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Essay

Mammalian Septins Nomenclature

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There are 10 known mammalian septin genes, some of which produce multiple splice variants. The current nomenclature for the genes and gene products is very confusing, with several different names having been given to the same gene product and distinct names given to splice variants of the same gene. Moreover, some names are based on those of yeast or *Drosophila* septins that are not the closest homologues. Therefore, we suggest that the mammalian septin field adopt a common nomenclature system, based on that adopted by the Mouse Genomic Nomenclature Committee and accepted by the

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Human Genome Organization Gene Nomenclature Committee. The human and mouse septin genes will be named *SEPT1–SEPT10* and *Sept1–Sept10*, respectively. Splice variants will be designated by an underscore followed by a lowercase "v" and a number, e.g., SEPT4_v1.

The septins are a family of proteins that were first discovered in the yeast *Saccharomyces cerevisiae* by analysis of mutants defective in cytokinesis and bud morphogenesis. It is now clear that they are widespread and probably ubiquitous in the fungi and animals, although apparently not in plants. Most if not all septins seem to bind and hydrolyze GTP and to participate in filament formation in vitro and probably in vivo. In addition to their widespread involvement in cytokinesis, the septins seem also to be involved in vesicle trafficking and other aspects of cell surface organization, and they may have other functions as well. For various trivial historical reasons, the current nomenclature for the mammalian septins is particularly chaotic and confusing. With the field still young but attracting increasing interest, there seems to be great value in rationalizing and simplifying the septin nomenclature at this time.

In accordance with the Mouse Genomic Nomenclature Committee nomenclature, the mouse genes will be named *Sept1–Sept10*, and the corresponding protein products will be SEPT1–SEPT10. Although these numbers do not correspond to the genetic distances between the septins (Figure 1), they do provide an unambiguous and consistent naming system. The Human Genome Organization Gene Nomenclature Committee-approved symbols will be *SEPT1–SEPT10* for the genes, and the corresponding gene products will be SEPT1–SEPT10. Although there are still too few sequences available to be certain, it seems likely that most or all septins of other vertebrates will prove to have unambiguous orthologues among the mammalian septins, in which case it would be desirable to name them by using the same system. For example, several fragments of septin genes from frog and zebrafish are available in GenBank as expressed sequence tags (ESTs), and these encode peptides that are highly related to particular mammalian septins. Therefore, we suggest that where possible other vertebrate septins be named using the same system as used for the mammalian proteins. Usually, the species being described would be obvious from the context, but it could also be indicated by adding, as a prefix, an abbreviation of the Latin binomial for the species (e.g., *Xl* for *Xenopus laevis*). For example, the frog septin A (GenBank no. AF212298), which is 89% similar in sequence to human SEPT2 but only 61% similar to the next most closely related human septin, would now be named *Xl* SEPT2, or just SEPT2. (However, the prefix would not be a part of the official gene symbol.) At the same time, comparison of the yeast, *Caenorhabditis elegans* and *Drosophila* septins to the mammalian septins (Adam, Peifer, and Pringle, unpublished data) shows that the relationships are sufficiently complicated that the mammalian nomenclature scheme could not reasonably be applied to nonvertebrate septins.

The proposed symbols are reconciled with the previously used aliases for the mouse and human members of the septin family in Table 1. This table also provides selected GenBank accession numbers for the mouse and human septins, the N- and C-terminal sequences of the longest known variants (so as to provide an unambiguous means of identification), and the human chromosome loci.

Note that some septins currently have a multitude of distinct aliases (e.g., SEPT9 names include Sint1, Sep9, E-septin, SLP-a, MSF, SepD1, and Ov/Br septin), and SEPT6 has been named both Septin 6 and Sept2, which engenders considerable confusion in the literature and in database searches. Additionally, some vertebrate septins (e.g., Cdc10 or Pnutl) have been named after *Saccharomyces cerevisiae* or *Drosophila* septins that are not true orthologues (or even the closest homologues). Finally, at least four septin genes produce multiple splice variants, and these have also sometimes been given completely different names [e.g., SEPT4 splice variants include hCDCrel-2a, hCDCrel-2b, Bradeion-α and -B, ARTS, MART, and Pnutl2(variants 1–4)]. To make the genetic origin of these variants clear, we propose using the system adopted by the Mouse and Human Genome Nomenclature Committees. In this system, splice variants are distinguished by an underscore followed by a lowercase "v" and a number, as listed in Table 1, e.g., the mouse G-septin α would be named SEPT3_v1. Finally, we propose that if new, distinct septin genes are discovered, they and their products be given a new number in the sequence (e.g., SEPT11).

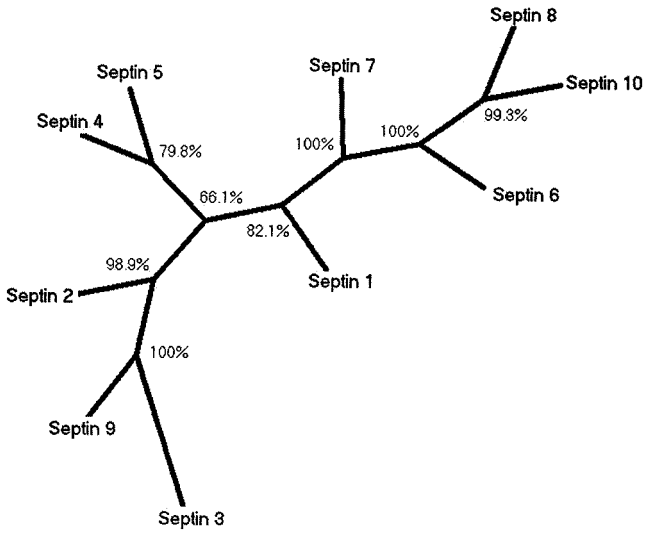

Figure 1. Unrooted phylogenetic tree of human septins. This consensus tree was generated using the Protpars program in the Phylip package. Each of the 1000 bootstrapped replicate data sets generated was analyzed 20 times, with the sequence input order randomized each time. The branch values (percentage) refer to the frequency with which a given branching pattern was produced. Strong support for any particular branch shown in the figure is indicated by values >90%, and moderate-to-weak support is indicated by values between 60 and 90%. Values <60% indicate no support for the given branching pattern. Segment lengths do not correspond to relatedness.

Table 1. Proposed nomenclature for mammalian septins

Approved mouse septin nomenclature (Locus/ protein)	Approved human septin nomenclature (Locus/ protein)	Mouse, rat septin aliases[a]	Mouse, rat GenBank accession nos. (selected)	Human septin aliases	N-terminal sequence (human, longest splice variant)	C-terminal sequence (human, longest splice variant)	Human GenBank accession nos (selected)	Human chromosome locus
Sept1/SEPT1	*SEPT1*/SEPT1	Diff6, Septin1	M37030, NM_017461	SEPT1	MDKEYVGF	QGEQSDAL.	NM_052838	16p11.1
Sept2/SEPT2	*SEPT2*/SEPT2	Nedd5, Septin2	NM_010891, D49382	Nedd5, Pnutl3, Diff6, KIAA0158	MSKQQPTQ	GGALGHHV.	NM_004404, AF038404	2q37.3
Sept3/ SEPT3_v1–3[b]	*SEPT3*/ SEPT3_v1–2[c]	G-septin(α,β,γ), Septin3(A–C)	AF111179(α), AF111180(β), AF111181(γ), NM_011889, NM_019375	Sep3[c]	MSELVPEP	EESHDSNP.	NM_019106	22q13.2
Sept4/ SEPT4_v1–6	*SEPT4*/ SEPT4_v1–6	H5, Sep4	NM_011129	H5, Bradeion(α,β), Pnutl2(variants 1–4), hCDCrel-2(a–b), ARTS,[d] MART[d]	MDRSLGWQ	QKQMKENY.	NM_004574, NM_080415–7, AF176379, AB008753, AB002110	17q23
Sept5/SEPT5	*SEPT5*/SEPT5	Cdcrel-1 Pnutl1[e]	NM_053931	Pnutl, hCDCrel-1A, B	MSTGLRYK	MKQQMQDQ.	Y11593, NM_002688	22q11.2
Sept6/SEPT6	*SEPT6*/SEPT6_v1–6	Septin6	NM_019942	SEPT2, Septin6(I–VI), KIAA0128	MAATDIAR	KRDKEKKN.	AF403058–62, AB023622,	Xq24
Sept7/SEPT7	*SEPT7*/SEPT7	Septin7, Cdc10	NM_022616	hCdc10	MVAQQKNLE	NKKKGKIF.	AF142759, NM_001788	7q36.1
Sept8/SEPT8	*SEPT8*/SEPT8		AA636820 (partial)	KIAA0202	MAATDLERFS[f]	RKDKDKKN.	D86957, BAA13193.1	5q31
Sept9/ SEPT9_v1–5	*SEPT9*/ SEPT9_v1–5	Sint1, Sep9, E-septin, SLP-a	NM_017380, AJ250723	AF17q25 gene, MSF(a–d), SEPT9, SepD1, Ov/Br septin, Pnutl4, KIAA0991	MKKSYSGGTR	EKEPEAPEM.	NM_006640, AB023208, AF189712, AF123052	17q25.3
Sept10/SEPT10	*SEPT10*/SEPT10		AV254985 (partial)	SEPT10, Sep1-like	MASSEVARHL	QGQYISQSE.	AF146760	8q11.23

Mouse locus symbols (italicized, first letter capitalized) are those approved by the Mouse Genomic Nomenclature Committee; human locus symbols (italicized, all capital letters) have been approved by the Human Genome Organization Gene Nomenclature Committee. Where possible, the Genbank accession numbers are those provided by the curated NCBI reference sequence project (*http://www.ncbi.nlm.nih.gov:80/locuslink/refseq.html*). Selected accession numbers for various septin splice variants are also provided.

[a] Aliasas can still be used to search the mouse genome informatics site for septin genes of interest (http://www.informatics.jax.org).

[b] Several of the septin genes produce multiple splice variants. We propose a consistent naming convention for the splice variants, as adopted by the Mouse and Human Genome Nomenclature Committees, in which an underscore and a "v" followed by a number is added as a suffix for each variant.

[c] Human ESTs exist encoding a C-terminal sequence identical to the unique C-terminal sequence of rat G-septin α. No human ESTs were found that correspond to the unique N-terminus of G-septin γ, and it is not clear if this is a true splice variant.

[d] ARTS and MART are splice variants of the *SEPT4* gene that lack the G4 motif (XKXD) found in typical septins. Uniquely, ARTS is localized to mitochondria, is essential for TGF-β-mediated apoptosis, and translocates to the nucleus when apoptosis occurs. It is not known if ARTS or MART binds guanine nucleotide. However, the name ARTS-1 is also used for a TNF-receptor-shedding aminopeptidase regulator, and *MART-1* is the gene name for a melanoma tumor antigen recognized by T cells. Therefore, despite the significant differences in the sequences and functions of these splice variants, we propose that they be named SEPT4_v5 and SEPT4_v6.

[e] Note: the N-terminus of the known rat SEPT5 (MDSLAAPQ-) is unrelated to that of the human SEPT5. There are splice variants of both human and rat SEPT5, but the 5′ ends have not been unambiguously determined.

[f] A partial sequence of a possible longer variant (that begins RRGSGCAR) has been described.