

In the beginning there was babble...

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“Go to, let us go down, and there confound their language, that they may not understand one another’s speech. ... Therefore is the name of it called Babel; because the Lord did there confound the language of all the earth...”

Genesis 11:7,9

Why do we need a unified nomenclature? To some extent we do not. Does it matter if we refer to that spherical fruit as an orange and you refer to it as an apple? In this case it is probably not a matter of life and death, but it can be annoying. In other cases, it can be critical. The German physician Robert Koch realized the importance of knowing exactly what microbe he was working with when he developed some of the techniques we still use today for isolating individual colonies. For example, it can be critical to know whether you have an infection of *Staphylococcus aureus* vs. *Mycobacterium tuberculosis*. Furthermore, it is important that we agree on the name. After all, you do not want your physician prescribing an inappropriate antibiotic simply because he/she was mistaken about the causative agent—“Oh, was it *Mycobacterium*? I’m sorry, I always get that confused with *Mycoplasma*.” Although not necessarily a matter of life and death, the same concerns apply to our research.

Consider a topic closer to home, the fungal *ATG* genes.¹ At one time there were at least 10 different names being used to identify these genes. For example, *APG1*, *AUT3*, *CVT10*, *GSA10*, *PAZ1* and *PDD7* all refer to the *Saccharomyces cerevisiae* gene we now call *ATG1*. To be honest, this aura of confusion was actually quite handy for a long time as it kept competitors out of the

field—they did not know what we were talking about. However, it got to the point where those of us working with these genes were having a hard time keeping them straight, so we had to agree on a unified nomenclature. The way this happened deserves a brief mention. The handful of labs working on fungal autophagy essentially got together at the first Gordon Research Conference on Autophagy in Stress, Development and Disease, and decided on a tentative name. Importantly, we checked various possibilities against the *Saccharomyces* Genome Database (the organization that is responsible for officially maintaining gene nomenclature in yeast) to be sure we were not choosing a name that was already being used to designate other genes. Unfortunately, checking with the official organization does not seem to happen very often in the case of human or mouse genes.

For human genes there are many examples that are confusing, such as *p38*: are we referring to *AHSA1*, *AIMP2* or *MAPK14*, all of which come up in a gene search through the HGNC database? The corresponding gene products have very different functions (an activator of heat shock 90kDa protein ATPase homolog 1, aminoacyl tRNA synthetase complex-interacting multifunctional protein 2, or mitogen-activated protein kinase 14).

Furthermore, multiple genes are aliased as *p38* in the NCBI Gene database (*AHSA1*, *AIMP2*, *CRK*, *GRAP2*, *HRB87F*, *MAPK1*, *MPK2*, *NURF38*, *RNF19A*, *SYP* and so on, and this does not even get into the variations such as *p38-2*, *p38a*, *p38Beta*, *p38beta2*, *p38 delta*, *p38gamma*, etc.) and a further range of “p38” proteins can be found in UniProtKB (including POLDIP2 and RPP38). For *p55* there are four possible genes noted with this as an alias by HGNC (*ERG*, *FSCN1*, *PIK3R3* and *PSMD12*), and for *p85* there are five possibilities (*ARHGEF7*, *PIK3R1*, *PIK3R2*, *PPP1R12C* and *PPP1R13B*). Even when we refer to *p62* there is the potential for confusion as this designation is used to refer not only to *SQSTM1*, but also to *KHDRBS1* and *NUP62*. Of course a gene that is named as “p” followed by a number is prone to potential confusion, and that is one reason that the HGNC recommends against using this type of designation (in addition to the fact that the molecular mass can vary between isoforms and species, making this type of name particularly meaningless). However, there are many examples that are not limited to the “p” nomenclature, such as the name *CAP* that corresponds to at least six different genes. We can see yet another example in autophagy: Bif-1 (Bax-interacting factor 1)/endophilin B1 associates

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with BECN1/Beclin 1/beclin1/beclin-1 via its interaction with UVRAG. A search in HGNC indicates that *BIF1* is a synonym for *ZBTB24* (zinc finger and BTB domain containing 24). However, Bif-1 is also referred to as SH3GLB1 (SH3-domain GRB2-like endophilin B1), which is encoded by a completely different gene than *ZBTB24*. Thus, Bif-1 is not the same as BIF1, but even if you work in the field of autophagy you might find this confusing. We suggest that this is not simply a matter of semantics; a misunderstanding of this nature can lead to a tremendous waste of time (and hence funds) spent working on the wrong gene/protein.

There are also reasons of self-interest that should prompt authors to use the official nomenclature. For example, some online journal articles are now being linked directly to databases.² The ability to do this automatically will depend on the use of the correct gene/protein names, and should enhance the visibility of the corresponding papers, potentially resulting in increased citations. In general, accurate curation of data requires the use of standardized nomenclature among the various model organisms.³

So, if we agree that there are reasons for a standardized nomenclature it is reasonable to ask who makes the decision about which name is the standard one, and/or who is in charge of maintaining the established nomenclature? Most model systems already have an organization in place for this purpose. As indicated above, the SGD does this for *Saccharomyces cerevisiae* (and the corresponding designations are generally observed for other fungi). Similarly, the HUGO Gene Nomenclature Committee (HGNC), the International Committee on Standardized Genetic Nomenclature for Mice, curators at the Rat Genome Database, and the Zebrafish Nomenclature Committee carry out this role for human, mouse, rat and zebrafish genes. Further sources for official gene names are listed on Wikipedia (http://en.wikipedia.org/wiki/Gene_nomenclature). In addition, there is substantial coordination among these committees so that, at least among the vertebrates, the gene names for orthologous genes are typically taken from the human gene. More

Table 1. Examples of model system nomenclature

	Gene		Protein
	WT	Mutant	
Human	<i>ULK1</i>	<i>ULK1^{-/-}</i>	ULK1
Mouse	<i>Ulk1</i>	<i>ulk1</i>	ULK1
Rat	<i>Ulk1</i>	<i>ulk1</i>	ULK1
Chicken	<i>ULK1</i>	<i>ULK1^{-/-}</i>	ULK1
Xenopus	<i>ulk1</i>	<i>ulk1</i>	ulk1
Zebrafish	<i>ulk1a</i>	<i>ulk1a</i>	Ulk1a
Caenorhabditis	<i>unc-51/atg-1^a</i>	<i>unc-51(-)^b</i>	UNC-51/ATG-1
Arabidopsis	<i>ATG1a</i>	<i>atg1a</i>	ATG1a
Yeast	<i>ATG1</i>	<i>atg1^c</i>	Atg1

^a*atg-1* is an alias; however, in this case the “other name” may actually help avoid confusion by clearly identifying the gene as a homolog of *ATG1*. Most of the *C. elegans atg* genes that have non-*atg* designations have “other names” that incorporate the yeast *ATG* nomenclature. For example, *lgg-1/atg-8.1* and *bec-1/atg-6*. We recommend that authors use both names at least for the initial time the gene is mentioned in a paper. ^bMutants can also be expressed by specific allele designations, as in *unc-51(e369)* or more generally as *unc-51(lof)* to indicate loss of function. ^cAllele designations typically take the form of the gene name followed by a dash and an allele number, as in *atg1-17*. This is one reason that a protein-protein interaction such as Atg12–Atg5 should not be abbreviated as “Atg12-5”.

information on the rationale behind a unified nomenclature can be found at the HGNC website (<http://www.genenames.org/about/FAQ/#whatisthehgnc>).

Therefore, to avoid future confusion, and to be consistent with the already established nomenclature for each field, we now ask authors to use the official gene and protein name for papers published in *Autophagy*. Note that although the HGNC

does not specifically indicate a rule for protein designations in their guidelines, it nonetheless recommends that the protein name be the same as the approved gene symbol, and be written in all uppercase letters. Thus, *BECN1* and BECN1 would be used when referring to the human gene and protein, or *Becn1* and BECN1 for the mouse or rat equivalents (Table 1 and Table 2). Indeed, both human and mouse

Table 2. Nomenclature guidelines and gene search/database URLs

Human	http://www.genenames.org/guidelines.html
	http://www.genenames.org/
Mouse	http://www.informatics.jax.org/mgihome/nomen/gene.shtml
	http://www.informatics.jax.org/
Rat	http://www.informatics.jax.org/mgihome/nomen/gene.shtml
	http://rgd.mcw.edu/
Chicken	http://projects.roslin.ac.uk/chickmap/nomenclature.html
	http://www.agnc.msstate.edu/
Xenopus	http://www.xenbase.org/gene/static/geneNomenclature.jsp
	http://www.xenbase.org/
Zebrafish	https://wiki.zfin.org/display/general/ZFIN+Zebrafish+Nomenclature+Guidelines
	http://zfin.org/
Arabidopsis	http://www.arabidopsis.org/portals/nomenclature/guidelines.jsp
	http://www.arabidopsis.org/
Caenorhabditis	http://www.wormbase.org/about/userguide/nomenclature
	http://www.wormbase.org/
Yeast	http://www.yeastgenome.org/help/community/nomenclature-conventions
	http://www.yeastgenome.org/

or rat proteins should be in all uppercase letters, despite the fact that few authors follow this convention.

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Note that we are not trying to establish a new convention, but rather are asking that authors abide by the already

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established conventions for these model systems. Now, that is not asking too much, is it?

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