

Comments on the distribution and phylogeny of type I polyketide synthases and nonribosomal peptide synthetases in eukaryotes

Wang et al. (1) report on the cataloging and phylogenetic analysis of gene clusters that encode nonribosomal peptide synthetases (NRPSs) and type I polyketide synthases (PKSs) in sequenced genomes from all three domains of life. We read this article with great interest. However, a few points require a more detailed discussion, and we would like to highlight some complementary analyses previously published by us and others.

Regarding the distribution of NRPS and PKS genes (figure 1 in ref. 1), we noticed that some lineages were poorly covered, despite a wealth of available genomic sequence data. For example, Wang et al. analyze three basidiomycete genomes and do not detect any NRPS or type I PKS genes (1). This could be misconstrued that these genes are rare or even absent in basidiomycetes. However, type I PKS and PKS-NRPS hybrid genes were previously predicted in 28 of 35 basidiomycete genomes investigated, with an average of four genes per genome (2). Also, basidiomycetes use NRPSs and NRPS-like enzymes for siderophore or pigment biosynthesis, respectively (e.g., ref. 3). Furthermore, Wang et al. analyze the genome of a single chlorophyte alga, *Chlorella variabilis*, and identify only a single NRPS gene (1). In reality, *C. variabilis* also contains a 63-kb PKS gene (accession no. XP_005847912). In a more representative analysis of chlorophyte

genomes, type I PKS genes were detected in eight of nine genomes examined, whereas NRPS genes were only found in two genomes (4).

Regarding the phylogeny of NRPS genes, we could not find any support for the suggested horizontal gene transfer of NRPS genes other than the increased similarity shown in figure 3 of ref. 1, which per se does not provide sufficient evidence for horizontal gene transfer. The state of the art is to provide multilevel evidence, including incongruent phylogenies, the analysis of codon use, genome statistics, etc. (5). In addition, we do not see how figure S6 in ref. 1 supports the general statement that “archaeal and eukaryotic NRPSs and PKSs appeared to be acquired from bacteria via horizontal gene transfer.” To this end, the phylogenetic tree in figure S6 constructed for less than 40 condensation domains is unlikely to serve as a suitable representation of the more than 1,000 NRPSs identified by Wang et al., many of which contain more than one condensation domain.

We hope that this additional information sharpens the view on eukaryotic PKSs provided by Wang et al. and further supports one of their most interesting findings, namely that PKS and NRPS genes occur in numerous different eukaryotic lineages.

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