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Use of metabolomics to identify bioactive compounds from grapevine eco-extracts that can impair fungal growth and production of mycotoxins by *Fusarium graminearum* and elucidate their mechanisms of action

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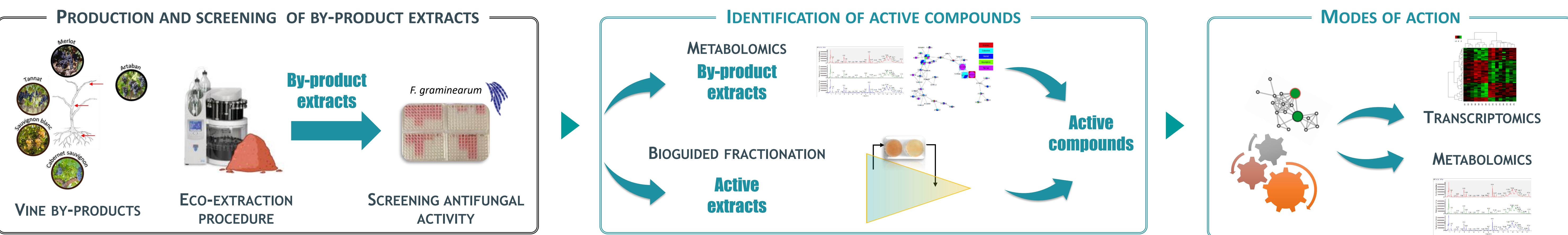
* These authors contributed equally to this work

PROBLEM STATEMENT AND OBJECTIVES

Fusarium Head Blight of small-grain cereals is a devastating fungal disease primarily caused by *Fusarium graminearum* in Europe. Beyond crop losses, *F. graminearum* poses potential health risks due to the production type B trichothecene (TCTB) mycotoxins including deoxynivalenol (DON) and 15-acetyldeoxynivalenol (15-ADON). The development of environmental-friendly strategies guaranteeing the safety of food and feed is a key challenge facing agriculture today.

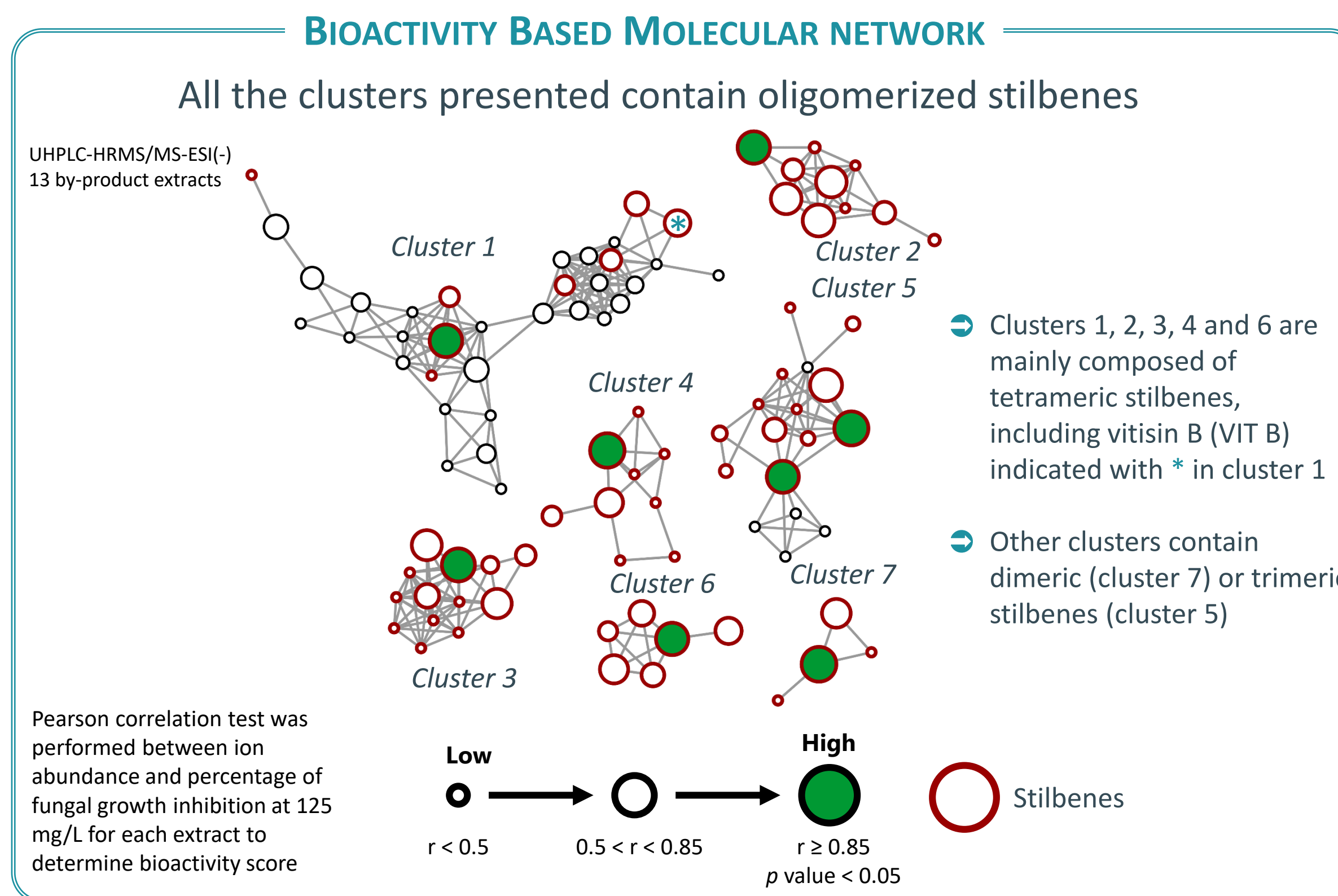
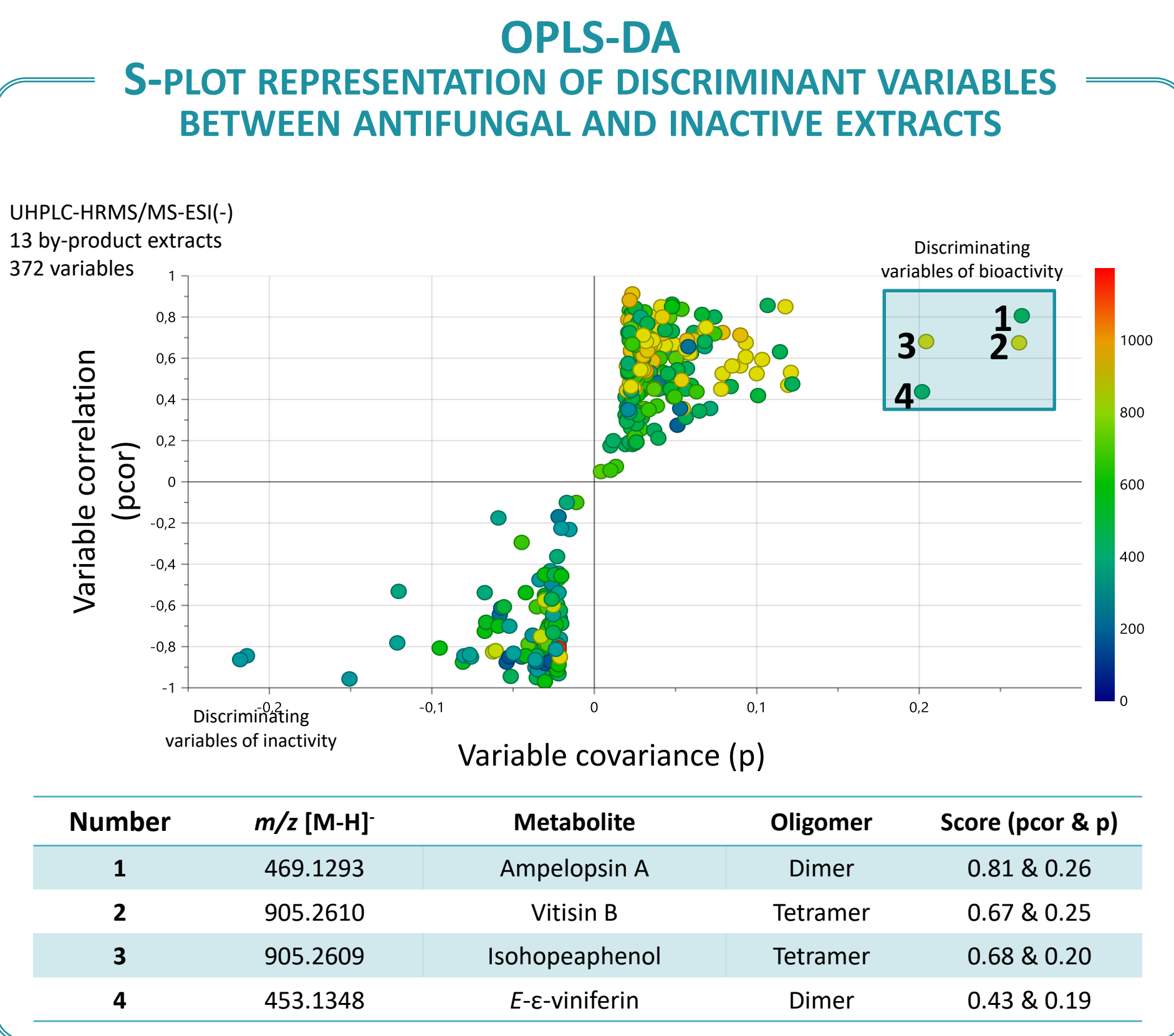
The goal of the present study is to investigate and exploit the biological activity of grapevine wastes to develop environmental-friendly solutions to counteract the growth of *F. graminearum* and its production of mycotoxins. In the first step, natural extracts from vine by-products were obtained using eco-extraction and were characterized for their antifungal and antimycotoxin activities. Identification of active molecules and their mechanisms of action were investigated using complementary omics approaches.

EXPERIMENTAL PROCEDURE



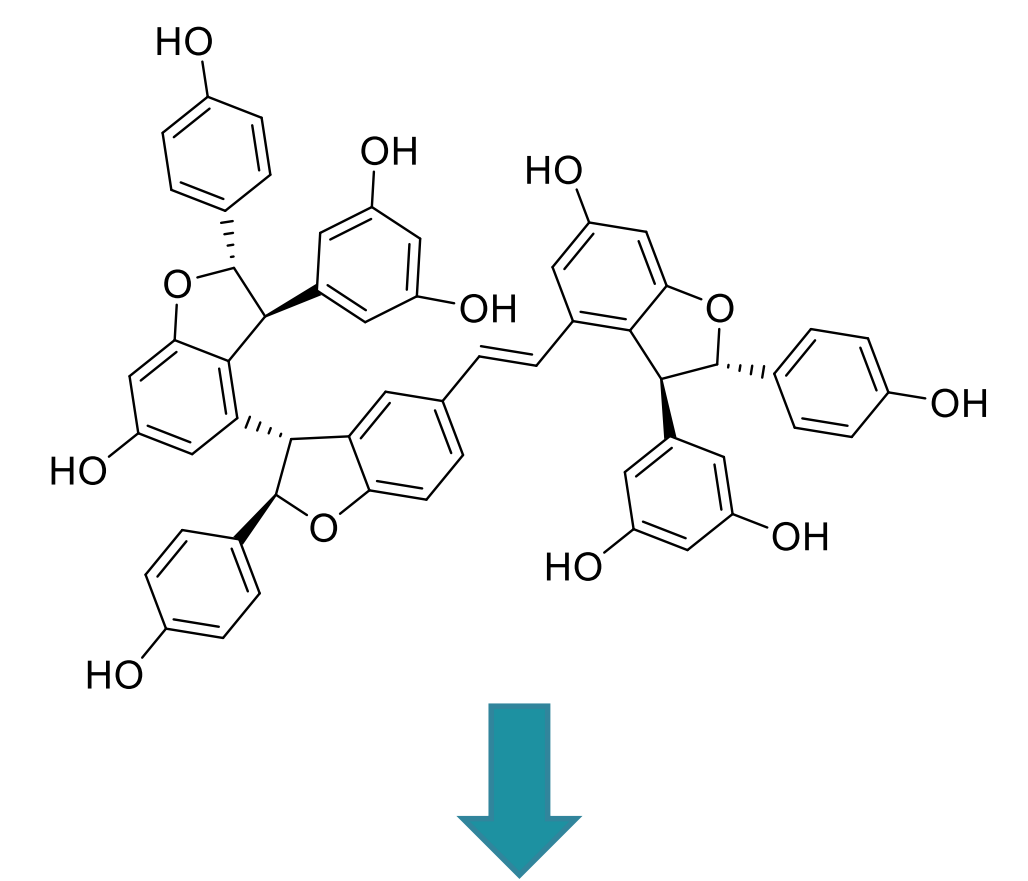
RESULTS

UNTARGETED METABOLOMICS AND MOLECULAR NETWORK TO EVIDENCE THE ACTIVE COMPOUNDS



OLIGOMERIC STILBENES APPEAR TO BE CORRELATED WITH ANTIFUNGAL ACTIVITY

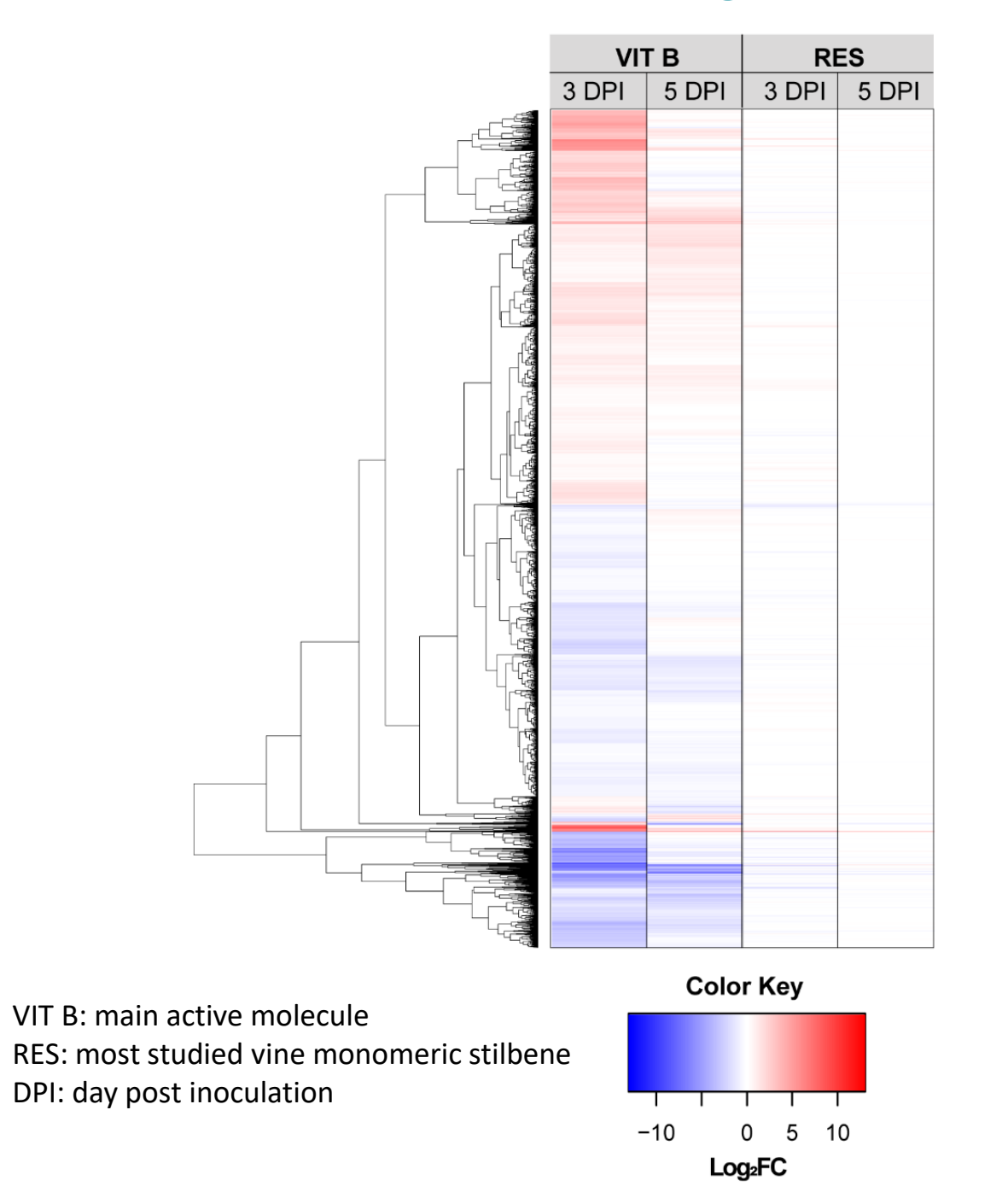
VIT B is the main stilbene quantified by HPLC-UV in most active root extracts



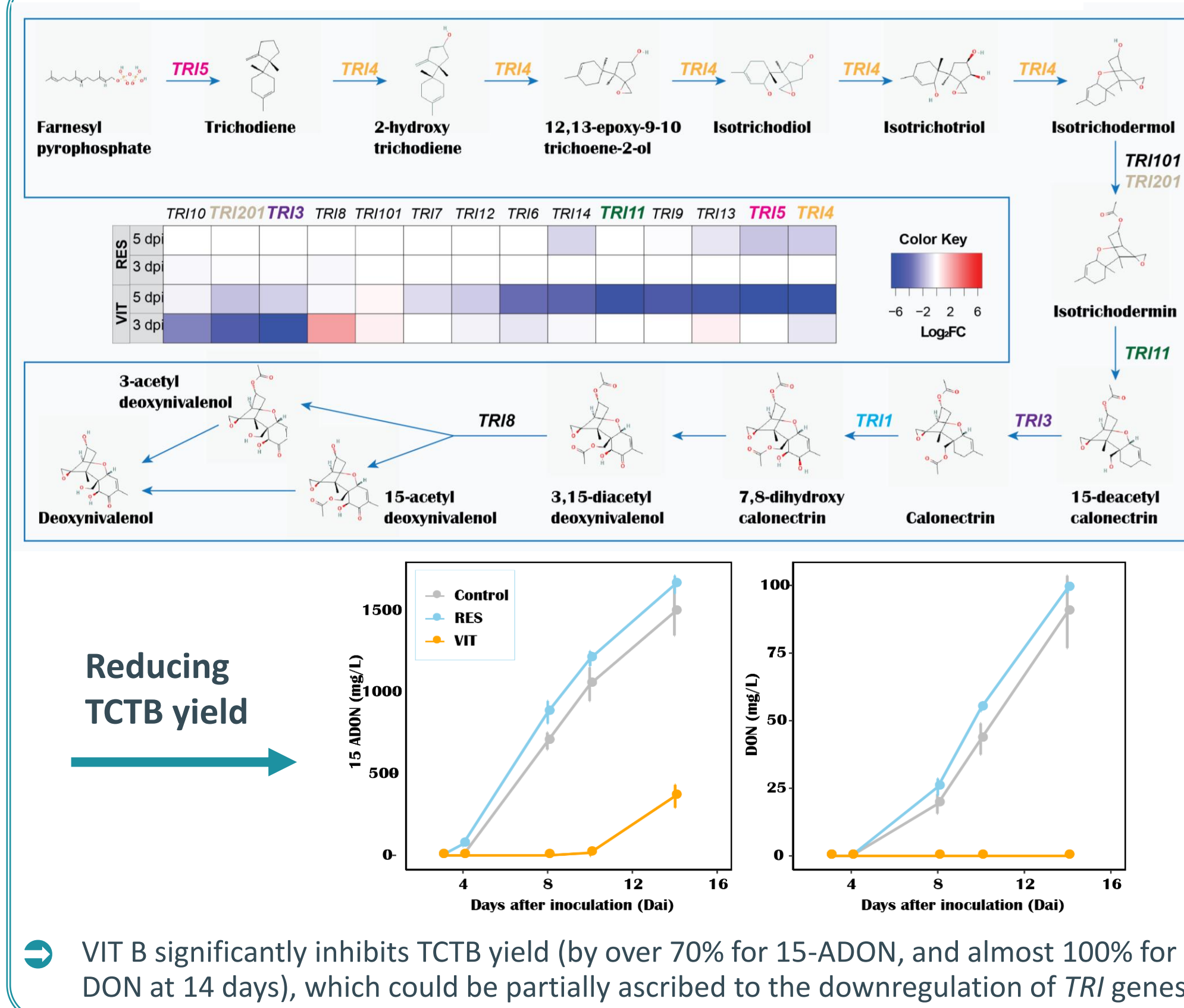
Isolation of VIT B from root extract using preparative HPLC

MULTI-OMICS APPROACH TO UNDERSTAND THE MODE OF ACTION OF VIT B AND E-RESVERATROL (RES)

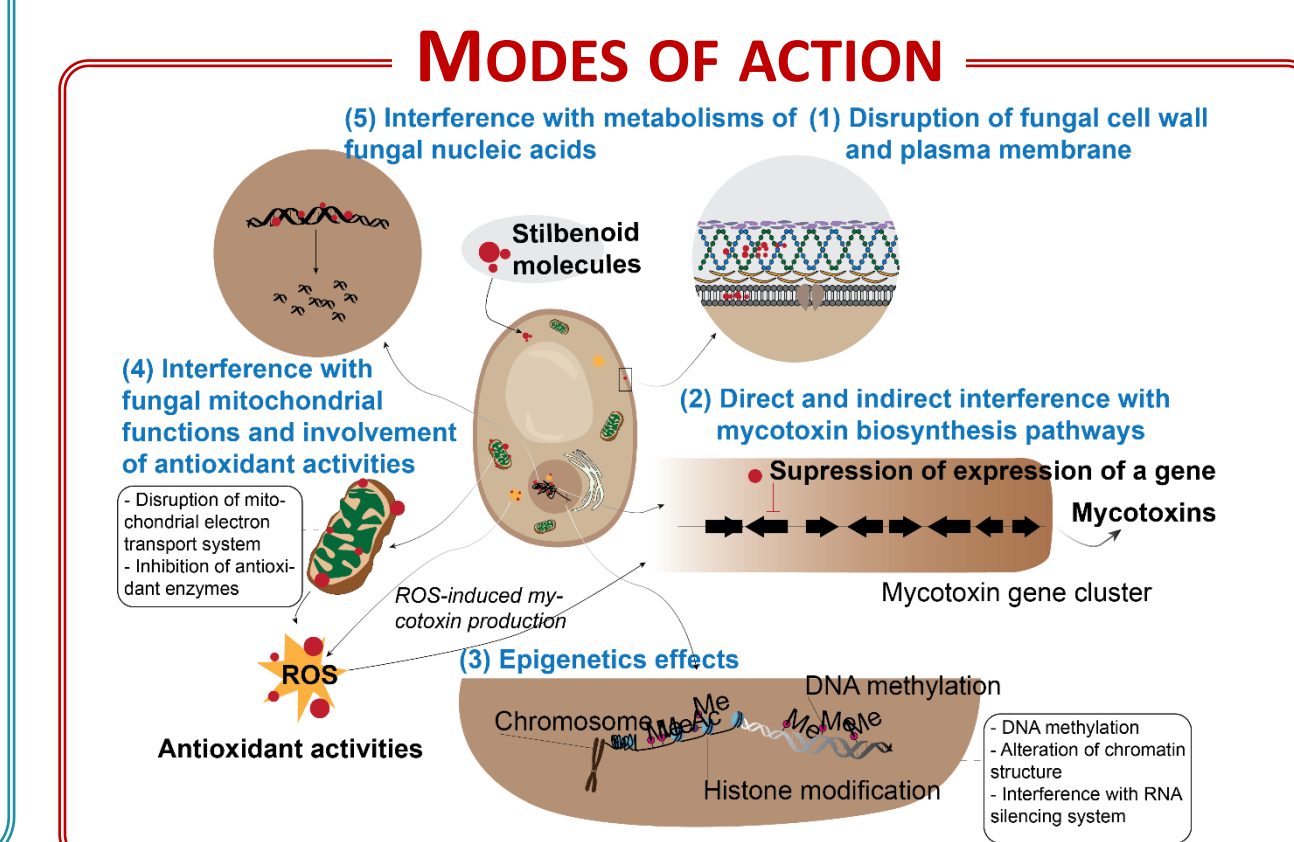
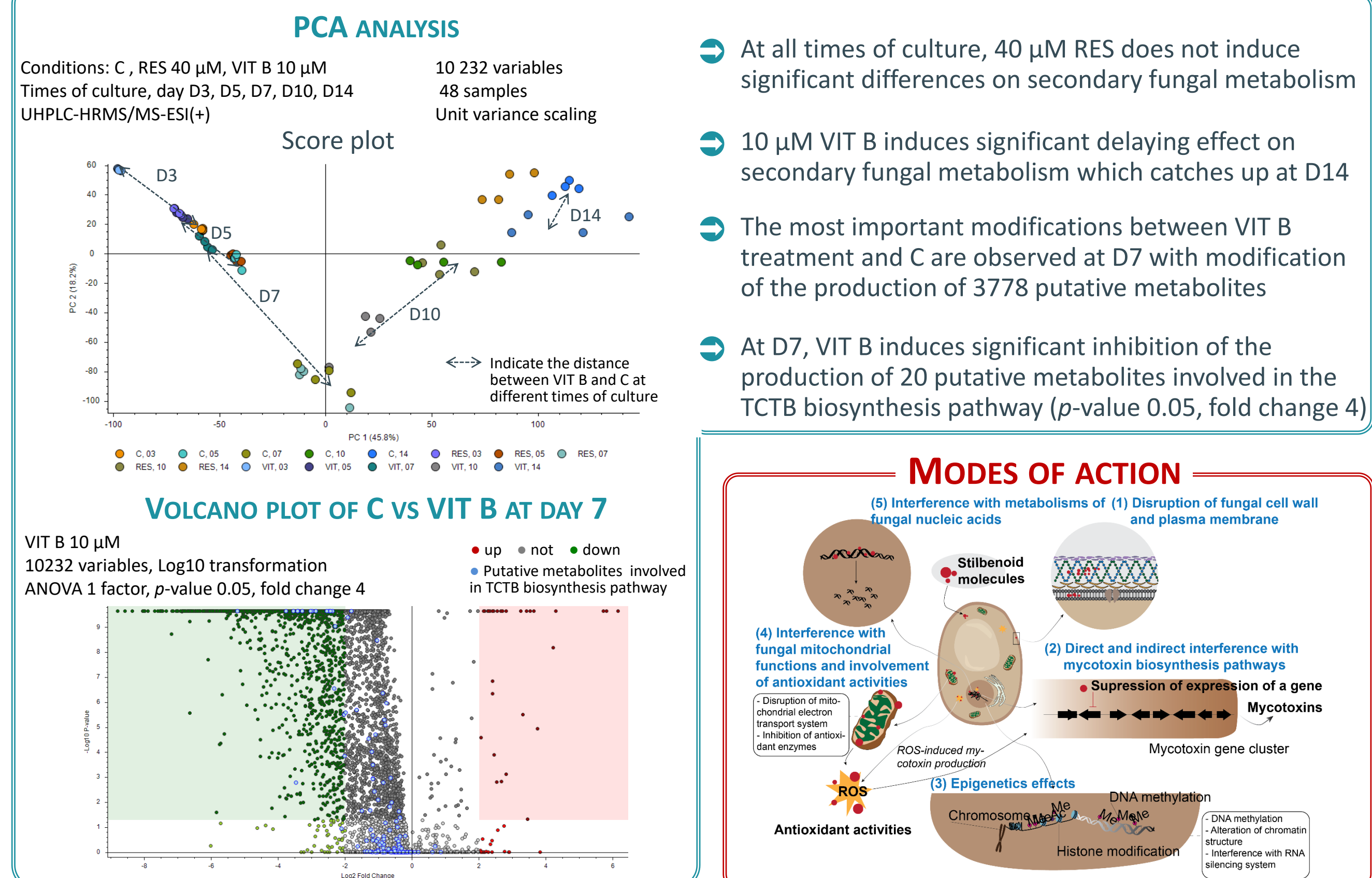
GLOBALY TRANSCRIPTOMIC REGULATION BY VIT B AND RES



DOWN-REGULATION OF TRI GENES BY VIT B AND RES



UNTARGETED METABOLOMICS OF FUNGAL SUPERNATANTS



CONCLUSIONS AND PERSPECTIVES

- Untargeted metabolomics combined with molecular network and bioguided fractionation allow us to identify oligomeric stilbenes, in particular VIT B, as predominant active antifungal and antimycotoxin metabolites in vine by-products
- VIT B (at a low concentration of 10 μM) induces significant modifications in secondary fungal metabolism of *F. graminearum*, especially in TCTB biosynthesis pathway
- Omics approaches provide a deeper insight into the mechanism of action of VIT B underlying its antifungal and antimycotoxin activity
- The ongoing *in-planta* assays will study bioactivities of the vine extracts towards developing environmental-friendly solutions

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