Cytoplasmic dynein nomenclature

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A variety of names has been used in the literature for the subunits of cytoplasmic dynein complexes. Thus, there is a strong need for a more definitive consensus statement on nomenclature. This is especially important for mammalian cytoplasmic dyneins, many subunits of which are encoded by multiple genes. We propose names for the mammalian cytoplasmic dynein subunit genes and proteins that reflect the phylogenetic relationships of the genes and the published studies clarifying the functions of the polypeptides. This nomenclature recognizes the two distinct cytoplasmic dynein complexes and has the flexibility to accommodate the discovery of new subunits and isoforms.

Cytoplasmic dynein is the major microtubule minus end-directed motor protein of the cell; it is involved in many essential cellular processes such as membrane trafficking and mitosis. The cytoplasmic dynein complex is resolved on SDS-polyacrylamide gels into subunit polypeptides of ~530 (dynein heavy chains), \sim 74 (intermediate chains), \sim 53–59 (light intermediate chains), and ~10–14 kD (light chains). Since mammalian cytoplasmic dynein was first identified and characterized (Paschal et al., 1987), further understanding of the subunit complexity of cytoplasmic dyneins has emerged (for review see Vallee et al., 2004; Pfister et al., 2005). Only a single heavy chain gene has been identified for the initially described form of cytoplasmic dynein, but two intermediate chain and two light intermediate chain genes have been found (Mikami et al., 1993; Zhang et al., 1993; Gill et al., 1994; Hughes et al., 1995; Vaughan and Vallee, 1995). Three light chain families have been identified, which appear to be shared among some, but not all, cytoplasmic

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and axonemal dynein complexes (King et al., 1996a,b, 1998; Bowman et al., 1999; Wilson et al., 2001). Also, it is now known that there are two distinct cytoplasmic dynein complexes: the originally characterized complex with six subunits and a second distinct complex with two subunits that have been identified to date—a unique heavy chain and a unique light intermediate chain (Gibbons et al., 1994; Tanaka et al., 1995; Vaughan et al., 1996; Grissom et al., 2002; Mikami et al., 2002). Information about the 13 cytoplasmic dynein polypeptides has come from various sources, and individual gene and protein names have not been coordinated in a systematic manner. This article introduces a nomenclature that has been updated from Vaughan et al. (1996) for use with both mouse and human genes and suggests common names for the two cytoplasmic dynein complexes and their diverse subunits.

Table I shows the recommended nomenclature for mammalian cytoplasmic dynein genes and proteins. Although based upon the earlier terminology that was used for dynein genes by the human and mouse genome projects, this revised nomenclature is modified to better reflect the phylogenetic relationships of the dynein genes and the published studies clarifying the functions of dynein subunits. This recommended nomenclature has been endorsed by the Human Genome Organization Gene Nomenclature Committee (HGNC) and the International Committee on Standardized Nomenclature for Mice. Moreover, it conforms to the guidelines of the International Union of Pure and Applied Chemistry (IUPAC)-International Union of Biochemistry and Molecular Biology Joint Commission on Biochemical Nomenclature.

The most obvious nomenclature change is that two cytoplasmic dynein complexes are now recognized: cytoplasmic dynein 1 and 2. Thus, the designations of their subunits start with DYNC1 and DYNC2, respectively. We retain the convention of grouping the subunits of these complexes into polypeptide families of similarly sized proteins: heavy (H), intermediate (I), light intermediate (LI), and light (L) chains. The cytoplasmic dynein 1 complex has three distinct light chain families, and to systematize the light chain nomenclature, additional letters are

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used to distinguish the three families: Tctex1 (T), Roadblock (RB), and LC8 (L). These light chains only have DYN as their initial designation because of the abundant evidence that light chains are shared with several axonemal dyneins (King, 2002). Individual members of all the gene families are assigned numbers as before. We also retain the practice of designating the alternatively spliced isoforms of the intermediate chain gene products with letters, which is in accordance with IUPAC standards (Vaughan et al., 1996). As appropriate, letters can also be used to distinguish alternatively spliced isoforms of members of other gene families. We use standard human and mouse gene formatting: italicized uppercase letters for human gene names (for example, DYNC1H1) and italicized initial uppercase followed by lowercase letters for mice (Dync1h1). For the formal names of proteins of both species, the same names in nonitalicized uppercase letters (DYNC1H1) are used.

Although it is recommended that the subunits be referred to by using their formal names in publications, the rich history of common names and the superficial similarities of some of the formal names are recognized. Thus, it is anticipated that a dynein polypeptide subunit will be identified at first mention with its formal name followed by a common name in parenthe-

ses, with subsequent mentions to the common name only: for example, DYNC1I2 (cytoplasmic dynein 1 intermediate chain 2). Also, a hyphen might be used on subsequent mentions to minimize a potential confusion between the letter I and number 1 in some fonts (for example, DYNC1-I2). However, it is highly recommended that the light chains in the LC8 and Roadblock families not be referred to by the aliases dynein light chain 1, 2, 2A, and 2B, as these names are a source of considerable confusion. We suggest that portions of this nomenclature system be adapted for cytoplasmic dyneins of other species as appropriate. In the future, this nomenclature scheme may also be readily adapted to incorporate additional cytoplasmic dynein components (should they be identified) as well as the genes and proteins of axonemal dyneins (Pazour et al., 2005).

Other researchers supporting the use of this nomenclature for the cytoplasmic dynein subunits include Victoria Allan, Linda Amos, David Asai, Peter Baas, Elisar Barbar, Stan Burgess, John Cooper, Steven Gross, Majid Hafezparast, Leah Haimo, Nobutaka Hirokawa, Peter Hook, Holger Hummerich, Ritsu Kamiya, Stephen J. King, Michael Koonce, Bo Liu, David Mitchell, Kazuhiro Oiwa, Gregory Pazour, David Pellman, Stephen Pilder, Samara Reck-Peterson, Vladimir Rodi-

Table I. Nomenclature of the mammalian cytoplasmic dynein subunits

Gene symbols				Revised protein symbols	Common protein names
Human		Mouse		Human	
Revised	Former	Revised	Former	and mouse	Human and mouse
Cytoplasmic dynein	1 complex				
DYNC1H1	DNCHI	Dync1h1	Dnchc1	DYNC1H1	Cytoplasmic dynein 1 heavy chain, conventional cytoplasmic dynein heavy chain, DHC1a, dynein 1, dynein heavy chain 1, MAP1C
DYNC111	DNCII	Dynclil	Dncic1	DYNC111	Cytoplasmic dynein 1 intermediate chain 1, IC-1, IC74-1, IC70
DYNC112	DNC12	Dync1i2	Dncic2	DYNC112	Cytoplasmic dynein 1 intermediate chain 2, IC-2, IC74-2
DYNC1LI1	DNCLII	Dync1li1	Dnclic 1	DYNC1LI1	Cytoplasmic dynein 1 light intermediate chain 1, LIC1
DYNC1LI2	DNCL12	Dync1li2	Dnclic2	DYNC1LI2	Cytoplasmic dynein 1 light intermediate chain 2, LIC2
DYNLT1	TCTEL1	Dynlt1	Tctex 1	DYNLT1	Dynein Tctex1 light chain 1, Tctex1
DYNLT3	TCTE1L	Dynlt3	Tcte11	DYNLT3	Dynein Tctex1 light chain 3, rp3
DYNLRB1	DNCL2A	Dynlrb 1	Dnclc2a	DYNLRB1	Dynein Roadblock light chain 1, Robl1
DYNLRB2	DNCL2B	Dynlrb2	Dnclc2b	DYNLRB2	Dynein Roadblock light chain 2, Robl2
DYNLL1	DNCL1	Dynll 1	Dnclc1	DYNLL1	Dynein LC8 light chain 1
DYNLL2	DNCL2	Dynll2	Dlc2	DYNLL2	Dynein LC8 light chain 2
Cytoplasmic dynein	2 complex				
DYNC2H1	DNCH2	Dync2h1	Dnchc2	DYNC2H1	Cytoplasmic dynein 2 heavy chain, IFT¹ dynein heavy chain, DHC1b, dynein heavy chain 2, DHC2
DYNC2LI1	n/a²	Dync2li1	n/a²	DYNC2LI1	Cytoplasmic dynein 2 light intermediate chain 1, D2LIC, LIC3

¹³ well-established cytoplasmic dynein components are currently identified; other components may exist. The former mouse and human gene nomenclatures are shown along side the revised nomenclature for both species. Also shown are the suggested common protein names followed by some of the alternative names that are currently in use. In accordance with the human and mouse nomenclature rules, all gene symbols are in italics, mice genes have an uppercase first letter and the rest are lower case, and human genes have all uppercase letters. All protein symbols are in uppercase normal fonts. The designation cytoplasmic dynein Tctex1 light chain 2 is not used to avoid confusion with the gene currently known as TCTEX2 (human) and Tctex2 (mouse), which is an axonemal dynein subunit. ¹IFT, intraflagellar transport.

²n/a, not available.

onov, Andreas Russ, Winfield Sale, William Saxton, David Sharp, Walter Steffen, Susan Strome, Ching-Hwa Sung, Kazuo Sutoh, Ronald Vale, Michael Welte, Xin Xiang, Li-yuan Yu-Lee, and Mingjie Zhang.

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References

- Bowman, A.B., R.S. Patel-King, S.E. Benashski, J.M. McCaffery, L.S. Goldstein, and S.M. King. 1999. *Drosophila* roadblock and *Chlamydomonas* LC7: a conserved family of dynein-associated proteins involved in axonal transport, flagellar motility, and mitosis. *J. Cell Biol.* 146:165–180.
- Gibbons, B.H., D.J. Asai, W.J. Tang, T.S. Hays, and I.R. Gibbons. 1994. Phylogeny and expression of axonemal and cytoplasmic dynein genes in sea urchins. *Mol. Biol. Cell.* 5:57–70.
- Gill, S.R., D.W. Cleveland, and T.A. Schroer. 1994. Characterization of DLC-A and DLC-B, two families of cytoplasmic dynein light chain subunits. *Mol. Biol. Cell.* 5:645–654.
- Grissom, P.M., E.A. Vaisberg, and J.R. McIntosh. 2002. Identification of a novel light intermediate chain (D2LIC) for mammalian cytoplasmic dynein 2. Mol. Biol. Cell. 13:817–829.
- Hughes, S.M., K.T. Vaughan, J.S. Herskovits, and R.B. Vallee. 1995. Molecular analysis of a cytoplasmic dynein light intermediate chain reveals homology to a family of ATPases. J. Cell Sci. 108:17–24.
- King, S.M. 2002. Dynein motors: structure, mechanochemistry and regulation. *In* Molecular Motors. M. Schliwa, editor. Wiley-VCH Verlag, Weinheim. 45–78.
- King, S.M., E. Barbarese, J.F. Dillman III, R.S. Patel-King, J.H. Carson, and K.K. Pfister. 1996a. Brain cytoplasmic and flagellar outer arm dyneins share a highly conserved Mr 8,000 light chain. J. Biol. Chem. 271:19358–19366.
- King, S.M., J.F. Dillman III, S.E. Benashski, R.J. Lye, R.S. Patel-King, and K.K. Pfister. 1996b. The mouse t-complex-encoded protein Tctex-1 is a light chain of brain cytoplasmic dynein. J. Biol. Chem. 271:32281–32287.
- King, S.M., E. Barbarese, J.F. Dillman III, S.E. Benashski, K.T. Do, R.S. Patel-King, and K.K. Pfister. 1998. Cytoplasmic dynein contains a family of differentially expressed light chains. *Biochemistry*. 37:15033–15041.
- Mikami, A., B.M. Paschal, M. Mazumdar, and R.B. Vallee. 1993. Molecular cloning of the retrograde transport motor cytoplasmic dynein (MAP 1C). *Neuron*. 10:787–796.
- Mikami, A., S.H. Tynan, T. Hama, K. Luby-Phelps, T. Saito, J.E. Crandall, J.C. Besharse, and R.B. Vallee. 2002. Molecular structure of cytoplasmic dynein 2 and its distribution in neuronal and ciliated cells. J. Cell Sci. 115:4801–4808.
- Paschal, B.M., H.S. Shpetner, and R.B. Vallee. 1987. MAP 1C is a microtubule-activated ATPase which translocates microtubules in vitro and has dynein-like properties. J. Cell Biol. 105:1273–1282.
- Pazour, G.J., N. Agrin, B.L. Walker, and G.B. Witman. 2005. Identification of predicted human outer dynein arm genes - candidates for primary ciliary dyskinesia genes. J. Med. Genet. 10.1136/jmg.200503300.
- Pfister, K.K., P.R. Shah, H. Hummerich, A. Russ, J. Cotton, A.A. Annuar, S.M. King, and E.M.C. Fisher. 2005. Genetic analysis of the cytoplasmic dynein subunit families. *Plos. Genetics*. In press.
- Tanaka, Y., Z. Zhang, and N. Hirokawa. 1995. Identification and molecular evolution of new dynein-like protein sequences in rat brain. J. Cell Sci. 108:1883–1893.
- Vallee, R.B., J.C. Williams, D. Varma, and L.E. Barnhart. 2004. Dynein: an ancient motor protein involved in multiple modes of transport. J. Neurobiol. 58:180_200
- Vaughan, K.T., and R.B. Vallee. 1995. Cytoplasmic dynein binds dynactin through a direct interaction between the intermediate chains and p150Glued. J. Cell Biol. 131:1507–1516.
- Vaughan, K.T., A. Mikami, B.M. Paschal, E.L. Holzbaur, S.M. Hughes, C.J. Echeverri, K.J. Moore, D.J. Gilbert, N.G. Copeland, N.A. Jenkins, and R.B. Vallee. 1996. Multiple mouse chromosomal loci for dynein-based motility. *Genomics*. 36:29–38.

- Wilson, M.J., M.W. Salata, S.J. Susalka, and K.K. Pfister. 2001. Light chains of mammalian cytoplasmic dynein: identification and characterization of a family of LC8 light chains. Cell Motil. Cytoskeleton. 49:229–240.
- Zhang, Z., Y. Tanaka, S. Nonaka, H. Aizawa, H. Kawasaki, T. Nakata, and N. Hirokawa. 1993. The primary structure of rat brain (cytoplasmic) dynein heavy chain, a cytoplasmic motor enzyme. *Proc. Natl. Acad. Sci. USA*. 90:7928–7932.