

DEPARTAMENT DE BIOQUÍMICA I BIOLOGIA MOLECULAR
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**EVOLUCIÓ DELS MECANISMES DE CONTROL
DEL METABOLISME DEL GLICOGEN**

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G. BIBLIOGRAFIA

- Abi-Rached, L., Gilles, A., Shiina, T., Pontarotti, P. and Inoko, H. (2002) Evidence of en bloc duplication in vertebrate genomes. *Nat Genet*, **31**, 100-105.
- Aflalo, C. and Azoulay, H. (1998) Binding of rat brain hexokinase to recombinant yeast mitochondria: effect of environmental factors and the source of porin. *J Bioenerg Biomembr*, **30**, 245-255.
- Agius, L., Centelles, J. and Cascante, M. (2002) Multiple glucose 6-phosphate pools or channelling of flux in diverse pathways? *Biochem Soc Trans*, **30**, 38-43.
- Agius, L. and Peak, M. (1997) Binding and translocation of glucokinase in hepatocytes. *Biochem Soc Trans*, **25**, 145-150.
- Ahmad, Z., Camici, M., DePaoli-Roach, A.A. and Roach, P.J. (1984) Glycogen synthase kinases. Classification of a rabbit liver casein and glycogen synthase kinase (casein kinase-1) as a distinct enzyme. *J Biol Chem*, **259**, 3420-3428.
- Aleshin, A.E., Zeng, C., Bourenkov, G.P., Bartunik, H.D., Fromm, H.J. and Honzatko, R.B. (1998) The mechanism of regulation of hexokinase: new insights from the crystal structure of recombinant human brain hexokinase complexed with glucose and glucose-6-phosphate. *Structure*, **6**, 39-50.
- Altschul, S.F., Madden, T.L., Schaffer, A.A., Zhang, J., Zhang, Z., Miller, W. and Lipman, D.J. (1997) Gapped BLAST and PSI-BLAST: a new generation of protein database search programs. *Nucleic Acids Res*, **25**, 3389-3402.
- Amores, A., Force, A., Yan, Y.L., Joly, L., Amemiya, C., Fritz, A., Ho, R.K., Langeland, J., Prince, V., Wang, Y.L., Westerfield, M., Ekker, M. and Postlethwait, J.H. (1998) Zebrafish hox clusters and vertebrate genome evolution. *Science*, **282**, 1711-1714.
- Ardehali, H., Printz, R.L., Whitesell, R.R., May, J.M. and Granner, D.K. (1999) Functional interaction between the N- and C-terminal halves of human hexokinase II. *J Biol Chem*, **274**, 15986-15989.
- Arden, C., Baltrusch, S. and Agius, L. (2006) Glucokinase regulatory protein is associated with mitochondria in hepatocytes. *FEBS Lett*, **580**, 2065-2070.
- Armstrong, C.G., Doherty, M.J. and Cohen, P.T. (1998) Identification of the separate domains in the hepatic glycogen-targeting subunit of protein phosphatase 1 that interact with phosphorylase a, glycogen and protein phosphatase 1. *Biochem J*, **336** (Pt 3), 699-704.
- Ball, S.G. and Morell, M.K. (2003) From bacterial glycogen to starch: understanding the biogenesis of the plant starch granule. *Annu Rev Plant Biol*, **54**, 207-233.
- Ballard, F.J. and Oliver, I.T. (1963) Glycogen metabolism in embryonic chick and neonatal rat liver. *Biochim Biophys Acta*, **71**, 578-588.

Baltrusch, S., Lenzen, S., Okar, D.A., Lange, A.J. and Tiedge, M. (2001) Characterization of glucokinase-binding protein epitopes by a phage-displayed peptide library. Identification of 6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase as a novel interaction partner. *J Biol Chem*, **276**, 43915-43923.

Battaglia, F.C. and Meschia, G. (1978) Principal substrates of fetal metabolism. *Physiol Rev*, **58**, 499-527.

BeltrandelRio, H. and Wilson, J.E. (1991) Hexokinase of rat brain mitochondria: relative importance of adenylate kinase and oxidative phosphorylation as sources of substrate ATP, and interaction with intramitochondrial compartments of ATP and ADP. *Arch Biochem Biophys*, **286**, 183-194.

BeltrandelRio, H. and Wilson, J.E. (1992a) Coordinated regulation of cerebral glycolytic and oxidative metabolism, mediated by mitochondrially bound hexokinase dependent on intramitochondrially generated ATP. *Arch Biochem Biophys*, **296**, 667-677.

BeltrandelRio, H. and Wilson, J.E. (1992b) Interaction of mitochondrially bound rat brain hexokinase with intramitochondrial compartments of ATP generated by oxidative phosphorylation and creatine kinase. *Arch Biochem Biophys*, **299**, 116-124.

Benner, S.A., Trabesinger, N. and Schreiber, D. (1998) Post-genomic science: converting primary structure into physiological function. *Adv Enzyme Regul*, **38**, 155-180.

Betran, E. and Long, M. (2002) Expansion of genome coding regions by acquisition of new genes. *Genetica*, **115**, 65-80.

Bork, P., Sander, C. and Valencia, A. (1993) Convergent evolution of similar enzymatic function on different protein folds: the hexokinase, ribokinase, and galactokinase families of sugar kinases. *Protein Sci*, **2**, 31-40.

Brown, J., Miller, D.M., Holloway, M.T. and Leve, G.D. (1967) Hexokinase isoenzymes in liver and adipose tissue of man and dog. *Science*, **155**, 205-207.

Browner, M.F., Nakano, K., Bang, A.G. and Fletterick, R.J. (1989) Human muscle glycogen synthase cDNA sequence: a negatively charged protein with an asymmetric charge distribution. *Proc Natl Acad Sci U S A*, **86**, 1443-1447.

Burt, C.T., Glonek, T. and Barany, M. (1976) Analysis of phosphate metabolites, the intracellular pH, and the state of adenosine triphosphate in intact muscle by phosphorus nuclear magnetic resonance. *J Biol Chem*, **251**, 2584-2591.

Buschiazzo, A., Ugalde, J.E., Guerin, M.E., Shepard, W., Ugalde, R.A. and Alzari, P.M. (2004) Crystal structure of glycogen synthase: homologous enzymes catalyze glycogen synthesis and degradation. *Embo J*, **23**, 3196-3205.

Canestro, C., Bassham, S. and Postlethwait, J.H. (2003) Seeing chordate evolution through the *Ciona* genome sequence. *Genome Biol*, **4**, 208.

- Carabaza, A., Ricart, M.D., Mor, A., Guinovart, J.J. and Ciudad, C.J. (1990) Role of AMP on the activation of glycogen synthase and phosphorylase by adenosine, fructose, and glutamine in rat hepatocytes. *J Biol Chem*, **265**, 2724-2732.
- Cardenas, M.L. (1997) Kinetic behaviour of vertebrate hexokinases with emphasis on hexokinase D (IV). *Biochem Soc Trans*, **25**, 131-135.
- Cárdenas, M.L. (1995) *Glucokinase: its regulation and role in liver metabolism*. Springer-Verlag, Austin, Texas.
- Cardenas, M.L., Cornish-Bowden, A. and Ureta, T. (1998) Evolution and regulatory role of the hexokinases. *Biochim Biophys Acta*, **1401**, 242-264.
- Cid, E. (2002) Glicogen sintasa muscular: Elements de control de la distribució subcel·lular i identificació de residus crítics per a la catàlisi. *Departament de Bioquímica i Biologia Molecular, Facultat de Química*. Universitat de Barcelona, Barcelona.
- Cid, E., Cifuentes, D., Baque, S., Ferrer, J.C. and Guinovart, J.J. (2005) Determinants of the nucleocytoplasmic shuttling of muscle glycogen synthase. *FEBS J*, **272**, 3197-3213.
- Cid, E., Geremia, R.A., Guinovart, J.J. and Ferrer, J.C. (2002) Glycogen synthase: towards a minimum catalytic unit? *FEBS Lett*, **528**, 5-11.
- Cid, E., Gomis, R.R., Geremia, R.A., Guinovart, J.J. and Ferrer, J.C. (2000) Identification of two essential glutamic acid residues in glycogen synthase. *J Biol Chem*, **275**, 33614-33621.
- Cohen, P. and Hardie, D.G. (1991) The actions of cyclic AMP on biosynthetic processes are mediated indirectly by cyclic AMP-dependent protein kinase. *Biochim Biophys Acta*, **1094**, 292-299.
- Couronne, O., Poliakov, A., Bray, N., Ishkhanov, T., Ryaboy, D., Rubin, E., Pachter, L. and Dubchak, I. (2003) Strategies and tools for whole-genome alignments. *Genome Res*, **13**, 73-80.
- Coutinho, P.M., Deleury, E., Davies, G.J. and Henrissat, B. (2003) An evolving hierarchical family classification for glycosyltransferases. *J Mol Biol*, **328**, 307-317.
- Danial, N.N., Gramm, C.F., Scorrano, L., Zhang, C.Y., Krauss, S., Ranger, A.M., Datta, S.R., Greenberg, M.E., Licklider, L.J., Lowell, B.B., Gygi, S.P. and Korsmeyer, S.J. (2003) BAD and glucokinase reside in a mitochondrial complex that integrates glycolysis and apoptosis. *Nature*, **424**, 952-956.
- Dawkins, M.J. (1963) Glycogen Synthesis and Breakdown in Fetal and Newborn Rat Liver. *Ann N Y Acad Sci*, **111**, 203-211.

de la Iglesia, N., Mukhtar, M., Seoane, J., Guinovart, J.J. and Agius, L. (2000) The role of the regulatory protein of glucokinase in the glucose sensory mechanism of the hepatocyte. *J Biol Chem*, **275**, 10597-10603.

de la Iglesia, N., Veiga-da-Cunha, M., Van Schaftingen, E., Guinovart, J.J. and Ferrer, J.C. (1999) Glucokinase regulatory protein is essential for the proper subcellular localisation of liver glucokinase. *FEBS Lett*, **456**, 332-338.

Delsuc, F., Brinkmann, H., Chourrout, D. and Philippe, H. (2006) Tunicates and not cephalochordates are the closest living relatives of vertebrates. *Nature*, **439**, 965-968.

Dentin, R., Pegorier, J.P., Benhamed, F., Foufelle, F., Ferre, P., Fauveau, V., Magnuson, M.A., Girard, J. and Postic, C. (2004) Hepatic glucokinase is required for the synergistic action of ChREBP and SREBP-1c on glycolytic and lipogenic gene expression. *J Biol Chem*, **279**, 20314-20326.

DeRisi, J.L., Iyer, V.R. and Brown, P.O. (1997) Exploring the metabolic and genetic control of gene expression on a genomic scale. *Science*, **278**, 680-686.

Dietrich, F.S., Voegeli, S., Brachat, S., Lerch, A., Gates, K., Steiner, S., Mohr, C., Pohlmann, R., Luedi, P., Choi, S., Wing, R.A., Flavier, A., Gaffney, T.D. and Philippsen, P. (2004) The *Ashbya gossypii* genome as a tool for mapping the ancient *Saccharomyces cerevisiae* genome. *Science*, **304**, 304-307.

Duret, L. (2002) Evolution of synonymous codon usage in metazoans. *Curr Opin Genet Dev*, **12**, 640-649.

Ellsworth, D.L., Hewett-Emmett, D. and Li, W.H. (1994) Evolution of base composition in the insulin and insulin-like growth factor genes. *Mol Biol Evol*, **11**, 875-885.

Fang, T.Y., Alechina, O., Aleshin, A.E., Fromm, H.J. and Honzatko, R.B. (1998) Identification of a phosphate regulatory site and a low affinity binding site for glucose 6-phosphate in the N-terminal half of human brain hexokinase. *J Biol Chem*, **273**, 19548-19553.

Farkas, I., Hardy, T.A., DePaoli-Roach, A.A. and Roach, P.J. (1990) Isolation of the GSY1 gene encoding yeast glycogen synthase and evidence for the existence of a second gene. *J Biol Chem*, **265**, 20879-20886.

Farkas, I., Hardy, T.A., Goebel, M.G. and Roach, P.J. (1991) Two glycogen synthase isoforms in *Saccharomyces cerevisiae* are coded by distinct genes that are differentially controlled. *J Biol Chem*, **266**, 15602-15607.

Farkas, I., Toth, B., Vereb, G., Csontos, C. and Gergely, P. (1988) Activation/dephosphorylation of rabbit muscle glycogen synthase by the catalytic subunits of protein phosphatase-1 and 2A. *Acta Biochim Biophys Hung*, **23**, 231-246.

Fernandez-Novell, J.M., Arino, J., Vilaro, S., Bellido, D. and Guinovart, J.J. (1992a) Role of glucose 6-phosphate in the translocation of glycogen synthase in rat hepatocytes. *Biochem J*, **288** (Pt 2), 497-501.

Fernandez-Novell, J.M., Arino, J., Vilaro, S. and Guinovart, J.J. (1992b) Glucose induces the translocation and the aggregation of glycogen synthase in rat hepatocytes. *Biochem J*, **281** (Pt 2), 443-448.

Fernandez-Novell, J.M., Lopez-Iglesias, C., Ferrer, J.C. and Guinovart, J.J. (2002) Zonal distribution of glycogen synthesis in isolated rat hepatocytes. *FEBS Lett*, **531**, 222-228.

Ferrer, J.C., Baque, S. and Guinovart, J.J. (1997) Muscle glycogen synthase translocates from the cell nucleus to the cytosol in response to glucose. *FEBS Lett*, **415**, 249-252.

Ferrer, J.C., Favre, C., Gomis, R.R., Fernandez-Novell, J.M., Garcia-Rocha, M., de la Iglesia, N., Cid, E. and Guinovart, J.J. (2003) Control of glycogen deposition. *FEBS Lett*, **546**, 127-132.

Fong, N.M., Jensen, T.C., Shah, A.S., Parekh, N.N., Saltiel, A.R. and Brady, M.J. (2000) Identification of binding sites on protein targeting to glycogen for enzymes of glycogen metabolism. *J Biol Chem*, **275**, 35034-35039.

Fothergill-Gilmore, L.A. and Michels, P.A. (1993) Evolution of glycolysis. *Prog Biophys Mol Biol*, **59**, 105-235.

Friedman, D.L. and Larner, J. (1962) Interconversion of two forms of muscle UDPG-alpha-glucan transglucosylase by a phosphorylation-dephosphorylation reaction sequence. *Biochim Biophys Acta*, **64**, 185-186.

Gancedo, J.M., Clifton, D. and Fraenkel, D.G. (1977) Yeast hexokinase mutants. *J Biol Chem*, **252**, 4443-4444.

Garcia-Rocha, M., Roca, A., De La Iglesia, N., Baba, O., Fernandez-Novell, J.M., Ferrer, J.C. and Guinovart, J.J. (2001) Intracellular distribution of glycogen synthase and glycogen in primary cultured rat hepatocytes. *Biochem J*, **357**, 17-24.

Garfinkel, L., Garfinkel, D., Matsiras, P. and Matschinsky, B. (1987) Kinetic properties of hexokinase as assembled with a microcomputer data base. *Biochem J*, **244**, 351-357.

Gasa, R., Jensen, P.B., Berman, H.K., Brady, M.J., DePaoli-Roach, A.A. and Newgard, C.B. (2000) Distinctive regulatory and metabolic properties of glycogen-targeting subunits of protein phosphatase-1 (PTG, GL, GM/RGI) expressed in hepatocytes. *J Biol Chem*, **275**, 26396-26403.

Girard, J., Ferre, P., Pegorier, J.P. and Duee, P.H. (1992) Adaptations of glucose and fatty acid metabolism during perinatal period and suckling-weaning transition. *Physiol Rev*, **72**, 507-562.

Goldsmith, E.J., Sprang, S.R., Hamlin, R., Xuong, N.H. and Fletterick, R.J. (1989) Domain separation in the activation of glycogen phosphorylase a. *Science*, **245**, 528-532.

Gomis, R.R., Cid, E., Garcia-Rocha, M., Ferrer, J.C. and Guinovart, J.J. (2002) Liver glycogen synthase but not the muscle isoform differentiates between glucose 6-phosphate produced by glucokinase or hexokinase. *J Biol Chem*, **277**, 23246-23252.

Gomis, R.R., Favre, C., Garcia-Rocha, M., Fernandez-Novell, J.M., Ferrer, J.C. and Guinovart, J.J. (2003) Glucose 6-phosphate produced by gluconeogenesis and by glucokinase is equally effective in activating hepatic glycogen synthase. *J Biol Chem*, **278**, 9740-9746.

Gomis, R.R., Ferrer, J.C. and Guinovart, J.J. (2000) Shared control of hepatic glycogen synthesis by glycogen synthase and glucokinase. *Biochem J*, **351 Pt 3**, 811-816.

Gottlob, K., Majewski, N., Kennedy, S., Kandel, E., Robey, R.B. and Hay, N. (2001) Inhibition of early apoptotic events by Akt/PKB is dependent on the first committed step of glycolysis and mitochondrial hexokinase. *Genes Dev*, **15**, 1406-1418.

Green, A.R., Aiston, S., Greenberg, C.C., Freeman, S., Poucher, S.M., Brady, M.J. and Agius, L. (2004) The glycogenic action of protein targeting to glycogen in hepatocytes involves multiple mechanisms including phosphorylase inactivation and glycogen synthase translocation. *J Biol Chem*, **279**, 46474-46482.

Hahn, M.W. and Wray, G.A. (2002) The g-value paradox. *Evol Dev*, **4**, 73-75.

Hampson, L.J. and Agius, L. (2005) Increased potency and efficacy of combined phosphorylase inactivation and glucokinase activation in control of hepatocyte glycogen metabolism. *Diabetes*, **54**, 617-623.

Hanashiro, I. and Roach, P.J. (2002) Mutations of muscle glycogen synthase that disable activation by glucose 6-phosphate. *Arch Biochem Biophys*, **397**, 286-292.

Henrissat, B., Deleury, E. and Coutinho, P.M. (2002) Glycogen metabolism loss: a common marker of parasitic behaviour in bacteria? *Trends Genet*, **18**, 437-440.

Hershfield, M.S. and Nemeth, A.M. (1968) Placental transport of free palmitic and linoleic acids in the guinea pig. *J Lipid Res*, **9**, 460-468.

Hillier, L.W., Miller, W., Birney, E., Warren, W., Hardison, R.C., Ponting, C.P., Bork, P., Burt, D.W., Groenen, M.A., Delany, M.E., Dodgson, J.B., Chinwalla, A.T., Cliften, P.F., Clifton, S.W., Delehaunty, K.D., Fronick, C., Fulton, R.S., Graves, T.A., Kremitzki, C., Layman, D., Magrini, V., McPherson, J.D., Miner, T.L., Minx, P., Nash, W.E., Nhan, M.N., Nelson, J.O., Oddy, L.G., Pohl, C.S.,

Randall-Maher, J., Smith, S.M., Wallis, J.W., Yang, S.P., Romanov, M.N., Rondelli, C.M., Paton, B., Smith, J., Morrice, D., Daniels, L., Tempest, H.G., Robertson, L., Masabanda, J.S., Griffin, D.K., Vignal, A., Fillon, V., Jacobsson, L., Kerje, S., Andersson, L., Crooijmans, R.P., Aerts, J., van der Poel, J.J., Ellegren, H., Caldwell, R.B., Hubbard, S.J., Grafham, D.V., Kierzek, A.M., McLaren, S.R., Overton, I.M., Arakawa, H., Beattie, K.J., Bezzubov, Y., Boardman, P.E., Bonfield, J.K., Croning, M.D., Davies, R.M., Francis, M.D., Humphray, S.J., Scott, C.E., Taylor, R.G., Tickle, C., Brown, W.R., Rogers, J., Buerstedde, J.M., Wilson, S.A., Stubbs, L., Ovcharenko, I., Gordon, L., Lucas, S., Miller, M.M., Inoko, H., Shiina, T., Kaufman, J., Salomonsen, J., Skjoedt, K., Wong, G.K., Wang, J., Liu, B., Yu, J., Yang, H., Nefedov, M., Koriabine, M., Dejong, P.J., Goodstadt, L., Webber, C., Dickens, N.J., Letunic, I., Suyama, M., Torrents, D., von Mering, C., Zdobnov, E.M., Makova, K., Nekrutenko, A., Elnitski, L., Eswara, P., King, D.C., Yang, S., Tyekucheva, S., Radakrishnan, A., Harris, R.S., Chiaromonte, F., Taylor, J., He, J., Rijkels, M., Griffiths-Jones, S., Ureta-Vidal, A., Hoffman, M.M., Severin, J., Searle, S.M., Law, A.S., Speed, D., Waddington, D., Cheng, Z., Tuzun, E., Eichler, E., Bao, Z., Flicek, P., Shteynberg, D.D., Brent, M.R., Bye, J.M., Huckle, E.J., Chatterji, S., Dewey, C., Pachter, L., Kouranov, A., Mourelatos, Z., Hatzigeorgiou, A.G., Paterson, A.H., Ivarie, R., Brandstrom, M., Axelsson, E., Backstrom, N., Berlin, S., Webster, M.T., Pourquie, O., Reymond, A., Ucla, C., Antonarakis, S.E., Long, M., Emerson, J.J., Betran, E., Dupanloup, I., Kaessmann, H., Hinrichs, A.S., Bejerano, G., Furey, T.S., Harte, R.A., Raney, B., Siepel, A., Kent, W.J., Haussler, D., Eyraes, E., Castelo, R., Abril, J.F., Castellano, S., Camara, F., Parra, G., Guigo, R., Bourque, G., Tesler, G., Pevzner, P.A., Smit, A., Fulton, L.A., Mardis, E.R. and Wilson, R.K. (2004) Sequence and comparative analysis of the chicken genome provide unique perspectives on vertebrate evolution. *Nature*, **432**, 695-716.

Horcajada, C., Cid, E., Guinovart, J.J., Verdaguer, N. and Ferrer, J.C. (2003) Crystallization and preliminary X-ray analysis of the glycogen synthase from *Pyrococcus abyssi*. *Acta Crystallogr D Biol Crystallogr*, **59**, 2322-2324.

Horcajada, C., Guinovart, J.J., Fita, I. and Ferrer, J.C. (2006) Crystal structure of an archaeal glycogen synthase: insights into oligomerization and substrate binding of eukaryotic glycogen synthases. *J Biol Chem*, **281**, 2923-2931.

Ingebritsen, T.S. and Cohen, P. (1983) Protein phosphatases: properties and role in cellular regulation. *Science*, **221**, 331-338.

Ingebritsen, T.S., Foulkes, J.G. and Cohen, P. (1983) The protein phosphatases involved in cellular regulation. 2. Glycogen metabolism. *Eur J Biochem*, **132**, 263-274.

Itarte, E. and Huang, K.P. (1979) Purification and properties of cyclic AMP-independent glycogen synthase kinase 1 from rabbit skeletal muscle. *J Biol Chem*, **254**, 4052-4057.

Iynedjian, P.B., Ucla, C. and Mach, B. (1987) Molecular cloning of glucokinase cDNA. Developmental and dietary regulation of glucokinase mRNA in rat liver. *J Biol Chem*, **262**, 6032-6038.

Jaillon, O., Aury, J.M., Brunet, F., Petit, J.L., Stange-Thomann, N., Mauceli, E., Bouneau, L., Fischer, C., Ozouf-Costaz, C., Bernot, A., Nicaud, S., Jaffe, D., Fisher, S., Lutfalla, G., Dossat, C., Segurens, B., Dasilva, C., Salanoubat, M., Levy, M., Boudet, N., Castellano, S., Anthouard, V., Jubin, C., Castelli, V., Katinka, M., Vacherie, B., Biemont, C., Skalli, Z., Cattolico, L., Poulain, J., De Berardinis, V., Cruaud, C., Duprat, S., Brottier, P., Coutanceau, J.P., Gouzy, J., Parra, G., Lardier, G., Chapple, C., McKernan, K.J., McEwan, P., Bosak, S., Kellis, M., Volff, J.N., Guigo, R., Zody, M.C., Mesirov, J., Lindblad-Toh, K., Birren, B., Nusbaum, C., Kahn, D., Robinson-Rechavi, M., Laudet, V., Schachter, V., Quetier, F., Saurin, W., Scarpelli, C., Wincker, P., Lander, E.S., Weissenbach, J. and Roest Crolius, H. (2004) Genome duplication in the teleost fish *Tetraodon nigroviridis* reveals the early vertebrate proto-karyotype. *Nature*, **431**, 946-957.

Jang, J.C., Leon, P., Zhou, L. and Sheen, J. (1997) Hexokinase as a sugar sensor in higher plants. *Plant Cell*, **9**, 5-19.

Jenness, R. (1974) Proceedings: Biosynthesis and composition of milk. *J Invest Dermatol*, **63**, 109-118.

Jones, C.T. and Rolph, T.P. (1985) Metabolism during fetal life: a functional assessment of metabolic development. *Physiol Rev*, **65**, 357-430.

Joost, H.G., Bell, G.I., Best, J.D., Birnbaum, M.J., Charron, M.J., Chen, Y.T., Doege, H., James, D.E., Lodish, H.F., Moley, K.H., Moley, J.F., Mueckler, M., Rogers, S., Schurmann, A., Seino, S. and Thorens, B. (2002) Nomenclature of the GLUT/SLC2A family of sugar/polyol transport facilitators. *Am J Physiol Endocrinol Metab*, **282**, E974-976.

Kaji, A., Trayser, K.A. and Colowick, S.P. (1961) Multiple forms of yeast hexokinase. *Ann N Y Acad Sci*, **94**, 798-811.

Kamata, K., Mitsuya, M., Nishimura, T., Eiki, J. and Nagata, Y. (2004) Structural basis for allosteric regulation of the monomeric allosteric enzyme human glucokinase. *Structure (Camb)*, **12**, 429-438.

Kanzaki, M. and Pessin, J.E. (2003) Insulin signaling: GLUT4 vesicles exit via the exocyst. *Curr Biol*, **13**, R574-576.

Kim, J.W. and Dang, C.V. (2005) Multifaceted roles of glycolytic enzymes. *Trends Biochem Sci*, **30**, 142-150.

Kim, Y.B., Peroni, O.D., Aschenbach, W.G., Minokoshi, Y., Kotani, K., Zisman, A., Kahn, C.R., Goodyear, L.J. and Kahn, B.B. (2005) Muscle-specific deletion of the *Glut4* glucose transporter alters multiple regulatory steps in glycogen metabolism. *Mol Cell Biol*, **25**, 9713-9723.

Kirschner, M. and Gerhart, J. (1998) Evolvability. *Proc Natl Acad Sci U S A*, **95**, 8420-8427.

Kogure, K., Shinohara, Y. and Terada, H. (1993) Evolution of the type II hexokinase gene by duplication and fusion of the glucokinase gene with conservation of its organization. *J Biol Chem*, **268**, 8422-8424.

Krissinel, E. and Henrick, K. (2004) Secondary-structure matching (SSM), a new tool for fast protein structure alignment in three dimensions. *Acta Crystallogr D Biol Crystallogr*, **60**, 2256-2268.

Kuser, P.R., Krauchenco, S., Antunes, O.A. and Polikarpov, I. (2000) The high resolution crystal structure of yeast hexokinase PII with the correct primary sequence provides new insights into its mechanism of action. *J Biol Chem*, **275**, 20814-20821.

L. F. Leloir and Cardini, C.E. (1957) Biosynthesis of glycogen from uridine diphosphate glucose. *J. Am. Chem. Soc.*, **79**, 6340-6341.

Lachaal, M. and Jung, C.Y. (1993) Interaction of facilitative glucose transporter with glucokinase and its modulation by ADP and glucose-6-phosphate. *J Cell Physiol*, **156**, 326-332.

Lander, E.S., Linton, L.M., Birren, B., Nusbaum, C., Zody, M.C., Baldwin, J., Devon, K., Dewar, K., Doyle, M., FitzHugh, W., Funke, R., Gage, D., Harris, K., Heaford, A., Howland, J., Kann, L., Lehoczky, J., LeVine, R., McEwan, P., McKernan, K., Meldrim, J., Mesirov, J.P., Miranda, C., Morris, W., Naylor, J., Raymond, C., Rosetti, M., Santos, R., Sheridan, A., Sougnez, C., Stange-Thomann, N., Stojanovic, N., Subramanian, A., Wyman, D., Rogers, J., Sulston, J., Ainscough, R., Beck, S., Bentley, D., Burton, J., Clee, C., Carter, N., Coulson, A., Deadman, R., Deloukas, P., Dunham, A., Dunham, I., Durbin, R., French, L., Grafham, D., Gregory, S., Hubbard, T., Humphray, S., Hunt, A., Jones, M., Lloyd, C., McMurray, A., Matthews, L., Mercer, S., Milne, S., Mullikin, J.C., Mungall, A., Plumb, R., Ross, M., Shownkeen, R., Sims, S., Waterston, R.H., Wilson, R.K., Hillier, L.W., McPherson, J.D., Marra, M.A., Mardis, E.R., Fulton, L.A., Chinwalla, A.T., Pepin, K.H., Gish, W.R., Chissole, S.L., Wendl, M.C., Delehaunty, K.D., Miner, T.L., Delehaunty, A., Kramer, J.B., Cook, L.L., Fulton, R.S., Johnson, D.L., Minx, P.J., Clifton, S.W., Hawkins, T., Branscomb, E., Predki, P., Richardson, P., Wenning, S., Slezak, T., Doggett, N., Cheng, J.F., Olsen, A., Lucas, S., Elkin, C., Uberbacher, E., Frazier, M., Gibbs, R.A., Muzny, D.M., Scherer, S.E., Bouck, J.B., Sodergren, E.J., Worley, K.C., Rives, C.M., Gorrell, J.H., Metzker, M.L., Naylor, S.L., Kucherlapati, R.S., Nelson, D.L., Weinstock, G.M., Sakaki, Y., Fujiyama, A., Hattori, M., Yada, T., Toyoda, A., Itoh, T., Kawagoe, C., Watanabe, H., Totoki, Y., Taylor, T., Weissenbach, J., Heilig, R., Saurin, W., Artiguenave, F., Brottier, P., Bruls, T., Pelletier, E., Robert, C., Wincker, P., Smith, D.R., Doucette-Stamm, L., Rubenfield, M., Weinstock, K., Lee, H.M., Dubois, J., Rosenthal, A., Platzer, M., Nyakatura, G., Taudien, S., Rump, A., Yang, H., Yu, J., Wang, J., Huang, G., Gu, J., Hood, L., Rowen, L., Madan, A., Qin, S., Davis, R.W., Federspiel, N.A., Abola, A.P., Proctor, M.J., Myers, R.M., Schmutz, J., Dickson, M., Grimwood, J., Cox, D.R., Olson, M.V., Kaul, R., Shimizu, N., Kawasaki, K., Minoshima, S., Evans, G.A., Athanasiou, M., Schultz, R., Roe, B.A., Chen, F., Pan, H., Ramser, J., Lehrach, H., Reinhardt, R., McCombie, W.R., de la Bastide, M., Dedhia, N., Blocker, H., Hornischer, K., Nordsiek, G., Agarwala, R., Aravind, L., Bailey, J.A., Bateman,

A., Batzoglou, S., Birney, E., Bork, P., Brown, D.G., Burge, C.B., Cerutti, L., Chen, H.C., Church, D., Clamp, M., Copley, R.R., Doerks, T., Eddy, S.R., Eichler, E.E., Furey, T.S., Galagan, J., Gilbert, J.G., Harmon, C., Hayashizaki, Y., Haussler, D., Hermjakob, H., Hokamp, K., Jang, W., Johnson, L.S., Jones, T.A., Kasif, S., Kasprzyk, A., Kennedy, S., Kent, W.J., Kitts, P., Koonin, E.V., Korf, I., Kulp, D., Lancet, D., Lowe, T.M., McLysaght, A., Mikkelsen, T., Moran, J.V., Mulder, N., Pollara, V.J., Ponting, C.P., Schuler, G., Schultz, J., Slater, G., Smit, A.F., Stupka, E., Szustakowski, J., Thierry-Mieg, D., Thierry-Mieg, J., Wagner, L., Wallis, J., Wheeler, R., Williams, A., Wolf, Y.I., Wolfe, K.H., Yang, S.P., Yeh, R.F., Collins, F., Guyer, M.S., Peterson, J., Felsenfeld, A., Wetterstrand, K.A., Patrinos, A., Morgan, M.J., de Jong, P., Catanese, J.J., Osoegawa, K., Shizuya, H., Choi, S. and Chen, Y.J. (2001) Initial sequencing and analysis of the human genome. *Nature*, **409**, 860-921.

Leloir, L.F., Olavarria, J.M., Goldemberg, S.H. and Carminatti, H. (1959) Biosynthesis of glycogen from uridine diphosphate glucose. *Arch Biochem Biophys*, **81**, 508-520.

Levine, M. and Tjian, R. (2003) Transcription regulation and animal diversity. *Nature*, **424**, 147-151.

Liberles, D.A. (2001) Evaluation of methods for determination of a reconstructed history of gene sequence evolution. *Mol Biol Evol*, **18**, 2040-2047.

Lindblad-Toh, K., Wade, C.M., Mikkelsen, T.S., Karlsson, E.K., Jaffe, D.B., Kamal, M., Clamp, M., Chang, J.L., Kulbokas, E.J., 3rd, Zody, M.C., Mauceli, E., Xie, X., Breen, M., Wayne, R.K., Ostrander, E.A., Ponting, C.P., Galibert, F., Smith, D.R., DeJong, P.J., Kirkness, E., Alvarez, P., Biagi, T., Brockman, W., Butler, J., Chin, C.W., Cook, A., Cuff, J., Daly, M.J., DeCaprio, D., Gnerre, S., Grabherr, M., Kellis, M., Kleber, M., Bardeleben, C., Goodstadt, L., Heger, A., Hitte, C., Kim, L., Koepfli, K.P., Parker, H.G., Pollinger, J.P., Searle, S.M., Sutter, N.B., Thomas, R., Webber, C., Baldwin, J., Abebe, A., Abouelleil, A., Aftuck, L., Ait-Zahra, M., Aldredge, T., Allen, N., An, P., Anderson, S., Antoine, C., Arachchi, H., Aslam, A., Ayotte, L., Bachantsang, P., Barry, A., Bayul, T., Benamara, M., Berlin, A., Bessette, D., Blitshteyn, B., Bloom, T., Blye, J., Boguslavskiy, L., Bonnet, C., Boukhgalter, B., Brown, A., Cahill, P., Calixte, N., Camarata, J., Cheshatsang, Y., Chu, J., Citroen, M., Collymore, A., Cooke, P., Dawoe, T., Daza, R., Decktor, K., DeGray, S., Dhargay, N., Dooley, K., Dorje, P., Dorjee, K., Dorris, L., Duffey, N., Dupes, A., Egbiremolen, O., Elong, R., Falk, J., Farina, A., Faro, S., Ferguson, D., Ferreira, P., Fisher, S., FitzGerald, M., Foley, K., Foley, C., Franke, A., Friedrich, D., Gage, D., Garber, M., Gearin, G., Giannoukos, G., Goode, T., Goyette, A., Graham, J., Grandbois, E., Gyaltsen, K., Hafez, N., Hagopian, D., Hagos, B., Hall, J., Healy, C., Hegarty, R., Honan, T., Horn, A., Houde, N., Hughes, L., Hunnicutt, L., Husby, M., Jester, B., Jones, C., Kamat, A., Kanga, B., Kells, C., Khazanovich, D., Kieu, A.C., Kisner, P., Kumar, M., Lance, K., Landers, T., Lara, M., Lee, W., Leger, J.P., Lennon, N., Leuper, L., LeVine, S., Liu, J., Liu, X., Lokyitsang, Y., Lokyitsang, T., Lui, A., Macdonald, J., Major, J., Marabella, R., Maru, K., Matthews, C., McDonough, S., Mehta, T., Meldrim, J., Melnikov, A., Meneus, L., Mihalev, A., Mihova, T., Miller, K., Mittelman, R., Mlenga, V., Mulrain, L., Munson, G.,

Navidi, A., Naylor, J., Nguyen, T., Nguyen, N., Nguyen, C., Nicol, R., Norbu, N., Norbu, C., Novod, N., Nyima, T., Olandt, P., O'Neill, B., O'Neill, K., Osman, S., Oyono, L., Patti, C., Perrin, D., Phunkhang, P., Pierre, F., Priest, M., Rachupka, A., Raghuraman, S., Rameau, R., Ray, V., Raymond, C., Rege, F., Rise, C., Rogers, J., Rogov, P., Sahalie, J., Settipalli, S., Sharpe, T., Shea, T., Sheehan, M., Sherpa, N., Shi, J., Shih, D., Sloan, J., Smith, C., Sparrow, T., Stalker, J., Stange-Thomann, N., Stavropoulos, S., Stone, C., Stone, S., Sykes, S., Tchuinga, P., Tenzing, P., Tesfaye, S., Thoulutsang, D., Thoulutsang, Y., Topham, K., Topping, I., Tsamla, T., Vassiliev, H., Venkataraman, V., Vo, A., Wangchuk, T., Wangdi, T., Weiland, M., Wilkinson, J., Wilson, A., Yadav, S., Yang, S., Yang, X., Young, G., Yu, Q., Zainoun, J., Zembek, L., Zimmer, A. and Lander, E.S. (2005) Genome sequence, comparative analysis and haplotype structure of the domestic dog. *Nature*, **438**, 803-819.

Lomako, J., Lomako, W.M. and Whelan, W.J. (2004) Glycogenin: the primer for mammalian and yeast glycogen synthesis. *Biochim Biophys Acta*, **1673**, 45-55.

Lynch, M. and Conery, J.S. (2000) The evolutionary fate and consequences of duplicate genes. *Science*, **290**, 1151-1155.

Machida, K., Ohta, Y. and Osada, H. (2006) Suppression of apoptosis by cyclophilin D via stabilization of hexokinase II mitochondrial binding in cancer cells. *J Biol Chem*.

Maier, T., Jenni, S. and Ban, N. (2006) Architecture of mammalian fatty acid synthase at 4.5 Å resolution. *Science*, **311**, 1258-1262.

Majewski, N., Nogueira, V., Bhaskar, P., Coy, P.E., Skeen, J.E., Gottlob, K., Chandel, N.S., Thompson, C.B., Robey, R.B. and Hay, N. (2004) Hexokinase-mitochondria interaction mediated by Akt is required to inhibit apoptosis in the presence or absence of Bax and Bak. *Mol Cell*, **16**, 819-830.

Malaisse, W.J., Malaisse-Lagae, F., Davies, D.R., Vandercammen, A. and Van Schaftingen, E. (1990) Regulation of glucokinase by a fructose-1-phosphate-sensitive protein in pancreatic islets. *Eur J Biochem*, **190**, 539-545.

Mayordomo, I. and Sanz, P. (2001) Human pancreatic glucokinase (GlkB) complements the glucose signalling defect of *Saccharomyces cerevisiae* hxx2 mutants. *Yeast*, **18**, 1309-1316.

Melendez, R., Melendez-Hevia, E. and Canela, E.I. (1999) The fractal structure of glycogen: A clever solution to optimize cell metabolism. *Biophys J*, **77**, 1327-1332.

Melendez, R., Melendez-Hevia, E. and Cascante, M. (1997) How did glycogen structure evolve to satisfy the requirement for rapid mobilization of glucose? A problem of physical constraints in structure building. *J Mol Evol*, **45**, 446-455.

Mu, J. and Roach, P.J. (1998) Characterization of human glycogenin-2, a self-glucosylating initiator of liver glycogen metabolism. *J Biol Chem*, **273**, 34850-34856.

- Mu, J., Skurat, A.V. and Roach, P.J. (1997) Glycogenin-2, a novel self-glycosylating protein involved in liver glycogen biosynthesis. *J Biol Chem*, **272**, 27589-27597.
- Mulichak, A.M., Wilson, J.E., Padmanabhan, K. and Garavito, R.M. (1998) The structure of mammalian hexokinase-1. *Nat Struct Biol*, **5**, 555-560.
- Narkewicz, M.R., Iynedjian, P.B., Ferre, P. and Girard, J. (1990) Insulin and triiodothyronine induce glucokinase mRNA in primary cultures of neonatal rat hepatocytes. *Biochem J*, **271**, 585-589.
- Newgard, C.B., Brady, M.J., O'Doherty, R.M. and Saltiel, A.R. (2000) Organizing glucose disposal: emerging roles of the glycogen targeting subunits of protein phosphatase-1. *Diabetes*, **49**, 1967-1977.
- Newgard, C.B., Nakano, K., Hwang, P.K. and Fletterick, R.J. (1986) Sequence analysis of the cDNA encoding human liver glycogen phosphorylase reveals tissue-specific codon usage. *Proc Natl Acad Sci U S A*, **83**, 8132-8136.
- Nobrega, M.A., Zhu, Y., Plajzer-Frick, I., Afzal, V. and Rubin, E.M. (2004) Megabase deletions of gene deserts result in viable mice. *Nature*, **431**, 988-993.
- Novak, M., Melichar, V. and Hahn, P. (1964) Postnatal Changes in the Blood Serum Content of Glycerol and Fatty Acids in Human Infants. *Biol Neonat*, **7**, 179-184.
- Nuttall, F.Q., Gannon, M.C., Bai, G. and Lee, E.Y. (1994) Primary structure of human liver glycogen synthase deduced by cDNA cloning. *Arch Biochem Biophys*, **311**, 443-449.
- O'Doherty, R.M., Lehman, D.L., Seoane, J., Gomez-Foix, A.M., Guinovart, J.J. and Newgard, C.B. (1996) Differential metabolic effects of adenovirus-mediated glucokinase and hexokinase I overexpression in rat primary hepatocytes. *J Biol Chem*, **271**, 20524-20530.
- Ohtsubo, K., Takamatsu, S., Minowa, M.T., Yoshida, A., Takeuchi, M. and Marth, J.D. (2005) Dietary and genetic control of glucose transporter 2 glycosylation promotes insulin secretion in suppressing diabetes. *Cell*, **123**, 1307-1321.
- Ossareh-Nazari, B., Bachelier, F. and Dargemont, C. (1997) Evidence for a role of CRM1 in signal-mediated nuclear protein export. *Science*, **278**, 141-144.
- Pastorino, J.G., Hoek, J.B. and Shulga, N. (2005) Activation of glycogen synthase kinase 3 β disrupts the binding of hexokinase II to mitochondria by phosphorylating voltage-dependent anion channel and potentiates chemotherapy-induced cytotoxicity. *Cancer Res*, **65**, 10545-10554.

- Pastorino, J.G., Shulga, N. and Hoek, J.B. (2002) Mitochondrial binding of hexokinase II inhibits Bax-induced cytochrome c release and apoptosis. *J Biol Chem*, **277**, 7610-7618.
- Peden, J.F. (1999) Analysis of Codon Usage. University of Nottingham, Nottingham, UK.
- Pederson, B.A., Cheng, C., Wilson, W.A. and Roach, P.J. (2000) Regulation of glycogen synthase. Identification of residues involved in regulation by the allosteric ligand glucose-6-P and by phosphorylation. *J Biol Chem*, **275**, 27753-27761.
- Penso, J. and Beitner, R. (1998) Clotrimazole and bifonazole detach hexokinase from mitochondria of melanoma cells. *Eur J Pharmacol*, **342**, 113-117.
- Perdereau, D., Narkewicz, M., Coupe, C., Ferre, P. and Girard, J. (1990) Hormonal control of specific gene expression in the rat liver during the suckling-weaning transition. *Adv Enzyme Regul*, **30**, 91-108.
- Postic, C., Leturque, A., Printz, R.L., Maulard, P., Loizeau, M., Granner, D.K. and Girard, J. (1994) Development and regulation of glucose transporter and hexokinase expression in rat. *Am J Physiol*, **266**, E548-559.
- Postic, C., Shiota, M., Niswender, K.D., Jetton, T.L., Chen, Y., Moates, J.M., Shelton, K.D., Lindner, J., Cherrington, A.D. and Magnuson, M.A. (1999) Dual roles for glucokinase in glucose homeostasis as determined by liver and pancreatic beta cell-specific gene knock-outs using Cre recombinase. *J Biol Chem*, **274**, 305-315.
- Printen, J.A., Brady, M.J. and Saltiel, A.R. (1997) PTG, a protein phosphatase 1-binding protein with a role in glycogen metabolism. *Science*, **275**, 1475-1478.
- Printz, R.L., Koch, S., Potter, L.R., O'Doherty, R.M., Tiesinga, J.J., Moritz, S. and Granner, D.K. (1993) Hexokinase II mRNA and gene structure, regulation by insulin, and evolution. *J Biol Chem*, **268**, 5209-5219.
- Rabuazzo, A.M., Patane, G., Anello, M., Piro, S., Vigneri, R. and Purrello, F. (1997) Hexokinase shift to mitochondria is associated with an increased sensitivity to glucose in rat pancreatic islets. *Diabetes*, **46**, 1148-1152.
- Roach, P.J. (1990) Control of glycogen synthase by hierarchal protein phosphorylation. *Faseb J*, **4**, 2961-2968.
- Roach, P.J., Cao, Y., Corbett, C.A., DePaoli-Roach, A.A., Farkas, I., Fiol, C.J., Flotow, H., Graves, P.R., Hardy, T.A., Hrubey, T.W. and et al. (1991) Glycogen metabolism and signal transduction in mammals and yeast. *Adv Enzyme Regul*, **31**, 101-120.
- Roach, P.J., DePaoli-Roach, A.A. and Larner, J. (1978) Ca²⁺-stimulated phosphorylation of muscle glycogen synthase by phosphorylase b kinase. *J Cyclic Nucleotide Res*, **4**, 245-257.

Roach, P.J. and Larner, J. (1976) Rabbit skeletal muscle glycogen synthase. II. Enzyme phosphorylation state and effector concentrations as interacting control parameters. *J Biol Chem*, **251**, 1920-1925.

Roach, P.J., Takeda, Y. and Larner, J. (1976) Rabbit skeletal muscle glycogen synthase. I. Relationship between phosphorylation state and kinetic properties. *J Biol Chem*, **251**, 1913-1919.

Rodin, S.N. and Parkhomchuk, D.V. (2004) Position-associated GC asymmetry of gene duplicates. *J Mol Evol*, **59**, 372-384.

Rodriguez, A., De La Cera, T., Herrero, P. and Moreno, F. (2001) The hexokinase 2 protein regulates the expression of the GLK1, HXK1 and HXK2 genes of *Saccharomyces cerevisiae*. *Biochem J*, **355**, 625-631.

Salavert, A., Itarte, E., Massague, J. and Guinovart, J.J. (1979) Multiple phosphorylation of rabbit muscle glycogen synthase by glycogen synthase kinase-1. Relationship between phosphorylation state and kinetic properties. *FEBS Lett*, **106**, 279-283.

Saltiel, A.R. (2001) New perspectives into the molecular pathogenesis and treatment of type 2 diabetes. *Cell*, **104**, 517-529.

Scannell, D.R., Byrne, K.P., Gordon, J.L., Wong, S. and Wolfe, K.H. (2006) Multiple rounds of speciation associated with reciprocal gene loss in polyploid yeasts. *Nature*, **440**, 341-345.

Seoane, J., Barbera, A., Telemaque-Potts, S., Newgard, C.B. and Guinovart, J.J. (1999) Glucokinase overexpression restores glucose utilization and storage in cultured hepatocytes from male Zucker diabetic fatty rats. *J Biol Chem*, **274**, 31833-31838.

Seoane, J., Gomez-Foix, A.M., O'Doherty, R.M., Gomez-Ara, C., Newgard, C.B. and Guinovart, J.J. (1996) Glucose 6-phosphate produced by glucokinase, but not hexokinase I, promotes the activation of hepatic glycogen synthase. *J Biol Chem*, **271**, 23756-23760.

Shelley, H.J. (1964) Carbohydrate Reserves in the Newborn Infant. *Br Med J*, **5378**, 273-275.

Skurat, A.V. and Dietrich, A.D. (2004) Phosphorylation of Ser640 in muscle glycogen synthase by DYRK family protein kinases. *J Biol Chem*, **279**, 2490-2498.

Skurat, A.V. and Roach, P.J. (1995) Phosphorylation of sites 3a and 3b (Ser640 and Ser644) in the control of rabbit muscle glycogen synthase. *J Biol Chem*, **270**, 12491-12497.

Skurat, A.V., Wang, Y. and Roach, P.J. (1994) Rabbit skeletal muscle glycogen synthase expressed in COS cells. Identification of regulatory phosphorylation sites. *J Biol Chem*, **269**, 25534-25542.

Sprang, S.R., Acharya, K.R., Goldsmith, E.J., Stuart, D.I., Varvill, K., Fletterick, R.J., Madsen, N.B. and Johnson, L.N. (1988) Structural changes in glycogen phosphorylase induced by phosphorylation. *Nature*, **336**, 215-221.

Sprang, S.R., Withers, S.G., Goldsmith, E.J., Fletterick, R.J. and Madsen, N.B. (1991) Structural basis for the activation of glycogen phosphorylase b by adenosine monophosphate. *Science*, **254**, 1367-1371.

Srere, P.A. and Ovadi, J. (1990) Enzyme-enzyme interactions and their metabolic role. *FEBS Lett*, **268**, 360-364.

Steensberg, A., Febbraio, M.A., Osada, T., Schjerling, P., van Hall, G., Saltin, B. and Pedersen, B.K. (2001) Interleukin-6 production in contracting human skeletal muscle is influenced by pre-exercise muscle glycogen content. *J Physiol*, **537**, 633-639.

Su, A.I., Wiltshire, T., Batalov, S., Lapp, H., Ching, K.A., Block, D., Zhang, J., Soden, R., Hayakawa, M., Kreiman, G., Cooke, M.P., Walker, J.R. and Hogenesch, J.B. (2004) A gene atlas of the mouse and human protein-encoding transcriptomes. *Proc Natl Acad Sci U S A*, **101**, 6062-6067.

Sui, D. and Wilson, J.E. (1997) Structural determinants for the intracellular localization of the isozymes of mammalian hexokinase: intracellular localization of fusion constructs incorporating structural elements from the hexokinase isozymes and the green fluorescent protein. *Arch Biochem Biophys*, **345**, 111-125.

Thorens, B. (2001) GLUT2 in pancreatic and extra-pancreatic gluco-detection (review). *Mol Membr Biol*, **18**, 265-273.

Uldry, M. and Thorens, B. (2004) The SLC2 family of facilitated hexose and polyol transporters. *Pflugers Arch*.

Ureta, T. and Radojkovic, J. (1987) Organisation of glucose metabolism: A model of compartments by poly-isozymic complexes. In Clegg, J.S. (ed.), *The organisation of cell metabolism*. Plenum Publishing Corporation.

Van Duyne, C.M. (1965) Free fatty acid metabolism during perinatal life. *Biol Neonat*, **9**, 115-123.

van Schaftingen, E., Veiga-da-Cunha, M. and Niculescu, L. (1997) The regulatory protein of glucokinase. *Biochem Soc Trans*, **25**, 136-140.

Veiga-da-Cunha, M., Courtois, S., Michel, A., Gosselain, E. and Van Schaftingen, E. (1996) Amino acid conservation in animal glucokinases. Identification of residues implicated in the interaction with the regulatory protein. *J Biol Chem*, **271**, 6292-6297.

Villar-Palasi, C. (1991) Substrate specific activation by glucose 6-phosphate of the dephosphorylation of muscle glycogen synthase. *Biochim Biophys Acta*, **1095**, 261-267.

Villar-Palasi, C. and Guinovart, J.J. (1997) The role of glucose 6-phosphate in the control of glycogen synthase. *Faseb J*, **11**, 544-558.

Vinogradov, A.E. (2003) Isochores and tissue-specificity. *Nucleic Acids Res*, **31**, 5212-5220.

Vinuela, E., Salas, M. and Sols, A. (1963) Glucokinase and hexokinase in liver in relation to glycogen synthesis. *J Biol Chem*, **238**, 1175-1177.

Walmsley, A.R., Barrett, M.P., Bringaud, F. and Gould, G.W. (1998) Sugar transporters from bacteria, parasites and mammals: structure-activity relationships. *Trends Biochem Sci*, **23**, 476-481.

Waterston, R.H., Lindblad-Toh, K., Birney, E., Rogers, J., Abril, J.F., Agarwal, P., Agarwala, R., Ainscough, R., Alexandersson, M., An, P., Antonarakis, S.E., Attwood, J., Baertsch, R., Bailey, J., Barlow, K., Beck, S., Berry, E., Birren, B., Bloom, T., Bork, P., Botcherby, M., Bray, N., Brent, M.R., Brown, D.G., Brown, S.D., Bult, C., Burton, J., Butler, J., Campbell, R.D., Carninci, P., Cawley, S., Chiaromonte, F., Chinwalla, A.T., Church, D.M., Clamp, M., Clee, C., Collins, F.S., Cook, L.L., Copley, R.R., Coulson, A., Couronne, O., Cuff, J., Curwen, V., Cutts, T., Daly, M., David, R., Davies, J., Delehaunty, K.D., Deri, J., Dermitzakis, E.T., Dewey, C., Dickens, N.J., Diekhans, M., Dodge, S., Dubchak, I., Dunn, D.M., Eddy, S.R., Elnitski, L., Emes, R.D., Eswara, P., Eyras, E., Felsenfeld, A., Fewell, G.A., Flicek, P., Foley, K., Frankel, W.N., Fulton, L.A., Fulton, R.S., Furey, T.S., Gage, D., Gibbs, R.A., Glusman, G., Gnerre, S., Goldman, N., Goodstadt, L., Grafham, D., Graves, T.A., Green, E.D., Gregory, S., Guigo, R., Guyer, M., Hardison, R.C., Haussler, D., Hayashizaki, Y., Hillier, L.W., Hinrichs, A., Hlavina, W., Holzer, T., Hsu, F., Hua, A., Hubbard, T., Hunt, A., Jackson, I., Jaffe, D.B., Johnson, L.S., Jones, M., Jones, T.A., Joy, A., Kamal, M., Karlsson, E.K., Karolchik, D., Kasprzyk, A., Kawai, J., Keibler, E., Kells, C., Kent, W.J., Kirby, A., Kolbe, D.L., Korf, I., Kucherlapati, R.S., Kulbokas, E.J., Kulp, D., Landers, T., Leger, J.P., Leonard, S., Letunic, I., Levine, R., Li, J., Li, M., Lloyd, C., Lucas, S., Ma, B., Maglott, D.R., Mardis, E.R., Matthews, L., Mauceli, E., Mayer, J.H., McCarthy, M., McCombie, W.R., McLaren, S., McLay, K., McPherson, J.D., Meldrim, J., Meredith, B., Mesirov, J.P., Miller, W., Miner, T.L., Mongin, E., Montgomery, K.T., Morgan, M., Mott, R., Mullikin, J.C., Muzny, D.M., Nash, W.E., Nelson, J.O., Nhan, M.N., Nicol, R., Ning, Z., Nusbaum, C., O'Connor, M.J., Okazaki, Y., Oliver, K., Overton-Larty, E., Pachter, L., Parra, G., Pepin, K.H., Peterson, J., Pevzner, P., Plumb, R., Pohl, C.S., Poliakov, A., Ponce, T.C., Ponting, C.P., Potter, S., Quail, M., Reymond, A., Roe, B.A., Roskin, K.M., Rubin, E.M., Rust, A.G., Santos, R., Sapojnikov, V., Schultz, B., Schultz, J., Schwartz, M.S., Schwartz, S., Scott, C., Seaman, S., Searle, S., Sharpe, T., Sheridan, A., Shownkeen, R., Sims, S., Singer, J.B., Slater, G., Smit, A., Smith, D.R., Spencer, B., Stabenau, A., Stange-Thomann, N., Sugnet, C., Suyama, M., Tesler, G., Thompson, J., Torrents, D., Trevaskis, E., Tromp, J., Ucla, C., Ureta-Vidal, A., Vinson, J.P., Von Niederhausern, A.C., Wade, C.M., Wall, M., Weber, R.J., Weiss, R.B., Wendl, M.C., West, A.P., Wetterstrand, K., Wheeler, R., Whelan, S., Wierzbowski, J., Willey, D., Williams, S., Wilson, R.K., Winter, E., Worley, K.C., Wyman, D., Yang, S., Yang, S.P., Zdobnov, E.M., Zody, M.C. and Lander, E.S.

(2002) Initial sequencing and comparative analysis of the mouse genome. *Nature*, **420**, 520-562.

Watson, R.T. and Pessin, J.E. (2006) Bridging the GAP between insulin signaling and GLUT4 translocation. *Trends Biochem Sci*, **31**, 215-222.

Wilson, J.E. (1997) An introduction to the isoenzymes of mammalian hexokinase types I-III. *Biochem Soc Trans*, **25**, 103-107.

Wilson, J.E. (2003) Isozymes of mammalian hexokinase: structure, subcellular localization and metabolic function. *J Exp Biol*, **206**, 2049-2057.

Wilson, W.A., Skurat, A.V., Probst, B., de Paoli-Roach, A., Roach, P.J. and Rutter, J. (2005) Control of mammalian glycogen synthase by PAS kinase. *Proc Natl Acad Sci U S A*, **102**, 16596-16601.

Woodgett, J.R., Tonks, N.K. and Cohen, P. (1982) Identification of a calmodulin-dependent glycogen synthase kinase in rabbit skeletal muscle, distinct from phosphorylase kinase. *FEBS Lett*, **148**, 5-11.

Wright, F. (1990) The 'effective number of codons' used in a gene. *Gene*, **87**, 23-29.

Wu, J., Liu, J., Thompson, I., Oliver, C.J., Shenolikar, S. and Brautigan, D.L. (1998) A conserved domain for glycogen binding in protein phosphatase-1 targeting subunits. *FEBS Lett*, **439**, 185-191.

Xia, X., Xie, Z. and Li, W.H. (2003) Effects of GC content and mutational pressure on the lengths of exons and coding sequences. *J Mol Evol*, **56**, 362-370.

Yamashita, R., Suzuki, Y., Sugano, S. and Nakai, K. (2005) Genome-wide analysis reveals strong correlation between CpG islands with nearby transcription start sites of genes and their tissue specificity. *Gene*, **350**, 129-136.

Yang, R., Cao, L., Gasa, R., Brady, M.J., Sherry, A.D. and Newgard, C.B. (2002) Glycogen-targeting subunits and glucokinase differentially affect pathways of glycogen metabolism and their regulation in hepatocytes. *J Biol Chem*, **277**, 1514-1523.

Zeng, C., Aleshin, A.E., Hardie, J.B., Harrison, R.W. and Fromm, H.J. (1996) ATP-binding site of human brain hexokinase as studied by molecular modeling and site-directed mutagenesis. *Biochemistry*, **35**, 13157-13164.

Zvibel, I., Fiorino, A.S., Brill, S. and Reid, L.M. (1998) Phenotypic characterization of rat hepatoma cell lines and lineage-specific regulation of gene expression by differentiation agents. *Differentiation*, **63**, 215-223.