

**S1 Table. List of P450 families with majority of its members grouped in physical clusters.**

Family	Family size (total sequences)	Number of clustered members	Examples of functions in other organisms
CYP82	69	66	Biosynthesis of homoterpenes in <i>A. thaliana</i> [1], opioids in <i>Papaver somniferum</i> [2–4].
CYP71	51	45	Biosynthesis of monoterpenoids in mint species <i>Mentha x piperita</i> and <i>Mentha x spicata</i> [5], cyanogenic glucosides in cassava ( <i>Manihot esculenta</i> ) [6], furanocoumarins in several species [7], artemisinin in <i>Artemisia annua</i> [8], flavonoids in soybean ( <i>Glycine max</i> ) [9].
CYP81	50	42	Biosynthesis of indole glucosinolates in <i>A. thaliana</i> [10], isoflavonoid phytoalexins in <i>Medicago truncatula</i> , <i>G. echinata</i> and, <i>Lotus japonicus</i> [9], sesamin in <i>Sesamum spp.</i> [11]
CYP76	42	42	Biosynthesis of monoterpene volatiles in <i>A. thaliana</i> [12], monoterpene indole alkaloids in <i>Catharanthus roseus</i> [13,14], sesquiterpene volatiles in sandalwood ( <i>Santalum album</i> ) [15], phytoalexins in rice ( <i>Oryza sativa</i> ) [16,17], tanshinones in Chinese sage ( <i>Salvia miltiorrhiza</i> ) [18], pigment betalain in beetroot ( <i>Beta vulgaris</i> ) [19]. Metabolism of xenobiotics in <i>A. thaliana</i> [20].
CYP72	36	33	Biosynthesis of monoterpene indole alkaloids in <i>C. roseus</i> [14,21], glycyrrhizin in licorice ( <i>Glycyrrhiza</i> ) [22], saponins in <i>M. truncatula</i> [23].
CYP79	26	25	Biosynthesis of cyanogenic glucosides in sorghum [24], cassava ( <i>M. esculenta</i> ) [25] and other plant species, glucosinolates in brassicaceae [26–28].
CYP89	25	21	Chlorophyll degradation in <i>A. thaliana</i> [29].
CYP75	24	23	Biosynthesis of flavonoids in <i>Petunia x hybrida</i> , <i>A. thaliana</i> , <i>Gentiana triflora</i> , <i>C. roseus</i> , etc. [9]
CYP716	23	12	Biosynthesis of saponins in <i>M. truncatula</i> [30] and <i>Maesa lanceolata</i> [31,32].
CYP706	21	19	Biosynthesis of sesquiterpenoids in cotton ( <i>Gossypium arboreum</i> ) [33].
CYP87	20	15	Biosynthesis of saponins in <i>Maesa lanceolata</i> [31].
CYP714	16	13	Degradation or biosynthesis of hormones (gibberelins) in rice ( <i>O. sativa</i> ) [34].
CYP736	13	11	Unknown. Pathogen response in grapevine <i>V. vinifera</i> [35].
CYP728	11	9	Unknown.
CYP80	10	9	Alkaloid biosynthesis in barberry ( <i>Berberis stolonifera</i> ) [36] and California poppy ( <i>Eschscholzia californica</i> ) [37].
CYP96	9	9	Biosynthesis of cuticular wax in <i>A. thaliana</i> [38].
CYP721	8	8	Unknown.
CYP74	7	7	Biosynthesis of jasmonates and C6 volatiles in <i>A. thaliana</i> and other plants [39–41].
CYP92	7	5	Unknown.
CYP93	7	6	Biosynthesis of flavonoids in soybean ( <i>G. max</i> ), <i>Glycyrrhiza echinata</i> , <i>Gerbera hybrid</i> , <i>Antirrhinum majus</i> , <i>Torrenia hybrid</i> , etc. [9,42]
CYP712	6	5	Unknown.

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