

# Credits

## 1. Illustration and text revision team

**Illustrator (except caricatures and PDB molecular graphics):** Julio Xerfan, MD.

**Molecular Graphics Designer:** Fabiana Carneiro, PhD.

**Caricaturist:** Bruno Matos Vieira, PhD.

**Text reviewer:** Franklin David Rumjanek, PhD.

## 2. Complete list of references from which illustrations were reprinted:

**Figure 1.1:** Moreira D, López-García P. Ten reasons to exclude viruses from the tree of life. *Nat. Rev. Microbiol.* 7:306–311, 2009.

**Figures 1.2 and 1.4:** Saphiro R. El origen de la vida. *Investigacion y Ciencia* 371, Prensa Cientifica SA, 2007.

**Figure 1.8:** Stevens J, Corper AL, Basler CF, Taubenberger JK, Palese P, Wilson IA. Structure of the uncleaved human H1 hemagglutinin from the extinct 1918 influenza virus. *Science* 303:1866–1870, 2004.

**Figure Box 1.1:** Taubenberger JK, Reid AH, Fanning TG. El virus de la gripe de 1918. *Temas Investigacion y Ciencia* 48, 2007.

**Figure 1.10:** Goodsell DS, *The Machinery of Life*, second edition, Springer, 2009, ISBN 978-0-387-84924-9; Burton DR, Weiss RA. AIDS/HIV. A boost for HIV vaccine design. *Science*. 329:770–773, 2010; and Cardoso RM, Zwick MB, Stanfield RL, Kunert R, Binley JM, Katinger H, Burton DR, Wilson IA. Broadly neutralizing anti-HIV antibody 4E10 recognizes a helical conformation of a highly conserved fusion-associated motif in gp41. *Immunity* 22:163–173, 2005.

**Figure 2.1:** Goodsell DS, *The Machinery of Life*, second edition, Springer, 2009, ISBN 978-0-387-84924-9.

**Figure 2.2:** Dobson CM, Gerrard JA, Pratt AJ, *Foundations of Chemical Biology*, Oxford University Press, 2001, ISBN 978-0-19-924899-5.

- Figure 2.5:** Ribeiro MMB, Melo MN, Serrano ID, Santos NC, Castanho MARB. Drug-lipid interaction evaluation: why a nineteenth century solution? *TiPS*, 31:449–454, 2010.
- Figure 2.14c, d:** Ruetsch SB, Kamath Y, Weigmann H-D. Photodegradation of human hair: a microscopy study, in *Comprehensive Series in Photosciences* 3:175–205, 2001.
- Figure 3.9:** Santos NC, Ter-Ovanesyan E, Zasadzinski JA, Prieto M, Castanho MA. Filipin-induced lesions in planar phospholipid bilayers imaged by atomic force microscopy. *Biophys J.* 75:1869–1873, 1998; Alves CS, Melo MN, Franquelim HG, Ferre R, Planas M, Feliu L, Bardají E, Kowalczyk W, Andreu D, Santos NC, Fernandes MX, Castanho MA. Escherichia coli cell surface perturbation and disruption induced by antimicrobial peptides BP100 and pepR. *J. Biol. Chem.* 285:27536–27544, 2010.
- Figure 3.10 :** Mouritsen Ole G., Andersen OS. Do we need a new biomembrane model. In *Search of a new biomembrane model.* *Biol. Skr. Vid. Selsk* 49:7–12, 1998.
- Figure 3.11:** Franquelim HG, Loura LM, Santos NC, Castanho MA. Sifuvirtide screens rigid membrane surfaces. Establishment of a correlation between efficacy and membrane domain selectivity among HIV fusion inhibitor peptides. *J. Am. Chem. Soc.* 130:6215–6223, 2008; and Franquelim HG, Gaspar D, Veiga AS, Santos NC, Castanho MA. Decoding distinct membrane interactions of HIV-1 fusion inhibitors using a combined atomic force and fluorescence microscopy approach. *Biochim. Biophys. Acta.* 1828:1777–1785, 2013.
- Figure 6.1a:** Pasteur L. Études sur la bière ses maladies, causes qui les provoquent, procédé pour la rendre inaltérable; avec une théorie nouvelle de la fermentation. Gauthier-Villars Ed., Paris, 1876. ([https://openlibrary.org/books/OL24165461M/%C3%89tudes\\_sur\\_la\\_bi%C3%A8re](https://openlibrary.org/books/OL24165461M/%C3%89tudes_sur_la_bi%C3%A8re))
- Figure 6.2:** Harden A, Young WJ. The Alcoholic ferment of yeast-juice. *Proc. Royal Soc. Lond. B* 77:405–520, 1906.
- Figure Box 6.2:** de Meis L, in *Calcium and Cellular Metabolism: Transport and Regulation*, chapter 8. Plenum Press, NY, 1997.
- Figure Box 6.4:** Gatenby RA, Gillies RJ. Why do cancers have high aerobic glycolysis? *Nat. Rev. Cancer* 4:891–899, 2004.
- Figure Box 6.5:** Keilin D. On Cytochrome, a Respiratory Pigment, Common to Animals, Yeast, and Higher Plants. *Proc. R. Soc. Lond. B* 98:312–339, 1925.
- Figure 6.8:** Belitser VA, Tsybakova ET. The mechanism of phosphorylation associated with respiration. *Biokhimiya* 4:516–535, 1939.
- Figure 6.21:** Davies KM, Strauss M, Daum B, Kief JH, Osiewicz HD, Rycovska A, Zickermann V, Kühlbrandt W. Macromolecular organization of ATP synthase and complex I in whole mitochondria. *Proc. Natl. Acad. Sci. USA* 108:14121–14126, 2011.
- Figure 6.25c:** Ricquier D, Bouillaud F. The uncoupling protein homologues: UCP1, UCP2, UCP3, StUCP and AtUCP. *Biochem J.* 345:161–179, 2000.
- Figure Box 6.7:** van Marken Lichtenbelt WD, Vanhommerig JW, Smulders NM, Drossaerts JM, Kemerink GJ, Bouvy ND, Schrauwen P, Teule GJ. *New Engl.*

J. Med. 360:1500–1508, 2009 ; and Cypess AM, Lehman S, Williams G, Tal I, Rodman D, Goldfine AB, Kuo FC, Palmer EL, Tseng YH, Doria A, Kolodny GM, Kahn CR. *New Engl. J. Med.* 360:1509–1517, 2009.

**Figure Box 7.1:** Lusk G. *The elements of the science of human nutrition.* W. B. Saunders Company, 1917 (<http://chestofbooks.com/health/nutrition/Science/index.html#.VLL1B3uMGVc>).

**Figure 7.5:** Zhou ZH, McCarthy DB, O'Connor CM, Reed LJ, Stoops JK. The remarkable structural and functional organization of the eukaryotic pyruvate dehydrogenase complexes. *Proc. Natl. Acad. Sci. USA* 98:14802–14807, 2001.

**Figure 8.2a:** Biston P, Van Cauter E, Ofek G, Linkowski P, Polonsky KS, Degaute JP. Diurnal variations in cardiovascular function and glucose regulation in normotensive humans. *Hypertension* 28:863–871, 1996.

**Figure 8.2b:** Matschinsky F, Liang Y, Kesavan P, Wang L, Froguel P, Velho G, Cohen D, Permutt MA, Tanizawa Y, Jetton TL, et al. Glucokinase as pancreatic beta cell glucose sensor and diabetes gene. *J. Clin. Invest.* 92:2092–2098, 1993.

**Figure 8.3:** Cárdenas ML, Cornish-Bowden A, Ureta T. Evolution and regulatory role of the hexokinases. *Biochim. Biophys. Acta* 1401:242–264, 1998.

**Figure Box 8.2:** Matschinsky FM. Regulation of pancreatic beta-cell glucokinase: from basics to therapeutics. *Diabetes* 51:S394–S404, 2002.

**Figure Box 8.3:** Ferrer JC, Favre C, Gomis RR, Fernández-Novell JM, García-Rocha M, de la Iglesia N, Cid E, Guinovart JJ. Control of glycogen deposition. *FEBS Lett.* 546:127–132, 2003.

**Figure 8.9:** Pederson BA, Cheng C, Wilson WA, Roach PJ. 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, 2000.

**Figure Box 8.4:** Baskaran S, Roach PJ, DePaoli-Roach AA, Hurley TD. Structural basis for glucose-6-phosphate activation of glycogen synthase. *Proc Natl Acad Sci USA.* 107:17563–17568, 2010.

**Figure Box 8.5:** Zhang W, DePaoli-Roach AA, Roach PJ. Mechanism of multi-site phosphorylation and inactivation of rabbit muscle glycogen synthase. *Arch. Biochem. Biophys.* 304:219–225, 1993.

**Figure 8.10:** Fong NM, Jensen TC, Shah AS, Parekh NN, Saltiel AR, Brady MJ. Identification of binding sites on protein targeting to glycogen for enzymes of glycogen metabolism. *J Biol Chem.* 275:35034–35039, 2000.

**Figure Box 8.6:** Tong L. Structure and function of biotin-dependent carboxylases. *Cell. Mol. Life Sci.* 70:863–891, 2013.

**Figure 8.14:** Liu H, Liu JY, Wu X, Zhang JT. Biochemistry, molecular biology, and pharmacology of fatty acid synthase, an emerging therapeutic target and diagnosis/prognosis marker. *Int J Biochem Mol Biol.* 1:69–89, 2010.

**Figure Box 8.8:** Goodsell DS. *The machinery of life*, p. 32. Springer, New York ISBN: 978-0-387-84924-9. Second edition, 2009.

**Table 8.2:** Elia M. The inter-organ flux of substrates in fed and fasted man, as indicated by arterio-venous balance studies. *Nutr. Res. Rev.* 4:3–31, 1991.

- Figure Box 9.1:** Eaton SB, Konner M. Paleolithic nutrition. A consideration of its nature and current implications. *N. Engl. J. Med.* 312:283–289, 1985; Eaton SB. The ancestral human diet: what was it and should it be a paradigm for contemporary nutrition? *Proc. Nutr. Soc.* 65:1–6, 2006; Adler CJ, Dobney K, Weyrich LS, Kaidonis J, Walker AW, Haak W, Bradshaw CJ, Townsend G, Sołtysiak A, Alt KW, Parkhill J, Cooper A. Sequencing ancient calcified dental plaque shows changes in oral microbiota with dietary shifts of the Neolithic and Industrial revolutions. *Nat. Genet.* 45:450–455, 2013.
- Figures 9.1 and 9.15b, c:** Cahill G. Fuel metabolism in starvation. *Ann. Rev. Nutr.* 26:1–22, 2006.
- Figure 9.15a:** Owen OE. Ketone bodies as a fuel for the brain during starvation. *Biochem. Mol. Biol. Educ.* 33:246–251, 2005.
- Figure Box 9.3:** Löscher W, Potschka H. Drug resistance in brain diseases and the role of drug efflux transporters. *Nat. Rev. Neurosci.* 6:591–602, 2005.
- Figure 9.9:** Jitrapakdee S, St Maurice M, Rayment I, Cleland WW, Wallace JC, Attwood PV. Structure, mechanism and regulation of pyruvate carboxylase. *Biochem. J.* 413:369–387, 2008.
- Figure Box 9.5:** Michels PA, Rigden DJ. Evolutionary analysis of fructose 2,6-bisphosphate metabolism. *IUBMB Life* 58:133–141, 2006.
- Figure 9.15b:** Cunnane SC, Crawford MA. *Comp. Biochem. Physiol. A: Mol. Integr. Physiol.* Survival of the fattest: fat babies were the key to evolution of the large human brain. 136:17–26, 2003.
- Table 9.3:** Felig P. Amino acid metabolism in man. *Annu. Rev. Biochem.* 44:933–955, 1975.
- Figures 10.3 and 10.6:** Huxley HE. The double array of filaments in cross-striated muscle. *J. Biophys. Biochem. Cytol.* 3:631–648, 1957.
- Figures 10.4a and 10.7a:** Huxley HE. The mechanism of muscular contraction. *Science* 164:1356–1365, 1969.
- Figure 10.4b:** Slayter HS, Lowey S. Substructure of the myosin molecule as visualized by electron microscopy. *Proc. Natl. Acad. Sci. USA* 58:1611–1618, 1967.
- Figure 10.5:** Hanson J, Lowy J. The structure of F-actin and of actin filaments isolated from muscle. *J. Mol. Biol.* 6:46–60, 1963; and Geeves MA, Holmes KC. *Ann Rev Biochem* 68:687–728, 1999.
- Figure 10.10:** Newsholme EA & Leech TR. Physical activity: In non-athletes, athletes and patients, in “Functional biochemistry in health and disease”, chapter 13. Wiley-Blackwell, ISBN: 978-0-471-98820-5, 2010.
- Figure 10.13b and Figure Box 10.4:** Oakhill JS, Scott JW, Kemp BE. AMPK functions as an adenylate charge-regulated protein kinase. *Trends Endocrinol. Metab.* 23:125–132, 2012.
- Figure 11.1:** Finucane MM, Stevens GA, Cowan MJ, Danaei G, Lin JK, Paciorek CJ, Singh GM, Gutierrez HR, Lu Y, Bahalim AN, Farzadfar F, Riley LM, Ezzati M; Global Burden of Metabolic Risk Factors of Chronic Diseases Collaborating Group (Body Mass Index). National, regional, and global trends in body-mass index since 1980: systematic analysis of health examination

surveys and epidemiological studies with 960 country-years and 9.1 million participants. *Lancet* 377:557–567, 2011.

**Figure 11.3:** Hervey GR. The effects of lesions in the hypothalamus in parabiotic rats. *J. Physiol.* 145:336–352, 1959

**Figure 11.4:** Ingalls AM, Dickie MM, Snell GD. Obese, a new mutation in the house mouse. *J. Hered.* 41:317–318, 1950.

**Figure 11.6:** Valle M, Gascón F, Martos R, Bermudo F, Ceballos P, Suanes A. Relationship between high plasma leptin concentrations and metabolic syndrome in obese pre-pubertal children. *Int. J. Obes. Relat. Metab. Disord.* 27:13–18, 2003.

**Figure 11.8:** Vidarsdottir S, Roelfsema F, Streefland T, Holst JJ, Rehfeld JF, Pijl H. Short-term treatment with olanzapine does not modulate gut hormone secretion: olanzapine disintegrating versus standard tablets. *Eur. J. Endocrinol.* 162:75–83, 2010.

**Figure 11.9:** Kraly FS, Carty WJ, Resnick S, Smith GP. Effect of cholecystokinin on meal size and intermeal interval in the sham-feeding rat. *J. Comp. Physiol. Psychol.* 92:697–707, 1978.

**Figure 11.10:** Kojima M, Hosoda H, Date Y, Nakazato M, Matsuo H, Kangawa K. Ghrelin is a growth-hormone-releasing acylated peptide from stomach. *Nature* 402:656–660, 1999; Cummings DE, Weigle DS, Frayo RS, Breen PA, Ma MK, Dellinger EP, Purnell JQ. Plasma ghrelin levels after diet-induced weight loss or gastric bypass surgery. *N. Engl. J. Med.* 346:1623–1630, 2002; and Foster CM, Barkan A, Kasa-Vubu JZ, Jaffe C. Ghrelin concentrations reflect body mass index rather than feeding status in obese girls. *Pediatr. Res.* 62:731–734, 2007.

**Figure Box 11.4:** le Roux CW, Aylwin SJ, Batterham RL, Borg CM, Coyle F, Prasad V, Shurey S, Ghatei MA, Patel AG, Bloom SR. Gut hormone profiles following bariatric surgery favor an anorectic state, facilitate weight loss, and improve metabolic parameters. *Ann. Surg.* 243:108–114, 2006.

**Figure Box 11.5:** Kozak LP, Young ME. Heat from calcium cycling melts fat. *Nat. Med.* 18:1458–1459, 2012.

**Figure 11.15:** Westerterp KR. Diet induced thermogenesis. *Nutr. Metab.* 1:1–5, 2004; and Leibel RL, Rosenbaum M, Hirsch J. Changes in energy expenditure resulting from altered body weight. *N. Engl. J. Med.* 332:621–628, 1995.

**Figure 11.17:** Dayan CM, Panicker V. Novel insights into thyroid hormones from the study of common genetic variation. *Nat. Rev. Endocrinol* 5:211–218, 2009.

**Figure 11.20a:** Hotamisligil GS, Arner P, Caro JF, Atkinson RL, Spiegelman BM. Increased adipose tissue expression of tumor necrosis factor- $\alpha$  in human obesity and insulin resistance. *J. Clin. Invest.* 95:2409–2415, 1995.

**Figure Box 11.6:** Hotamisligil GS. Inflammation and metabolic disorders. *Nature* 444:860–867, 2006; and Hotamisligil GS, Erbay E. Nutrient sensing and inflammation in metabolic diseases. *Nat. Rev. Immunol.* 8:923–934, 2008.

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