

## 6 References

- Aijaz,S., Erskine,L., Jeffery,G., Bhattacharya,S.S., and Votruba,M. (2004). Developmental expression profile of the optic atrophy gene product: OPA1 is not localized exclusively in the mammalian retinal ganglion cell layer. *Invest Ophthalmol Vis. Sci* 45, 1667-1673.
- Alberts,B., Bray,D., Lewis,J., Raff,M., Roberts,K., and Watson,JD. (1995). Molecular biology of cell. New York: Garland Science.
- Alexander,C., Votruba,M., Pesch,U.E., Thiselton,D.L., Mayer,S., Moore,A., Rodriguez,M., Kellner,U., Leo-Kottler,B., Auburger,G., Bhattacharya,S.S., and Wissinger,B. (2000). OPA1, encoding a dynamin-related GTPase, is mutated in autosomal dominant optic atrophy linked to chromosome 3q28. *Nat Genet* 26, 211-215.
- Amati-Bonneau,P., Odent,S., Derrien,C., Pasquier,L., Malthiery,Y., Reynier,P., and Bonneau,D. (2003). The association of autosomal dominant optic atrophy and moderate deafness may be due to the R445H mutation in the OPA1 gene. *Am J Ophthalmol.* 136, 1170-1171.
- Amati-Bonneau,P., Guichet,A., Olichon,A., Chevrollier,A., Viala,F., Miot,S., Ayuso,C., Odent,S., Arrouet,C., Verny,C., Calmels,M.N., Simard,G., Belenguer,P., Wang,J., Puel,J.L., Hamel,C., Malthiery,Y., Bonneau,D., Lenaers,G., and Reynier,P. (2005). OPA1 R445H mutation in optic atrophy associated with sensorineural deafness. *Ann. Neurol.* 58, 958-963.
- Anderson,S., Bankier,A.T., Barrell,B.G., de Brujin,M.H., Coulson,A.R., Drouin,J., Eperon,I.C., Nierlich,D.P., Roe,B.A., Sanger,F., Schreier,P.H., Smith,A.J., Staden,R., and Young,I.G. (1981). Sequence and organization of the human mitochondrial genome. *Nature* 290, 457-465.
- Arnoult,D., Grodet,A., Lee,Y.J., Estaquier,J., and Blackstone,C. (2005). Release of OPA1 during apoptosis participates in the rapid and complete release of cytochrome c and subsequent mitochondrial fragmentation. *J. Biol. Chem.* 280, 35742-35750.
- Baxter,R.V., Ben Othmane,K., Rochelle,J.M., Stajich,J.E., Hulette,C., Dew-Knight,S., Bentati,F., Ben Hamida,M., Bel,S., Stenger,J.E., Gilbert,J.R., Pericak-Vance,M.A., and Vance,J.M. (2002). Ganglioside-induced differentiation-associated protein-1 is mutant in Charcot-Marie-Tooth disease type 4A/8q21. *Nat Genet* 30, 21-22.
- Beal,M.F. (2005). Mitochondria take center stage in aging and neurodegeneration. *Ann. Neurol.* 58, 495-505.
- Bradford,M.M. (1976). A rapid and sensitive method for the quantitation of microgram quantities of protein utilizing the principle of protein-dye binding. *Anal. Biochem* 72, 248-254.
- Breckenridge,D.G., Stojanovic,M., Marcellus,R.C., and Shore,G.C. (2003). Caspase cleavage product of BAP31 induces mitochondrial fission through endoplasmic reticulum calcium signals, enhancing cytochrome c release to the cytosol. *J Cell Biol* 160, 1115-1127.
- Brill,L.M., Salomon,A.R., Ficarro,S.B., Mukherji,M., Stettler-Gill,M., and Peters,E.C. (2004). Robust phosphoproteomic profiling of tyrosine phosphorylation sites from human T cells using immobilized metal affinity chromatography and tandem mass spectrometry. *Anal. Chem.* 76, 2763-2772.
- Capano,M. and Crompton,M. (2002). Biphasic translocation of Bax to mitochondria. *Biochem J* 367, 169-178.
- Carelli,V., Ross-Cisneros,F.N., and Sadun,A.A. (2002). Optic nerve degeneration and mitochondrial dysfunction: genetic and acquired optic neuropathies. *Neurochem. Int.* 40, 573-584.
- Carelli,V., Ross-Cisneros,F.N., and Sadun,A.A. (2004). Mitochondrial dysfunction as a cause of optic neuropathies. *Prog. Retin. Eye Res* 23, 53-89.
- Chen,H., Detmer,S.A., Ewald,A.J., Griffin,E.E., Fraser,S.E., and Chan,D.C. (2003). Mitofusins Mfn1 and Mfn2 coordinately regulate mitochondrial fusion and are essential for embryonic development. *J Cell Biol* 160, 189-200.

- Chen,H., Chomyn,A., and Chan,D.C. (2005). Disruption of fusion results in mitochondrial heterogeneity and dysfunction. *J Biol Chem.* 280, 26185-26192.
- Chomczynski,P. and Sacchi,N. (1987). Single-step method of RNA isolation by acid guanidinium thiocyanate-phenol-chloroform extraction. *Anal. Biochem* 162, 156-159.
- Cipolat,S., Martins,d.B., Dal Zilio,B., and Scorrano,L. (2004). OPA1 requires mitofusin 1 to promote mitochondrial fusion. *Proc. Natl. Acad. Sci U. S. A* 101, 15927-15932.
- Cipolat,S., Rudka,T., Hartmann,D., Costa,V., Serneels,L., Craessaerts,K., Metzger,K., Frezza,C., Annaert,W., D'Adamio,L., Derkx,C., Dejaegere,T., Pellegrini,L., D'Hooge,R., Scorrano,L., and De Strooper,B. (2006). Mitochondrial rhomboid PARL regulates cytochrome c release during apoptosis via OPA1-dependent cristae remodeling. *Cell* 126, 163-175.
- Cuddeback,S.M., Yamaguchi,H., Komatsu,K., Miyashita,T., Yamada,M., Wu,C., Singh,S., and Wang,H.G. (2001). Molecular cloning and characterization of Bif-1. A novel Src homology 3 domain-containing protein that associates with Bax. *J Biol Chem.* 276, 20559-20565.
- Danino,D. and Hinshaw,J.E. (2001). Dynamin family of mechanoenzymes. *Curr Opin Cell Biol* 13, 454-460.
- de St Groth,S.F. (1980). Monoclonal antibodies and how to make them. *Transplant. Proc.* 12, 447-450.
- Delettre,C., Lenaers,G., Griffoin,J.M., Gigarel,N., Lorenzo,C., Belenguer,P., Pelloquin,L., Grosgeorge,J., Turc-Carel,C., Perret,E., Astarie-Dequeker,C., Lasquellec,L., Arnaud,B., Ducommun,B., Kaplan,J., and Hamel,C.P. (2000). Nuclear gene OPA1, encoding a mitochondrial dynamin-related protein, is mutated in dominant optic atrophy. *Nat Genet* 26, 207-210.
- Delettre,C., Griffoin,J.M., Kaplan,J., Dollfus,H., Lorenz,B., Faivre,L., Lenaers,G., Belenguer,P., and Hamel,C.P. (2001). Mutation spectrum and splicing variants in the OPA1 gene. *Hum Genet* 109, 584-591.
- Delettre,C., Lenaers,G., Pelloquin,L., Belenguer,P., and Hamel,C.P. (2002). OPA1 (Kjer type) dominant optic atrophy: a novel mitochondrial disease. *Mol Genet Metab* 75, 97-107.
- Delettre,C., Lenaers,G., Belenguer,P., and Hamel,C.P. (2003). Gene structure and chromosomal localization of mouse Opal : its exclusion from the Bst locus. *BMC. Genet* 4, 8.
- Desagher,S. and Martinou,J.C. (2000). Mitochondria as the central control point of apoptosis. *Trends Cell Biol* 10, 369-377.
- Dimauro,S. and Davidzon,G. (2005). Mitochondrial DNA and disease. *Ann. Med.* 37, 222-232.
- Dubey,M., Hoda,S., Chan,W.K., Pimenta,A., Ortiz,D.D., and Shea,T.B. (2004). Reexpression of vimentin in differentiated neuroblastoma cells enhances elongation of axonal neurites. *J. Neurosci. Res.* 78, 245-249.
- Duvezin-Caubet,S., Jagasia,R., Wagener,J., Hofmann,S., Trifunovic,A., Hansson,A., Chomyn,A., Bauer,M.F., Attardi,G., Larsson,N.G., Neupert,W., and Reichert,A.S. (2006). Proteolytic processing of OPA1 links mitochondrial dysfunction to alterations in mitochondrial morphology. *J. Biol. Chem.*
- Eiberg,H., Kjer,B., Kjer,P., and Rosenberg,T. (1994). Dominant optic atrophy (OPA1) mapped to chromosome 3q region. I. Linkage analysis. *Hum Mol Genet* 3, 977-980.
- Elenius,V., Leinonen,M., and Airas,K. (1991). Rod thresholds in dominantly inherited juvenile optic atrophy. *Ophthalmologica* 202, 208-212.
- Falkenberg,M., Gaspari,M., Rantanen,A., Trifunovic,A., Larsson,N.G., and Gustafsson,C.M. (2002). Mitochondrial transcription factors B1 and B2 activate transcription of human mtDNA. *Nat Genet* 31, 289-294.
- Ferre,M., Amati-Bonneau,P., Tourmen,Y., Malthiery,Y., and Reynier,P. (2005). eOPA1: an online database for OPA1 mutations. *Hum Mutat.* 25, 423-428.

- Frank,S., Gaume,B., Bergmann-Leitner,E.S., Leitner,W.W., Robert,E.G., Catez,F., Smith,C.L., and Youle,R.J. (2001). The role of dynamin-related protein 1, a mediator of mitochondrial fission, in apoptosis. *Dev. Cell* 1, 515-525.
- Fransson,S., Ruusala,A., and Aspenstrom,P. (2006). The atypical Rho GTPases Miro-1 and Miro-2 have essential roles in mitochondrial trafficking. *Biochem. Biophys. Res. Commun.* 344, 500-510.
- Frey,T.G. and Mannella,C.A. (2000). The internal structure of mitochondria. *Trends in Biochemical Sciences* 25, 319-324.
- Frezza,C., Cipolat,S., Martins,d.B., Micaroni,M., Beznoussenko,G.V., Rudka,T., Bartoli,D., Polishuck,R.S., Danial,N.N., De Strooper,B., and Scorrano,L. (2006). OPA1 controls apoptotic cristae remodeling independently from mitochondrial fusion. *Cell* 126, 177-189.
- Fujiki,Y., Hubbard,A.L., Fowler,S., and Lazarow,P.B. (1982). Isolation of intracellular membranes by means of sodium carbonate treatment: application to endoplasmic reticulum. *J Cell Biol* 93, 97-102.
- Giles,R.E., Blanc,H., Cann,H.M., and Wallace,D.C. (1980). Maternal inheritance of human mitochondrial DNA. *Proc. Natl. Acad. Sci U. S. A* 77, 6715-6719.
- Goehler,H., Lalowski,M., Stelzl,U., Waelter,S., Stroedicke,M., Worm,U., Droege,A., Lindenberger,K.S., Knoblich,M., Haenig,C., Herbst,M., Suopanki,J., Scherzinger,E., Abraham,C., Bauer,B., Hasenbank,R., Fritzsche,A., Ludewig,A.H., Bussow,K., Coleman,S.H., Gutekunst,C.A., Landwehrmeyer,B.G., Lehrach,H., and Wanker,E.E. (2004). A protein interaction network links GIT1, an enhancer of huntingtin aggregation, to Huntington's disease. *Mol. Cell* 15, 853-865.
- Gray,M.W., Burger,G., and Lang,B.F. (1999). Mitochondrial evolution. *Science* 283, 1476-1481.
- Greg Ralston. Introduction to Analytical Ultracentrifugation. Beckman Coulter, Inc.
- Griffin,E.E., Graumann,J., and Chan,D.C. (2005). The WD40 protein Caf4p is a component of the mitochondrial fission machinery and recruits Dnm1p to mitochondria. *J Cell Biol* 170, 237-248.
- Gripasic,L., van der Wel,N.N., Orozco,I.J., Peters,P.J., and van der Bliek,A.M. (2004). Loss of the intermembrane space protein Mgm1/OPA1 induces swelling and localized constrictions along the lengths of mitochondria. *J Biol Chem.* 279, 18792-18798.
- Guillou,E., Bousquet,C., Daloyau,M., Emorine,L.J., and Belenguer,P. (2005). Msp1p is an intermembrane space dynamin-related protein that mediates mitochondrial fusion in a Dnm1p-dependent manner in *S. pombe*. *FEBS Lett.* 579, 1109-1116.
- Hall,S.C., Smith,D.M., Masiarz,F.R., Soo,V.W., Tran,H.M., Epstein,L.B., and Burlingame,A.L. (1993). Mass spectrometric and Edman sequencing of lipocortin I isolated by two-dimensional SDS/PAGE of human melanoma lysates. *Proc Natl Acad Sci U S A.* 90(5):1927-31
- Herlan,M., Vogel,F., Bornhovd,C., Neupert,W., and Reichert,A.S. (2003). Processing of Mgm1 by the rhomboid-type protease Pcp1 is required for maintenance of mitochondrial morphology and of mitochondrial DNA. *J Biol Chem.* 278, 27781-27788.
- Herlan,M., Bornhovd,C., Hell,K., Neupert,W., and Reichert,A.S. (2004). Alternative topogenesis of Mgm1 and mitochondrial morphology depend on ATP and a functional import motor. *J Cell Biol* 165, 167-173.
- Howell,N. (1997). Leber hereditary optic neuropathy: how do mitochondrial DNA mutations cause degeneration of the optic nerve? *J Bioenerg. Biomembr.* 29, 165-173.
- Ingerman,E., Perkins,E.M., Marino,M., Mears,J.A., McCaffery,J.M., Hinshaw,J.E., and Nunnari,J. (2005). Dnm1 forms spirals that are structurally tailored to fit mitochondria. *J Cell Biol* 170, 1021-1027.
- Ishihara,N., Jofuku,A., Eura,Y., and Mihara,K. (2003). Regulation of mitochondrial morphology by membrane potential, and DRP1-dependent division and FZO1-dependent fusion reaction in mammalian cells. *Biochem Biophys. Res Commun.* 301, 891-898.

- Ishihara,N., Eura,Y., and Mihara,K. (2004). Mitofusin 1 and 2 play distinct roles in mitochondrial fusion reactions via GTPase activity. *J Cell Sci* *117*, 6535-6546.
- Ishihara,N., Fujita,Y., Oka,T., and Mihara,K. (2006). Regulation of mitochondrial morphology through proteolytic cleavage of OPA1. *EMBO J* *25*, 2966-2977.
- Ito,A. (1999). Mitochondrial processing peptidase: multiple-site recognition of precursor proteins. *Biochem. Biophys. Res. Commun.* *265*, 611-616.
- Jagasia,R., Grote,P., Westermann,B., and Conradt,B. (2005). DRP-1-mediated mitochondrial fragmentation during EGL-1-induced cell death in *C. elegans*. *Nature* *433*, 754-760.
- James,D.I., Parone,P.A., Mattenberger,Y., and Martinou,J.C. (2003). hFis1, a novel component of the mammalian mitochondrial fission machinery. *J Biol Chem.* *278*, 36373-36379.
- John,G.B., Shang,Y., Li,L., Renken,C., Mannella,C.A., Selker,J.M., Rangell,L., Bennett,M.J., and Zha,J. (2005). The mitochondrial inner membrane protein mitoflin controls cristae morphology. *Mol Biol Cell* *16*, 1543-1554.
- Johnston,P.B., Gaster,R.N., Smith,V.C., and Tripathi,R.C. (1979). A clinicopathologic study of autosomal dominant optic atrophy. *Am J Ophthalmol.* *88*, 868-875.
- Ju,W.K., Misaka,T., Kushnareva,Y., Nakagomi,S., Agarwal,N., Kubo,Y., Lipton,S.A., and Bossy-Wetzel,E. (2005). OPA1 expression in the normal rat retina and optic nerve. *J Comp Neurol.* *488*, 1-10.
- Kamei,S., Chen-Kuo-Chang,M., Cazevieille,C., Lenaers,G., Olichon,A., Belenguer,P., Roussignol,G., Renard,N., Eybalin,M., Michelin,A., Delettre,C., Brabet,P., and Hamel,C.P. (2005). Expression of the Opal mitochondrial protein in retinal ganglion cells: its downregulation causes aggregation of the mitochondrial network. *Invest Ophthalmol Vis. Sci* *46*, 4288-4294.
- Karbowski,M., Jeong,S.Y., and Youle,R.J. (2004a). Endophilin B1 is required for the maintenance of mitochondrial morphology. *J Cell Biol* *166*, 1027-1039.
- Karbowski,M., Arnoult,D., Chen,H., Chan,D.C., Smith,C.L., and Youle,R.J. (2004b). Quantitation of mitochondrial dynamics by photolabeling of individual organelles shows that mitochondrial fusion is blocked during the Bax activation phase of apoptosis. *J Cell Biol* *164*, 493-499.
- Kim,J.Y., Hwang,J.M., Ko,H.S., Seong,M.W., Park,B.J., and Park,S.S. (2005). Mitochondrial DNA content is decreased in autosomal dominant optic atrophy. *Neurology* *64*, 966-972.
- Kim,N., Lim,D., Lee,S., and Kim,H. (2005). ASePCR: alternative splicing electronic RT-PCR in multiple tissues and organs. *Nucleic Acids Res.* *33*, W681-W685.
- Kjer,B., Eiberg,H., Kjer,P., and Rosenberg,T. (1996). Dominant optic atrophy mapped to chromosome 3q region. II. Clinical and epidemiological aspects. *Acta Ophthalmol. Scand* *74*, 3-7.
- Kjer,P., Jensen,O.A., and Klinken,L. (1983). Histopathology of eye, optic nerve and brain in a case of dominant optic atrophy. *Acta Ophthalmol. (Copenh)* *61*, 300-312.
- Kline,L.B. and Glaser,J.S. (1979). Dominant optic atrophy. The clinical profile. *Arch Ophthalmol.* *97*, 1680-1686.
- Koshiba,T., Detmer,S.A., Kaiser,J.T., Chen,H., McCaffery,J.M., and Chan,D.C. (2004). Structural basis of mitochondrial tethering by mitofusin complexes. *Science* *305*, 858-862.
- Kuhlenbaumer,G., Young,P., Hunermund,G., Ringelstein,B., and Stogbauer,F. (2002). Clinical features and molecular genetics of hereditary peripheral neuropathies. *J Neurol.* *249*, 1629-1650.
- Kuroda,S., Nakagawa,N., Tokunaga,C., Tatematsu,K., and Tanizawa,K. (1999). Mammalian homologue of the *Caenorhabditis elegans* UNC-76 protein involved in axonal outgrowth is a protein kinase C zeta-interacting protein. *J. Cell Biol.* *144*, 403-411.

- Laemmli,U.K. (1970). Cleavage of structural proteins during the assembly of the head of bacteriophage T4. *Nature* 227, 680-685.
- Larsson,N.G., Wang,J., Wilhelmsson,H., Oldfors,A., Rustin,P., Lewandoski,M., Barsh,G.S., and Clayton,D.A. (1998). Mitochondrial transcription factor A is necessary for mtDNA maintenance and embryogenesis in mice. *Nat Genet* 18, 231-236.
- Lee,Y.J., Jeong,S.Y., Karbowski,M., Smith,C.L., and Youle,R.J. (2004). Roles of the mammalian mitochondrial fission and fusion mediators Fis1, Drp1, and Opa1 in apoptosis. *Mol Biol Cell* 15, 5001-5011.
- Legros,F., Lombes,A., Frachon,P., and Rojo,M. (2002). Mitochondrial fusion in human cells is efficient, requires the inner membrane potential, and is mediated by mitofusins. *Mol Biol Cell* 13, 4343-4354.
- Lodi,R., Tonon,C., Valentino,M.L., Iotti,S., Clementi,V., Malucelli,E., Barboni,P., Longanesi,L., Schimpf,S., Wissinger,B., Baruzzi,A., Barbiroli,B., and Carelli,V. (2004). Deficit of in vivo mitochondrial ATP production in OPA1-related dominant optic atrophy. *Ann. Neurol.* 56, 719-723.
- Luciano,P. and Gelli,V. (1996). The mitochondrial processing peptidase: function and specificity. *Experientia* 52, 1077-1082.
- Malka,F., Guillery,O., Cifuentes-Diaz,C., Guillou,E., Belenguer,P., Lombes,A., and Rojo,M. (2005). Separate fusion of outer and inner mitochondrial membranes. *EMBO Rep.* 6, 853-859.
- Mancini,M., Anderson,B.O., Caldwell,E., Sedghinasab,M., Paty,P.B., and Hockenberry,D.M. (1997). Mitochondrial proliferation and paradoxical membrane depolarization during terminal differentiation and apoptosis in a human colon carcinoma cell line. *J Cell Biol* 138, 449-469.
- Mandel,H., Szargel,R., Labay,V., Elpeleg,O., Saada,A., Shalata,A., Anbinder,Y., Berkowitz,D., Hartman,C., Barak,M., Eriksson,S., and Cohen,N. (2001). The deoxyguanosine kinase gene is mutated in individuals with depleted hepatocerebral mitochondrial DNA. *Nat Genet* 29, 337-341.
- Marchbank,N.J., Craig,J.E., Leek,J.P., Toohey,M., Churchill,A.J., Markham,A.F., Mackey,D.A., Toomes,C., and Inglehearn,C.F. (2002). Deletion of the OPA1 gene in a dominant optic atrophy family: evidence that haploinsufficiency is the cause of disease. *J Med. Genet.* 39, e47.
- Mattenberger,Y., James,D.I., and Martinou,J.C. (2003). Fusion of mitochondria in mammalian cells is dependent on the mitochondrial inner membrane potential and independent of microtubules or actin. *FEBS Lett.* 538, 53-59.
- McQuibban,G.A., Saurya,S., and Freeman,M. (2003). Mitochondrial membrane remodelling regulated by a conserved rhomboid protease. *Nature* 423, 537-541.
- Meeusen,S., McCaffery,J.M., and Nunnari,J. (2004). Mitochondrial fusion intermediates revealed in vitro. *Science* 305, 1747-1752.
- Misaka,T., Miyashita,T., and Kubo,Y. (2002). Primary structure of a dynamin-related mouse mitochondrial GTPase and its distribution in brain, subcellular localization, and effect on mitochondrial morphology. *J Biol Chem.* 277, 15834-15842.
- Morris,J.A., Kandpal,G., Ma,L., and Austin,C.P. (2003). DISC1 (Disrupted-In-Schizophrenia 1) is a centrosome-associated protein that interacts with MAP1A, MIPT3, ATF4/5 and NUDEL: regulation and loss of interaction with mutation. *Hum. Mol. Genet.* 12, 1591-1608.
- Mozdy,A.D., McCaffery,J.M., and Shaw,J.M. (2000). Dnm1p GTPase-mediated mitochondrial fission is a multi-step process requiring the novel integral membrane component Fis1p. *J Cell Biol* 151, 367-380.
- Newman,N.J., Lott,M.T., and Wallace,D.C. (1991). The clinical characteristics of pedigrees of Leber's hereditary optic neuropathy with the 11778 mutation. *Am. J. Ophthalmol.* 111, 750-762.
- Niemann,A., Ruegg,M., La,P., V, Schenone,A., and Suter,U. (2005). Ganglioside-induced differentiation associated protein 1 is a regulator of the mitochondrial network: new implications for Charcot-Marie-Tooth disease. *J. Cell Biol.* 170, 1067-1078.

- Nikoskelainen,E.K., Huoponen,K., Juvonen,V., Lamminen,T., Nummelin,K., and Savontaus,M.L. (1996). Ophthalmologic findings in Leber hereditary optic neuropathy, with special reference to mtDNA mutations. *Ophthalmology* 103, 504-514.
- Nishino,I., Spinazzola,A., and Hirano,M. (1999). Thymidine phosphorylase gene mutations in MNGIE, a human mitochondrial disorder. *Science* 283, 689-692.
- Nunnari,J., Marshall,W.F., Straight,A., Murray,A., Sedat,J.W., and Walter,P. (1997). Mitochondrial transmission during mating in *Saccharomyces cerevisiae* is determined by mitochondrial fusion and fission and the intramitochondrial segregation of mitochondrial DNA. *Mol Biol Cell* 8, 1233-1242.
- Okamoto,K. and Shaw,J.M. (2005). Mitochondrial morphology and dynamics in yeast and multicellular eukaryotes. *Annu Rev Genet* 39, 503-536.
- Okamoto,P.M., Tripet,B., Litowski,J., Hodges,R.S., and Vallee,R.B. (1999). Multiple distinct coiled-coils are involved in dynamin self-assembly. *J Biol Chem*. 274, 10277-10286.
- Olichon,A., Emorine,L.J., Descoins,E., Pelloquin,L., Brichese,L., Gas,N., Guillou,E., Delettre,C., Valette,A., Hamel,C.P., Ducommun,B., Lenaers,G., and Belenguer,P. (2002). The human dynamin-related protein OPA1 is anchored to the mitochondrial inner membrane facing the inter-membrane space. *FEBS Lett.* 523, 171-176.
- Olichon,A., Baricault,L., Gas,N., Guillou,E., Valette,A., Belenguer,P., and Lenaers,G. (2003). Loss of OPA1 perturbs the mitochondrial inner membrane structure and integrity, leading to cytochrome c release and apoptosis. *J Biol Chem*. 278, 7743-7746.
- Olichon,A., Elachouri,G., Baricault,L., Delettre,C., Belenguer,P., and Lenaers,G. (2006). OPA1 alternate splicing uncouples an evolutionary conserved function in mitochondrial fusion from a vertebrate restricted function in apoptosis. *Cell Death Differ*.
- Olson,E.N. and Spizz,G. (1986). Fatty acylation of cellular proteins. Temporal and subcellular differences between palmitate and myristate acylation. *J. Biol. Chem.* 261, 2458-2466.
- Otera,H., Ohsakaya,S., Nagaura,Z., Ishihara,N., and Mihara,K. (2005). Export of mitochondrial AIF in response to proapoptotic stimuli depends on processing at the intermembrane space. *EMBO J* 24, 1375-1386.
- Otte,L., Wiedemann,U., Schlegel,B., Pires,J.R., Beyermann,M., Schmieder,P., Krause,G., Volkmer-Engert,R., Schneider-Mergener,J., and Oschkinat,H. (2003). WW domain sequence activity relationships identified using ligand recognition propensities of 42 WW domains. *Protein Sci* 12, 491-500.
- Payne,M., Yang,Z., Katz,B.J., Warner,J.E., Weight,C.J., Zhao,Y., Pearson,E.D., Treft,R.L., Hillman,T., Kennedy,R.J., Meire,F.M., and Zhang,K. (2004). Dominant optic atrophy, sensorineural hearing loss, ptosis, and ophthalmoplegia: a syndrome caused by a missense mutation in OPA1. *Am J Ophthalmol.* 138, 749-755.
- Pellegrini,L., Passer,B.J., Canelles,M., Lefterov,I., Ganjei,J.K., Fowlkes,B.J., Koonin,E.V., and D'Adamio,L. (2001). PAMP and PARL, two novel putative metalloproteases interacting with the COOH-terminus of Presenilin-1 and -2. *J Alzheimers Dis* 3, 181-190.
- Pesch,U.E., Leo-Kottler,B., Mayer,S., Jurklies,B., Kellner,U., Apfelstedt-Sylla,E., Zrenner,E., Alexander,C., and Wissinger,B. (2001). OPA1 mutations in patients with autosomal dominant optic atrophy and evidence for semi-dominant inheritance. *Hum. Mol. Genet.* 10, 1359-1368.
- Pesch,U.E., Fries,J.E., Bette,S., Kalbacher,H., Wissinger,B., Alexander,C., and Kohler,K. (2004). OPA1, the disease gene for autosomal dominant optic atrophy, is specifically expressed in ganglion cells and intrinsic neurons of the retina. *Invest Ophthalmol Vis. Sci* 45, 4217-4225.
- Pierrat,B., Simonen,M., Cueto,M., Mestan,J., Ferrigno,P., and Heim,J. (2001). SH3GLB, a new endophilin-related protein family featuring an SH3 domain. *Genomics* 71, 222-234.
- Pinton,P., Ferrari,D., Rapizzi,E., Di Virgilio,F., Pozzan,T., and Rizzuto,R. (2001). The Ca<sup>2+</sup> concentration of the endoplasmic reticulum is a key determinant of ceramide-induced apoptosis: significance for the molecular mechanism of Bcl-2 action. *EMBO J* 20, 2690-2701.

- Pollak,D.D., John,J., Schneider,A., Hoeger,H., and Lubec,G. (2006). Strain-dependent expression of signaling proteins in the mouse hippocampus. *Neuroscience* *138*, 149-158.
- Praefcke,G.J. and McMahon,H.T. (2004). The dynamin superfamily: universal membrane tubulation and fission molecules? *Nat Rev Mol Cell Biol* *5*, 133-147.
- Puomila,A., Huoponen,K., Mantyjarvi,M., Hamalainen,P., Paananen,R., Sankila,E.M., Savontaus,M.L., Somer,M., and Nikoskelainen,E. (2005). Dominant optic atrophy: correlation between clinical and molecular genetic studies. *Acta Ophthalmol Scand* *83*, 337-346.
- Rojo,M., Legros,F., Chateau,D., and Lombes,A. (2002). Membrane topology and mitochondrial targeting of mitofusins, ubiquitous mammalian homologs of the transmembrane GTPase Fzo. *J Cell Sci* *115*, 1663-1674.
- Saada,A., Shaag,A., Mandel,H., Nevo,Y., Eriksson,S., and Elpeleg,O. (2001). Mutant mitochondrial thymidine kinase in mitochondrial DNA depletion myopathy. *Nat Genet* *29*, 342-344.
- Sadun,A.A., Win,P.H., Ross-Cisneros,F.N., Walker,S.O., and Carelli,V. (2000). Leber's hereditary optic neuropathy differentially affects smaller axons in the optic nerve. *Trans. Am Ophthalmol. Soc.* *98*, 223-232.
- Sanger,F., Nicklen,S., and Coulson,A.R. (1977). DNA sequencing with chain-terminating inhibitors. *Proc. Natl. Acad. Sci U. S. A* *74*, 5463-5467.
- Santel,A. and Fuller,M.T. (2001). Control of mitochondrial morphology by a human mitofusin. *J Cell Sci* *114*, 867-874.
- Satoh,M., Hamamoto,T., Seo,N., Kagawa,Y., and Endo,H. (2003). Differential sublocalization of the dynamin-related protein OPA1 isoforms in mitochondria. *Biochem Biophys. Res Commun.* *300*, 482-493.
- Sesaki,H. and Jensen,R.E. (2001). UGO1 encodes an outer membrane protein required for mitochondrial fusion. *J. Cell Biol.* *152*, 1123-1134.
- Sesaki,H., Southard,S.M., Yaffe,M.P., and Jensen,R.E. (2003a). Mgm1p, a dynamin-related GTPase, is essential for fusion of the mitochondrial outer membrane. *Mol Biol Cell* *14*, 2342-2356.
- Sesaki,H., Southard,S.M., Hobbs,A.E., and Jensen,R.E. (2003b). Cells lacking Pcp1p/Ugo2p, a rhomboid-like protease required for Mgm1p processing, lose mtDNA and mitochondrial structure in a Dnm1p-dependent manner, but remain competent for mitochondrial fusion. *Biochem Biophys. Res Commun.* *308*, 276-283.
- Sesaki,H. and Jensen,R.E. (2004). Ugo1p links the Fzo1p and Mgm1p GTPases for mitochondrial fusion. *J Biol Chem.* *279*, 28298-28303.
- Shepard,K.A. and Yaffe,M.P. (1999). The yeast dynamin-like protein, Mgm1p, functions on the mitochondrial outer membrane to mediate mitochondrial inheritance. *J Cell Biol* *144*, 711-720.
- Shin,H.W., Takatsu,H., Mukai,H., Munekata,E., Murakami,K., and Nakayama,K. (1999). Intermolecular and interdomain interactions of a dynamin-related GTP-binding protein, Dnm1p/Vps1p-like protein. *J Biol Chem.* *274*, 2780-2785.
- Shoubridge,E.A. (2001). Nuclear genetic defects of oxidative phosphorylation. *Hum Mol Genet* *10*, 2277-2284.
- Smirnova,E., Griparic,L., Shurland,D.L., and van der Bliek,A.M. (2001). Dynamin-related protein Drp1 is required for mitochondrial division in mammalian cells. *Mol Biol Cell* *12*, 2245-2256.
- Smith,D.P. (1972). Diagnostic criteria in dominantly inherited juvenile optic atrophy. A report of three new families. *Am. J. Optom. Arch. Am. Acad. Optom.* *49*, 183-200.
- Spelbrink,J.N., Li,F.Y., Tiranti,V., Nikali,K., Yuan,Q.P., Tariq,M., Wanrooij,S., Garrido,N., Comi,G., Morandi,L., Santoro,L., Toscano,A., Fabrizi,G.M., Somer,H., Croxen,R., Beeson,D., Poulton,J., Suomalainen,A., Jacobs,H.T., Zeviani,M., and Larsson,C. (2001). Human mitochondrial DNA deletions associated with mutations in the gene encoding Twinkle, a phage T7 gene 4-like protein localized in mitochondria. *Nat Genet* *28*, 223-231.

- Stelzl,U., Worm,U., Lalowski,M., Haenig,C., Brembeck,F.H., Goehler,H., Stroedicke,M., Zenkner,M., Schoenherr,A., Koeppen,S., Timm,J., Mintzlaff,S., Abraham,C., Bock,N., Kietzmann,S., Goedde,A., Toksoz,E., Droege,A., Krobitsch,S., Korn,B., Birchmeier,W., Lehrach,H., and Wanker,E.E. (2005). A human protein-protein interaction network: a resource for annotating the proteome. *Cell* 122, 957-968.
- Sugioka,R., Shimizu,S., and Tsujimoto,Y. (2004). Fzo1, a protein involved in mitochondrial fusion, inhibits apoptosis. *J Biol Chem* 279, 52726-52734.
- Sweitzer,S.M. and Hinshaw,J.E. (1998). Dynamin undergoes a GTP-dependent conformational change causing vesiculation. *Cell* 93 , 1021-1029.
- Taylor,R.W. and Turnbull,D.M. (2005). Mitochondrial DNA mutations in human disease. *Nat Rev Genet* 6, 389-402.
- Thiselton,D.L., Alexander,C., Taanman,J.W., Brooks,S., Rosenberg,T., Eiberg,H., Andreasson,S., Van Regemorter,N., Munier,F.L., Moore,A.T., Bhattacharya,S.S., and Votruba,M. (2002). A comprehensive survey of mutations in the OPA1 gene in patients with autosomal dominant optic atrophy. *Invest Ophthalmol Vis Sci* 43, 1715-1724.
- Tieu,Q., Okreglak,V., Naylor,K., and Nunnari,J. (2002). The WD repeat protein, Mdvlp, functions as a molecular adaptor by interacting with Dnm1p and Fis1p during mitochondrial fission. *J Cell Biol* 158, 445-452.
- Tondera,D., Czauderna,F., Paulick,K., Schwarzer,R., Kaufmann,J., and Santel,A. (2005). The mitochondrial protein MTP18 contributes to mitochondrial fission in mammalian cells. *J Cell Sci* 118, 3049-3059.
- Toomes,C., Marchbank,N.J., Mackey,D.A., Craig,J.E., Newbury-Ecob,R.A., Bennett,C.P., Vize,C.J., Desai,S.P., Black,G.C., Patel,N., Teimory,M., Markham,A.F., Inglehearn,C.F., and Churchill,A.J. (2001). Spectrum, frequency and penetrance of OPA1 mutations in dominant optic atrophy. *Hum Mol Genet* 10, 1369-1378.
- Van Goethem,G., Dermaut,B., Lofgren,A., Martin,J.J., and Van Broeckhoven,C. (2001). Mutation of POLG is associated with progressive external ophthalmoplegia characterized by mtDNA deletions. *Nat Genet* 28, 211-212.
- Votruba,M., Moore,A.T., and Bhattacharya,S.S. (1998). Clinical features, molecular genetics, and pathophysiology of dominant optic atrophy. *J Med. Genet* 35, 793-800.
- von Mering,C., Krause,R., Snel,B., Cornell,M., Oliver,S.G., Fields,S. and Bork,P., (2002). Comparative assessment of large-scale data sets of protein-protein interactions. *Nature* 417, pp. 399-403.
- Wong,E.D., Wagner,J.A., Scott,S.V., Okreglak,V., Holewinske,T.J., Cassidy-Stone,A., and Nunnari,J. (2003). The intramitochondrial dynamin-related GTPase, Mgm1p, is a component of a protein complex that mediates mitochondrial fusion. *J Cell Biol* 160, 303-311.
- Yoon,Y., Krueger,E.W., Oswald,B.J., and McNiven,M.A. (2003). The mitochondrial protein hFis1 regulates mitochondrial fission in mammalian cells through an interaction with the dynamin-like protein DLP1. *Mol Cell Biol* 23, 5409-5420.
- Zuchner,S. and Vance,J.M. (2005). Emerging pathways for hereditary axonopathies. *J Mol Med*. 83, 935-943.
- Zuchner,S., De Jonghe,P., Jordanova,A., Claeys,K.G., Guergueltcheva,V., Cherninkova,S., Hamilton,S.R., Van Stavern,G., Krajewski,K.M., Stajich,J., Tournev,I., Verhoeven,K., Langerhorst,C.T., de Visser,M., Baas,F., Bird,T., Timmerman,V., Shy,M., and Vance,J.M. (2006). Axonal neuropathy with optic atrophy is caused by mutations in mitofusin 2. *Ann. Neurol.* 59, 276-281.