

# Subfunctionalization of paralog transcription factors contributes to regulation of alkaloid pathway branch choice in *Catharanthus roseus*

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**Manuscript Source:** <https://www.biorxiv.org/content/10.1101/2020.05.04.075671v2>

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### Research Paper Sections:

The sections of the research paper input text parsed in this audit.

[illegible]

Title      **Subfunctionalization of paralog transcription factors contributes to regulation of alkaloid pathway branch choice in *Catharanthus roseus***

**S1 [001]      SUMMARY**

**S1 [002]**      *Catharanthus roseus* produces a diverse range of specialized metabolites of the monoterpenoid indole alkaloid (MIA) class in a heavily branched pathway.

*Catharanthus roseus* produces a diverse range ...  
... of specialized metabolites ...  
... of the monoterpenoid indole alkaloid ...  
... (MIA) ...  
... class ...  
... in a heavily branched pathway.

**S1 [003]**      Recent great progress in identification of MIA biosynthesis genes revealed that the different pathway branch genes are expressed in a highly cell type- and organ-specific and stress-dependent manner.

Recent great progress ...  
... in identification ...  
... of MIA biosynthesis genes revealed ...  
... that the different pathway branch genes are expressed ...  
... in a highly cell type- ...  
... and organ-specific ...  
... and stress-dependent manner.

**S1 [004]**      This implies a complex control by specific transcription factors (TFs), only partly revealed today.

This implies a complex control ...  
... by specific transcription factors ...  
... (TFs), ...  
... only partly revealed today.

**S1 [005]**      We generated and mined a comprehensive compendium of publicly available *C. roseus* transcriptome data for MIA pathway branch-specific TFs.

We generated ...  
... and mined a comprehensive compendium ...  
... of publicly available *C. roseus* transcriptome data ...  
... for MIA pathway branch-specific TFs.

**S1 [006]**      Functional analysis was performed through extensive comparative gene expression analysis and profiling of over 40 MIA metabolites in the *C. roseus* flower petal expression system.

Functional analysis was performed ...

... through extensive comparative gene expression analysis ...  
... and profiling ...  
... of over 40 MIA metabolites ...  
... in the *C. roseus* flower petal expression system.

**S1 [007]** We identified additional members of the known BIS and ORCA regulators.

We identified additional members ...  
... of the known BIS ...  
... and ORCA regulators.

**S1 [008]** Further detailed study of the ORCA TFs suggests subfunctionalization of ORCA paralogs in terms of target gene-specific regulation and synergistic activity with the central jasmonate response regulator MYC2.

Further detailed study ...  
... of the ORCA TFs suggests subfunctionalization ...  
... of ORCA paralogs ...  
... in terms ...  
... of target gene-specific regulation ...  
... and synergistic activity ...  
... with the central jasmonate response regulator MYC2.

**S1 [009]** Moreover, we identified specific amino acid residues within the ORCA DNA-binding domains that contribute to the differential regulation of some MIA pathway branches.

Moreover, ...  
... we identified specific amino acid residues ...  
... within the ORCA DNA-binding domains ...  
... that contribute ...  
... to the differential regulation ...  
... of some MIA pathway branches.

**S1 [010]** Our results advance our understanding of TF paralog specificity for which, despite the common occurrence of closely related paralogs in many species, comparative studies are scarce.

Our results advance our understanding ...  
... of TF paralog specificity ...  
... for which, ...  
... despite the common occurrence ...  
... of closely related paralogs ...  
... in many species, ...  
... comparative studies are scarce.

**S1 [011]** SIGNIFICANCE STATEMENT

SIGNIFICANCE STATEMENT

**S1 [012]** A gene discovery program for regulators of monoterpenoid indole alkaloid biosynthesis in *Catharanthus roseus* advances our understanding of paralog specificity and subfunctionalization of the renowned class of ORCA transcription factors, particularly in terms of target gene-specificity and synergistic activity with other jasmonate-responsive transcription factors.

A gene discovery program ...  
... for regulators ...  
... of monoterpenoid indole alkaloid biosynthesis ...  
... in *Catharanthus roseus* advances our understanding ...  
... of paralog specificity ...  
... and subfunctionalization ...  
... of the renowned class ...  
... of ORCA transcription factors, ...  
... particularly ...  
... in terms ...  
... of target gene-specificity ...  
... and synergistic activity ...  
... with other jasmonate-responsive transcription factors.

## **S2 [013] INTRODUCTION**

**S2 [014]** Plant specialized metabolites are chemically diverse, typically species- or taxa-specific and have often evolved in adaptation to the ecological niche of the plant.

Plant specialized metabolites are chemically diverse, ...  
... typically species- ...  
... or taxa-specific ...  
... and have often evolved ...  
... in adaptation ...  
... to the ecological niche ...  
... of the plant.

**S2 [015]** Within the plant, their production often exclusively takes place in specific organs or cell types and may be up-regulated precisely in response to defined environmental conditions [for a review, see Colinas and Goossens (2018)].

Within the plant, ...  
... their production often exclusively takes place ...  
... in specific organs ...  
... or cell types ...  
... and may be up-regulated precisely ...  
... in response ...  
... to defined environmental conditions ...  
... [for a review, ...  
... see Colinas ...  
... and Goossens ...  
... (2018)].

**S2 [016]** The integration of internal cues, such as cell type environment and developmental stage, and external cues, such as the presence of pathogens or herbivores, is predominantly regulated at the transcriptional level by specific transcription factors (TFs).

The integration ...  
... of internal cues, ...  
... such as cell type environment ...  
... and developmental stage, ...  
... and external cues, ...  
... such as the presence ...  
... of pathogens ...  
... or herbivores, ...  
... is predominantly regulated ...  
... at the transcriptional level ...  
... by specific transcription factors ...  
... (TFs).

**S2 [017]** Different TFs might act independently or cooperatively, forming regulatory modules that ensure the optimal spatiotemporal expression of specific metabolic pathway genes.

Different TFs ...  
... might act independently ...  
... or cooperatively, ...  
... forming regulatory modules ...  
... that ensure the optimal spatiotemporal expression ...  
... of specific metabolic pathway genes.

**S2 [018]** The medicinal plant *Catharanthus roseus* is well-known as being the only source of the important anti-cancer compounds vinblastine and vincristine (van der Heijden et al., 2004).

The medicinal plant *Catharanthus roseus* is well-known ...  
... as being the only source ...  
... of the important anti-cancer compounds vinblastine ...  
... and vincristine ...  
... (van der Heijden et al., 2004).

**S2 [019]** These complex molecules belong to the class of monoterpenoid indole alkaloids (MIAs); around 150 different MIAs are estimated to occur in *C. roseus* (van der Heijden et al., 2004).

These complex molecules belong ...  
... to the class ...  
... of monoterpenoid indole alkaloids ...  
... (MIAs); ...  
... around 150 different MIAs are estimated ...  
... to occur ...  
... in *C. roseus* ...  
... (van der Heijden et al., 2004).

**S2 [020]** The identification of many of the involved biosynthetic enzymes has revealed that genes involved in the different MIA pathway steps and branches are expressed in a cell type-specific, organ-specific and stress-dependent manner, making this species an ideal model to study how a modular system of different TFs possibly regulates specialized metabolism (Courdavault et al., 2014; Dugé de Bernonville et al., 2015).

## **End of Sample Audit**

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