

Mini Review

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Cytochrome P450 Gene in Silkworm (*Bombyx mori*): A Review Article

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Abstract

To understand features of cytochrome P450 genes in silkworm, the advances in silkworm genome projects created a new genome wide analysis tool that enables us to seek cytochrome P450 genes constitutes and their diversities. This has provided not only an opportunity for divergence in their substrate specificity identification, but also for divergence in their regulatory attributes, such as differing patterns of induction, tissue specific expression, and developmental expression. However, different researchers so far made different efforts to identify number of cytochrome p450 genes in Bomboxy mori, they came up with slightly different numbers which ranges from 79 to 86 putative cytochrome p450 genes. Then, it urges us to undertake further investigate in order to arrive at certain consensuses putative cytochrome p450 genes number.

Introduction

Cytochrome P450 monooxygenases (termed CYPs or P450s originated from spectrophotometric peak at wavelength of the absorption maximum of the enzyme at 450nm) are collective name for the heme-protein containing enzymes that constitute a ubiquitous of hydrophobic, cysteinato-heme enzymes. They are one of the oldest and largest super-family. For their enzymatic reaction a variety of small and large molecular substrates are utilized. In general, terminal oxidase enzymes in electron transfer chains, categorized as P450-containing systems [1-4].

As the means of oxidation, P450 uses molecular oxygen, inserts one of its oxygen atoms into a substrate, and reduces second oxygen to a water molecule, using two electrons that are provided by NAD(P)H via a reductase protein. Since only one of the two oxygen atoms, initially present in O₂, remains in oxidized substrate which result in P450s as monooxygenases. Molecular oxygen, itself, is unreactive toward organic molecules at low temperatures either due to spin forbiddingness or to high barriers. Consequently, living systems mainly use enzymes that modify dioxygen to form capable of performing desired oxidation reaction. This modification can be achieved by metal-dependent oxygenases, like cytochromes P450 or non-heme metalloenzymes (e.g., methane monooxygenase), or by flavin-containing enzymes that do not possess a metal-based prosthetic group [4-7].

Indeed, P450s are important metabolic enzymes involved in metabolism not only of a wide range of endogenous compounds such as fatty acids, steroids, hormones or vitamins, but also exogenous substrates such as drugs, chemicals including environmental pollutants, such carcinogens as polycyclic aromatic hydrocarbons, and pesticides as well as plant toxics. Consequently, they are found virtually in all aerobic organisms, including organisms as diverse as in insects, plants, mammals, birds and bacteria [1,5-9]. Recently, due to the advancement in genome sequencing technology a huge number of P450 enzymes (more than 21,000 sequences of P450 genes) are accessible in the P450 database from all kingdoms of life [1]. The diversify of sequences encoded by a multiplicity genes, which have been arisen by gene duplication and adaptive diversification results in functional versatility of the p450 super-family i.e., gene duplication is basically a corner stone for evolution of gene family [3].

The crucial roles of P450s, in insects are synthesis and degradation of insect hormones including ecdysteroids and juvenoids and the detoxification or activation of such chemicals as plant toxins and insecticides in turn that is leading to increased resistance in insect populations. So far, most of them were isolated from dipteran and lepidopteran insect species and more specifically from pest or diseases vector species. So in insects, P450

genes can be assigned to one of four clades: CYP2, CYP3, CYP4 and the mitochondrial CYP clade. The CYP3 clade is subdivided again into the CYP6, CYP9, CYP28, CYP308–310, CYP317, CYP321, CYP324, CYP329, CYP332, CYP336–338 and CYP345–348 families. Indeed, Many CYP9 family members are known to participate in detoxification pathways associated with insecticide resistance. Hence, they are considered as key enzymes in order to visualize many metabolic pathways and based on these signals that enable to formulate desirable remedial actions [1, 10-11]. Having these in mind, this review aimed at P450s in silkworm species.

Cytochrome P450 Genes in *Bombyx Mori*

Based on the advances in silkworm genome projects, a new genome wide analysis of cytochrome P450s genes was performed by different scientists. Consequently, their finds revealed that *Bombyx mori* genome has not similar putative p450 gene numbers. That is Li and his colleagues were discovered that 86 putative P450s in silkworm genome, which are thought to belong to 32 subfamilies. Further, they made a comparative genomic analysis with *Drosophila melanogaster*, then the result revealed that the two insects have some similar P450 distribution patterns but still have some obvious differences. Especially, the diverse distribution exists in 7 p450 subfamilies, which are CYP4A, CYP4C, CYP4D, CYP6A, CYP6AE, CYP6B and CYP9A [11]. But, Li and his colleagues in other study, they came up with different result of predication number of putative p450s which was predicted that the genome of silkworm, *Bombyx mori*, has at least 79 P450 genes; however, P450 genes that are related to the catabolism of exogenous compounds were not reported [12]. On the contrary, Ai and his colleagues predicted that based on the same genome project and analysis of cytochrome P450 genes they obtained a total of 84 CYP-related sequences which could be classified into 26 families and 47 subfamilies according to standard nomenclature. According to their report out of total eighty four genes, seventy eight of them were appeared to be functional and six were probable pseudogenes. Furthermore, their result revealed that the distribution of *Bombyx mori* P450s in the genome depicted that most of them are tandem arranged on chromosomes, while merely 34 genes were present as singletons, with 8 clusters including 3 or more than 3 genes. On the other hand, they came up with *B. mori* and *H. armigera* CYP9A genes clustered in species-specific groups of three P450s, with the exception of the orthologous CYP9A22/CYP9A14 pair, which indicates that the gene expansions are independent species-specific events relative to the last common ancestor. As different phytophagous insects, *B. mori* and *H. armigera* encounter many predictably different chemistries and xenobiotics in their respective host plants and their distinct environments [3]. Hence, due to these dynamic and selective pressures on gene copies mechanisms exposed them to engage into a gradual modification which will create genes with specific

functions than their precursors. In general, we infer that these gene evolution scenario will drive insect P450s to diversify rapidly.

Conclusion

Even though different studies were resulted in different number of p450 genes, the attempt made in identification of putative cytochrome p450 gene numbers and their expression profiles provides new insights into the similarities and differences in the structure, evolution, expression, and functions of genes, and raises many interesting questions which will need further scrutiny and the orthologous relationships among different insect CYP9A genes as well. Hence, it needs further investigation at least to arrive on specific number of cytochrome p450 genes in *Bombyx mori* to avoid ambiguities.

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