

New and repurposed insecticides for mosquito control

Melanie Nolden, Sebastian Horstmann, Frederic Schmitt

envu™
Mosquito
Management



February 14., 2023

We protect the spaces society and nature share.



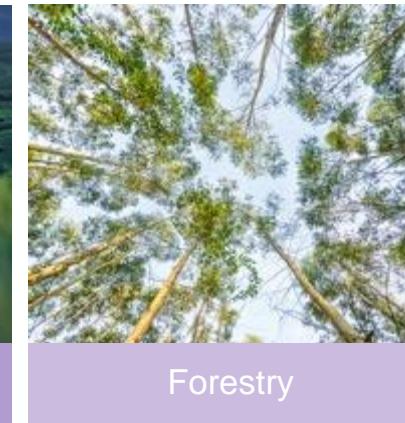
Professional Pest Mgmt.



Industrial Vegetation Mgmt.



Range & Pasture



Forestry



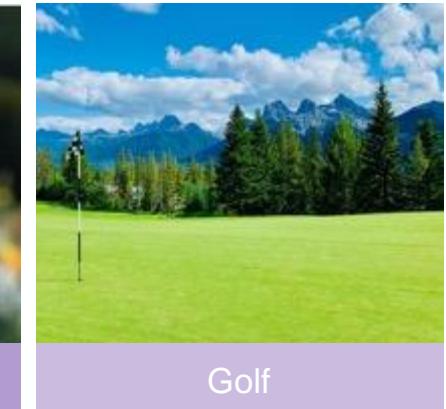
Mosquito Management



Lawn & Landscape



Ornamentals



Golf

Products in Mosquito Management



FLUDORA™ Fusion Deltamethrin + Clothianidine IRS

FICAM® Bendiocarb

K-OTHRINE® PolyZone Deltamethrin + Polyzone tech.



FLUDORA™ Co-Max Transfluthrin + Flupyradifurone Space sprays
(FFAST technology)

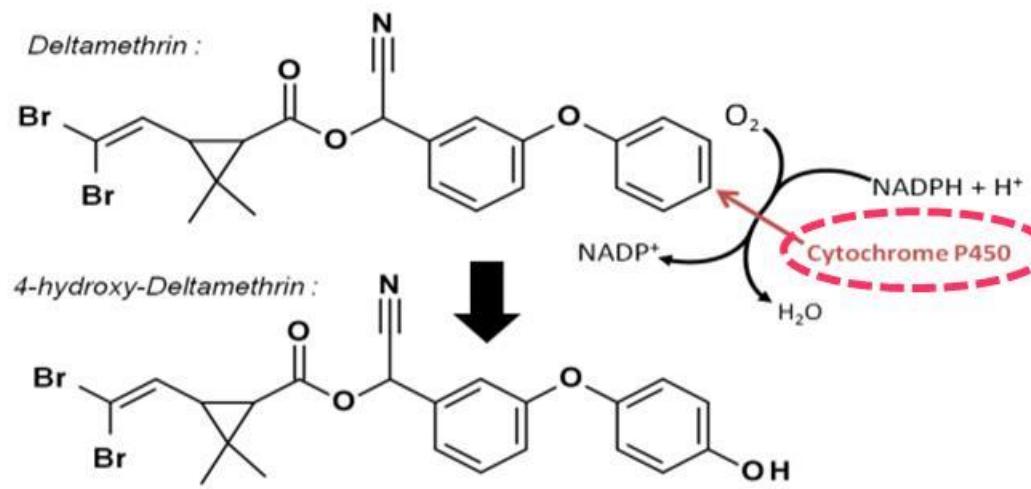
AQUA K-OTHRINE® Deltamethrin

AQUA RESLIN® Super Permethrin + S Biol. +PBO

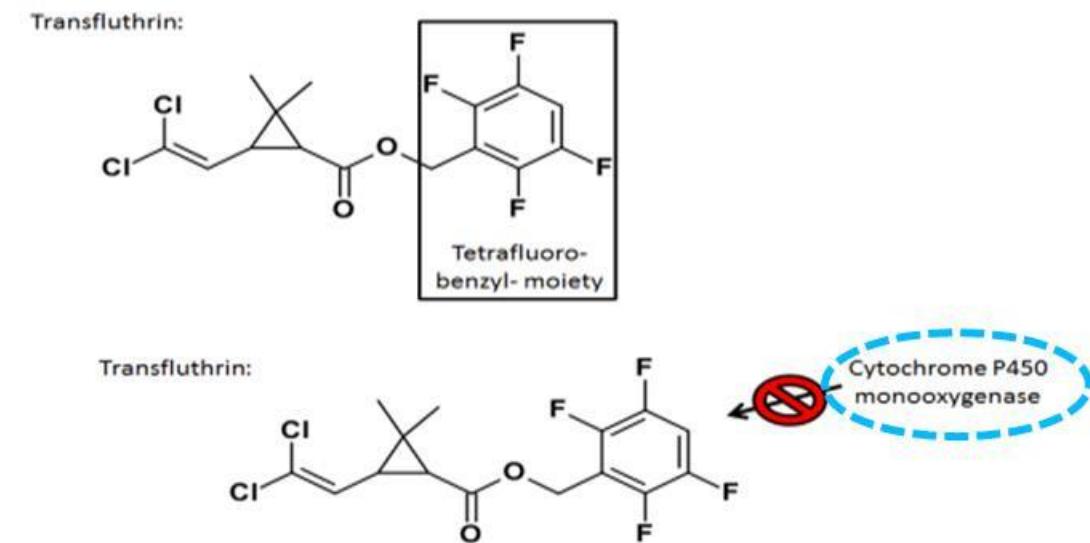


Bayothrin® (Transfluthrin) is resistant to P450 enzymes

General pyrethroid degradation scheme
(e.g.Deltamethrin):



Bayothrin® (Transfluthrin):
NO binding = NO degradation = NO resistance



RESEARCH ARTICLE

Contact Bioassays with Phenoxybenzyl and Tetrafluorobenzyl Pyrethroids against Target-Site and Metabolic Resistant Mosquitoes

Sebastian Horstmann*, Rainer Sonneck
Bayer CropScience AG, Monheim am Rhein, Germany

 PLOS ONE

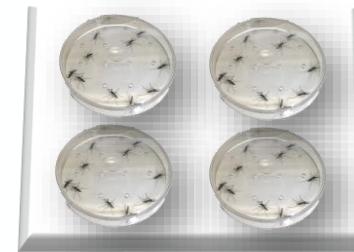
Transfluthrin – still active against resistant *An. funestus*

10 *Anopheles funestus* FUMOZ-R ♀

10 *Anopheles funestus* FANG ♀



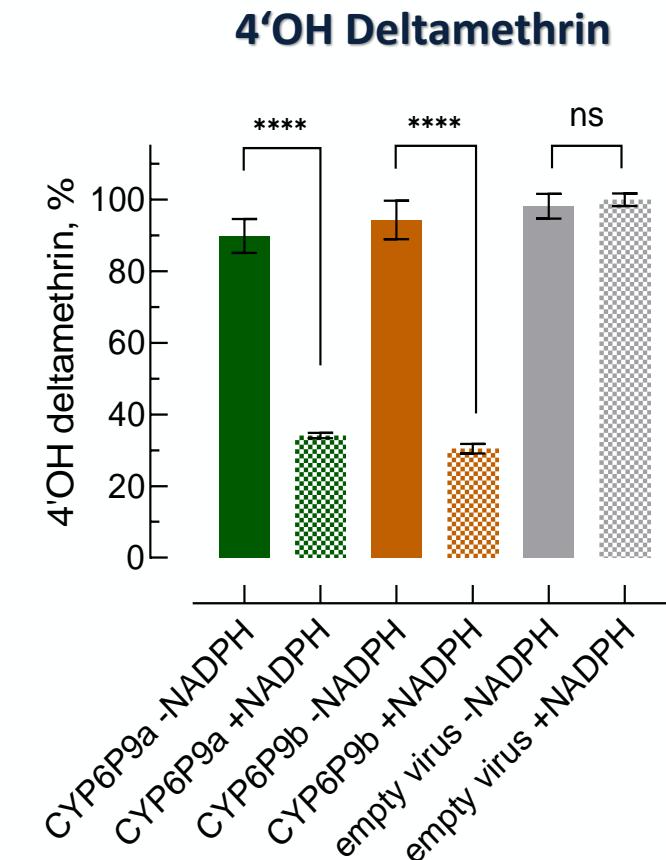
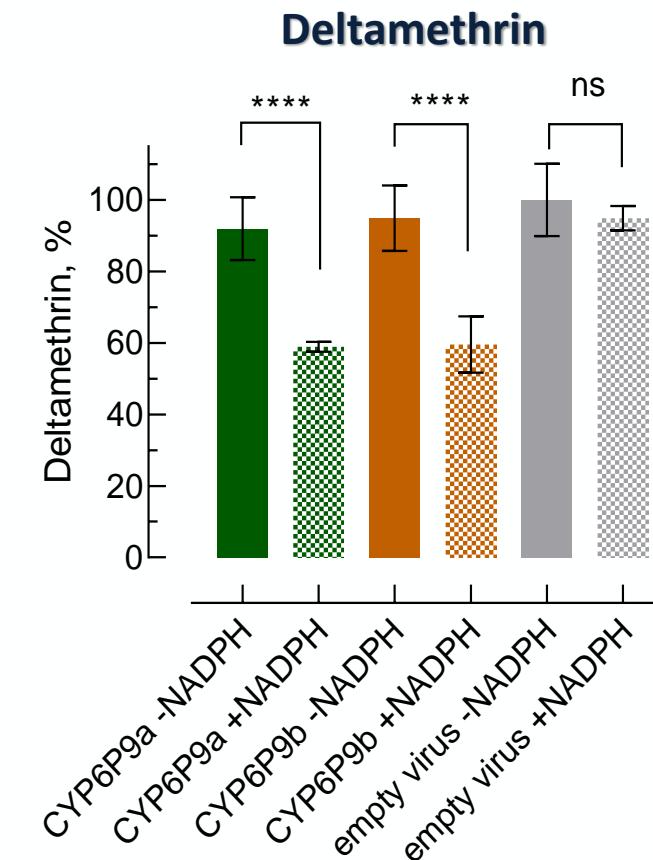
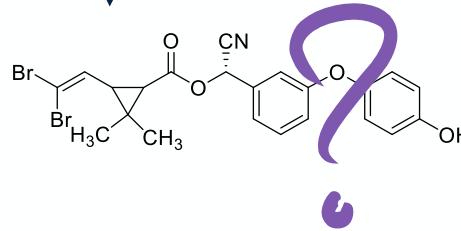
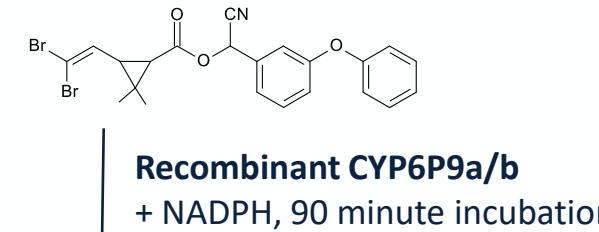
30 minutes exposure to different concentrations of insecticides



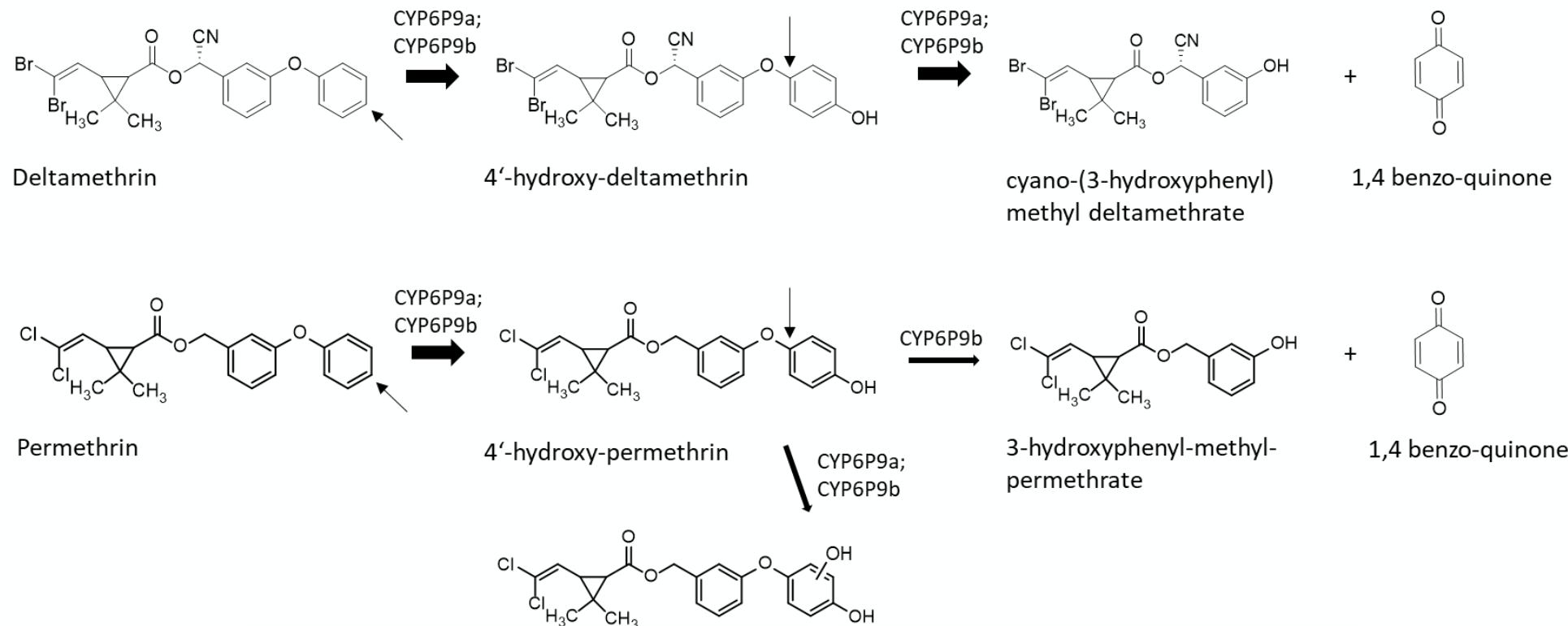
Calculation of lethal concentration 50 (LC₅₀)

Substances	LC ₅₀ in mg/m ² (FANG)
Deltamethrin	0.0206
Cypermethrin	0.0968
Permethrin	0.543
Transfluthrin	0.023

Deltamethrin and 4'OH deltamethrin metabolism



Sequential deltamethrin and permethrin metabolism by CYP6P9a and CYP6P9b



Contents lists available at ScienceDirect
Insect Biochemistry and Molecular Biology
journal homepage: www.elsevier.com/locate/ibmb

Cytochrome P450 6M2 from the malaria vector *Anopheles gambiae* metabolizes pyrethroids: Sequential metabolism of deltamethrin revealed

Bradley J. Stevenson^a, Jaclyn Bibby^b, Patricia Pignatelli^a, Sant Muangnoicharoen^a, Paul M. O'Neill^c, Lu-Yun Lian^d, Pie Müller^{a,c,f}, Dimitra Nikou^d, Andrew Steven^a, Janet Hemingway^a, Michael J. Sutcliffe^b, Mark J.I. Paine^{a,*}

^a Bayer AG, Crop Science Division, Alfred Nobell Str. 90, D-40709, Monheim am Rhein, Germany
^b Department of Victor Biology, Liverpool School of Tropical Medicine, Pembroke Place, Liverpool, L3 3QA, United Kingdom

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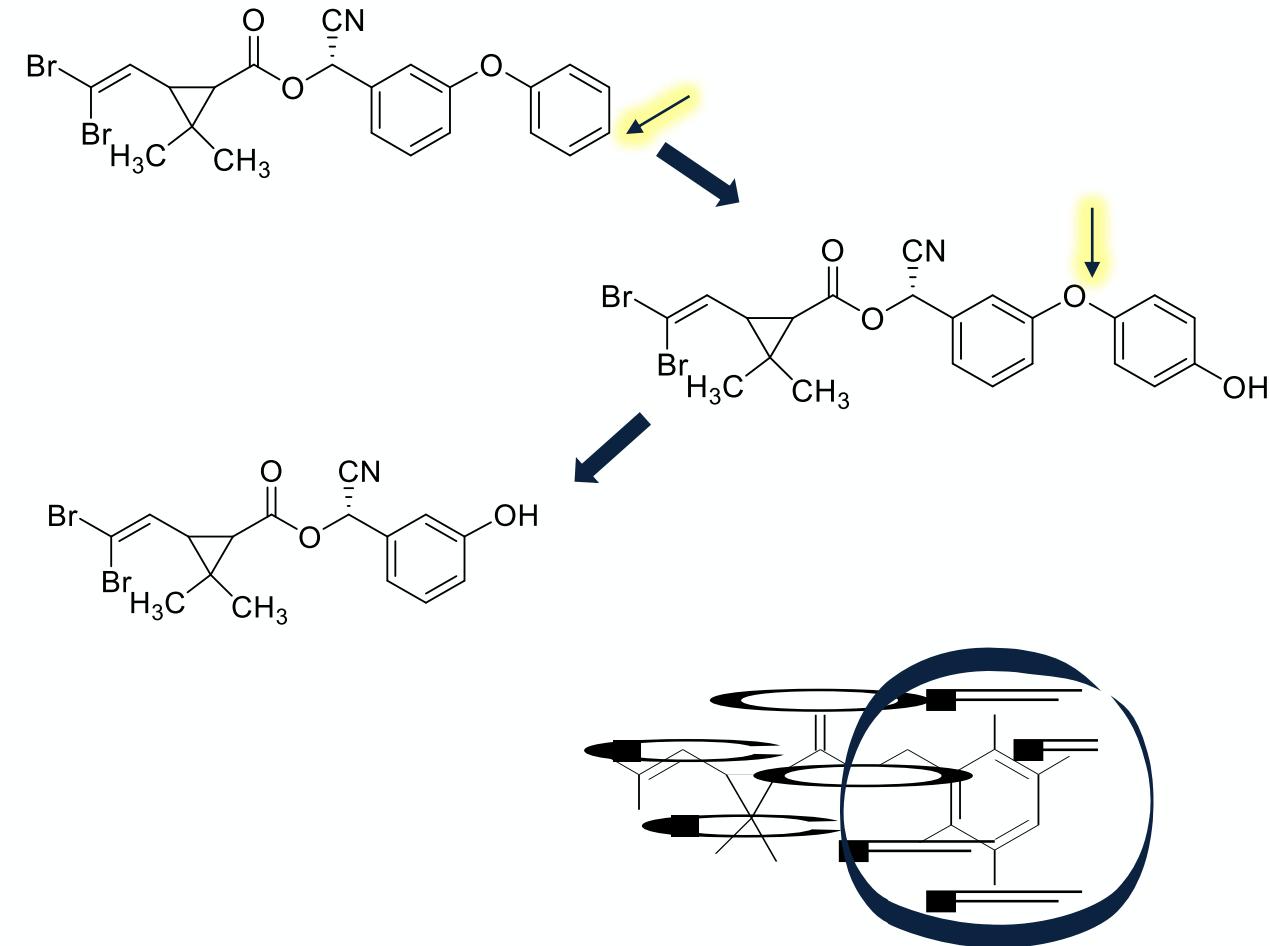
Sequential phase I metabolism of pyrethroids by duplicated CYP6P9 variants results in the loss of the terminal benzene moiety and determines resistance in the malaria mosquito *Anopheles funestus*

Melanie Nolden^{a,b}, Mark J.I. Paine^{b,*,*}, Ralf Nauen^{a,*}

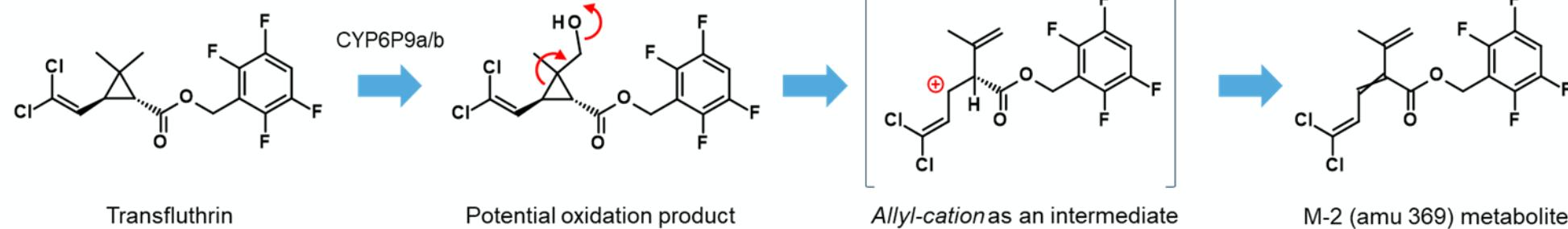
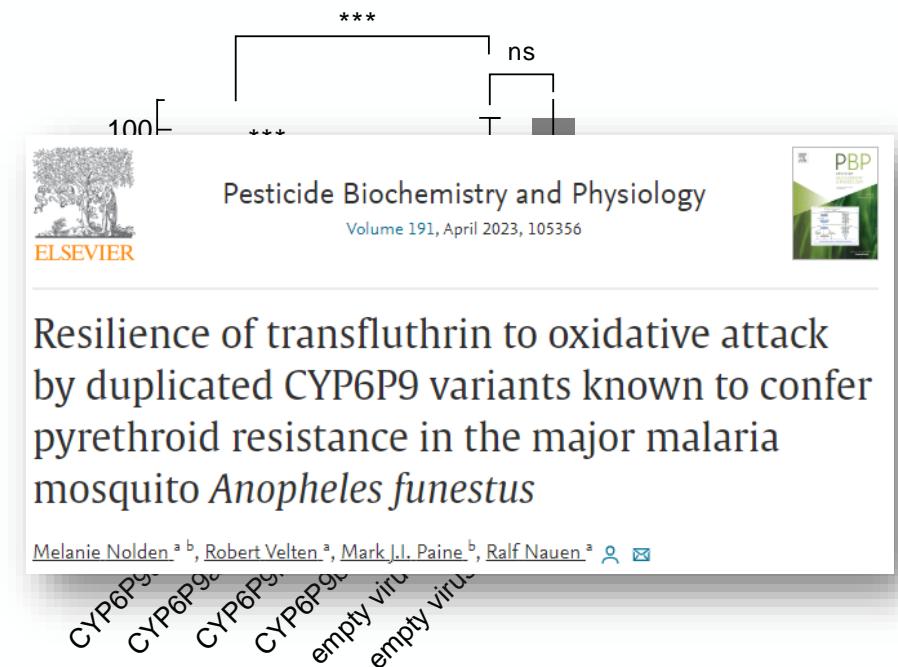
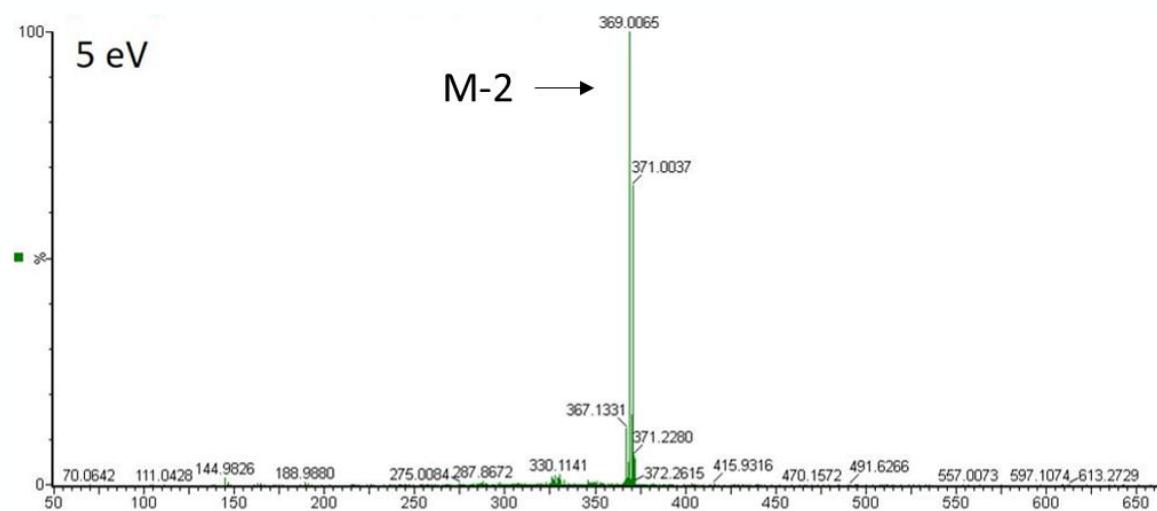
^a Bayer AG, Crop Science Division, Alfred Nobell Str. 90, D-40709, Monheim am Rhein, Germany
^b Department of Victor Biology, Liverpool School of Tropical Medicine, Pembroke Place, Liverpool, L3 3QA, United Kingdom

Transfluthrin – protected by P450 attacks?

Substances	LC ₅₀ in mg/m ² (FANG)	LC ₅₀ in mg/m ² (FUMOZ-R)	Resistance Ratio
Deltamethrin	0.0206	4.61	223
Cypermethrin	0.0968	7.54	77.9
Permethrin	0.543	4.21	7.76
Transfluthrin	0.023	0.0576	2.51



Proposed metabolic fate of transfluthrin



Take home messages

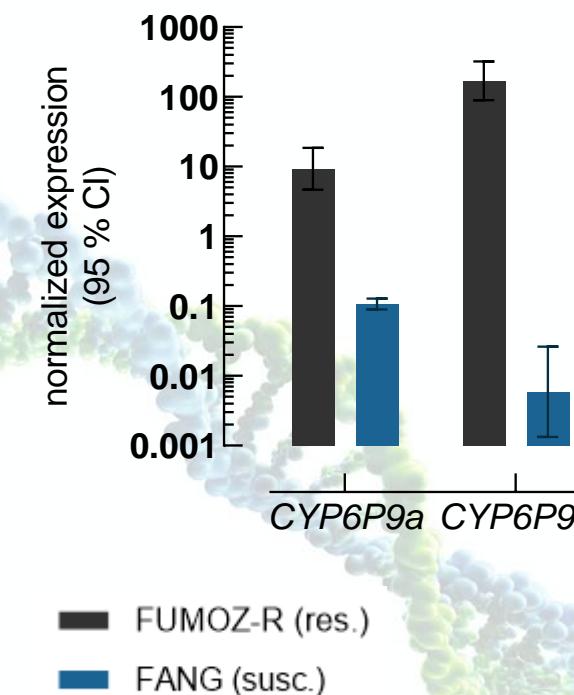
- At Envu we do research and product-development for vector control
- Pyrethroid resistance in *An. funestus* FUMOZ-R conferred by highly upregulated CYP6P9a/b
- **Transfluthrin** still active against highly pyrethroid resistant *An. funestus* FUMOZ-R
- Common **pyrethroids (deltamethrin, permethrin)** are easily processed at the phenoxybenzyl-moiety by two steps: hydroxylation and ether cleavage
- **Transfluthrin is protected by 1. fluorination and 2. lacking the phenoxybenzyl-ether**
- Transfluthrin metabolism revealed: likely an opening of cyclopropyl-ring

Thank You

Expression analysis revealed: upregulation of CYP6P9a and CYP6P9b

10 *Anopheles funestus* FUMOZ-R ♀
10 *Anopheles funestus* FANG ♀

RNA
cDNA
RT qPCR



Envu key figures

2022



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