 1 Nef protein sensitizes CD4(+) T lymphoid cells to apoptosis via functional upregulation of the CD95/CD95 ligand pathway. *Blood* 1999 Feb 1;93(3):1000-10.

Zeviani M et al. Deletions of mitochondrial DNA in Kearns-Sayre syndrome. *Neurology*. 1988 Sep;38(9):1339-46.

Zeviani M et al. Mitochondrial disorders. *Molecular Human Reproduction* 1997;3(2):133-148.

Zeviani M et al. Neurological disorders due to mutations of the mitochondrial genome. *Neuromuscul Disord* 1991;1:165-172.

Zeviani M et al. Maternally inherited myopathy and cardiomyopathy: Association with a mutation in mitochondrial DNA tRNA^{Leu}(UUR). *Lancet*. 1991; 338:143-7.

Zhang J and Piantadosi CA. Mitochondrial oxidative stress after carbon monoxide hypoxia in the rat brain. *J Clin Invest* 1992 Oct;90(4):1193-9.

Zhu X et al. Mitochondrial failures in Alzheimer's disease. *Am J Alzheimers Dis Other Demen* 2004 Nov-Dec;19(6):345-52. Review.

