Persistent Identifier: urn:nbn:de: 0294-sp-2017-Reinh-19-3

Lopez-Ruiz F; Mair W; Oliver RP. Proposal for a Unified Nomenclature for Target Site Mutations Associated with Resistance to Fungicides, an Update. In: Deising HB; Fraaije B; Mehl A; Oerke EC; Sierotzki H; Stammler G (Eds), "Modern Fungicides and Antifungal Compounds", Vol. VIII, pp. 121-126. © 2017 Deutsche Phytomedizinische Gesellschaft, Braunschweig, ISBN: 978-3-941261-15-0

Proposal for a Unified Nomenclature for Target Site Mutations Associated with Resistance to Fungicides, an Update

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ABSTRACT

Most cases of fungicide resistance have been linked to target site mutations. It is commonly observed that orthologous amino acids are selected by the same fungicides in different species but the amino acids have different numbers due to differences in the length of the protein. We proposed a system to unify the numbering by aligning all proteins to a reference or archetype sequence. All changes are given an italicised "label" based on the number of the amino acid in the archetype. This system was published in 2016 (Mair et *al.* 2016) based on information available in April 2016. We present here an update using new information.

INTRODUCTION

A system for unifying the nomenclature of target site mutations associated with fungicide resistance was based on alignments of target site proteins to a chosen archetype species (Mair et *al.* 2016). A key feature of the system was that it should be stable and capable of adding in new information as it becomes available. We present here new cases of target site mutation published or brought to our attention since April 2016.

The tables here list the new species and the label assigned to different amino acids changes. The new alignments are available at ccdm.curtin.edu.au.

Cytochrome b.

Table 1 CytB - Reference sequence from *Zymoseptoria tritici.*

Amino acid substitution(s) in archetype	Homologous position in other species	Reference
F129L	F129L in ALTETO	(Olaya et *al.* 2017)
G143A	G143A in RAMUCC	(Piotrowska et *al.* 2017)
	G143A in UNCINE	(Hall et *al.* 2017)

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Cyp51B.

The wheat eyespot pathogens *Tapesia (Oculimacula) acuformis* (PSDCHA) and *T. yallundae* (PSDCHE) differ in their natural sensitivities to triazole and imidazole DMIs (Albertini et *al.* 2003). The alignments to SEPTTR reveal a number of amino acids that may contribute to this situation. Other new mutations from *Penicillium digitatum, Pseudocercospora (Mycosphaerella) fijiensis* and *Pyrenopeziza brassicae* are listed.

Table 2 Cyp51B - Reference sequence from *Z. tritici*.

Amino acid substitution(s) in archetype	**Homologous position in other species**	**References**
L29	A29P in PSDCHA	(Albertini et *al.* 2003)
A35	S35T in PSDCHE	
L37	V37A in PSDCHA	
Q43	Q43H in PSDCHE	
S79	D78Y in PSDCHE	
D107V	E106K in PSDCHE	
Y137F	Y136H in PENIDI	(Wang et *al.* 2014)
A168	Q167H in PSDCHA	(Albertini et *al.* 2003)
N248	N244S in PSDCHE	
Q313	Q309H in PENIDI	(Wang et *al.* 2014)
H378	H380N in MYCOFI	(Chong et *al.* 2016)
A379G	A381G in MYCOFI	
D458	D460V in MYCOFI	(Chong et *al.* 2016)
Y459C/D/N/S/P/Δ	Y461D in MYCOFI	
G460D/Δ	G462A in MYCOFI	
Y461D/H/S	Y463D/H/N in MYCOFI	
G476S	G459S in PENIDI	(Hawkins & Fraaije, 2017; Wang et *al.* 2014)
	G460S in PYRPBR	(Carter et *al.* 2014)
D502	Y486H in PSDCHA	(Albertini et *al.* 2003)
S521	S505Q in PSDCHA	
	S505Q in PSDCHE	
F523	F506I in PENIDI	(Wang et *al.* 2014)
S524T	S508T in PYRPBR	(Carter et *al.* 2014)

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SDH subunits.

Reference sequences are from *Pyrenophora teres* f. sp. teres. *Venturia inaequalis*, *Stemphylium vesicarium*, *Uncinula necator* have been added to the alignments plus new mutations in Botrytis, *Z. tritici* and *A. alternata*.

Table 3 SdhB

Amino acid substitution(s) in archetype	Homologous position in other species	Reference
Y162	Y137C in VENTIN	(FRAC, 2016)
P230	P220L/T in SEPTTR	(Scalliet et *al.* 2012)
	P225F/H/L/T in BOTRCI	(Kleeman & Mehl, 2017)
	P225L in PLEOAL	(FRAC, 2016)
H277Y	H242R/Y in UNCINE	(Cherrad et *al.* 2017, Graf et *al*. 2017)
	H272Y/R in BOTREL	(FRAC, 2016)
	H272Y/R in PLEOAL	
T278	T268I in SEPTTR	

Table 4 SdhC

Amino acid substitution(s) in archetype	Homologous position in other species	Reference
K49E	NA	(FRAC, 2016)
R64K	NA	
	H151R in VENTIN	
G159	G169D in UNCINE	(Graf et *al*. 2017)

Table 5 SdhD

Amino acid substitution(s) in archetype	Homologous position in other species	Reference
R63	R47W in SEPTTR	(Dooley et *al.* 2016)
D124E/N	D123E in ALTEAL	(FRAC, 2016)

Oxathiapiprolin

Mutations conferring resistance to the new oomycete fungicide oxathiapiprolin have been discovered in oxysterol-binding proteins of *Phytophthora* species. *Phytophthora infestans* is chosen as the archetype species.

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Table 6 Oxysterol-binding protein (OSBP)-Related Proteins (ORP) - Reference sequence from *Phytophthora infestans* PiORP1 (NCBI gene accession number XP_002902250.1)

Amino acid substitution(s) in archetype	Homologous position in other species	Reference
L733W	NA	(Andreassi et *al.* 2013) (Miao et *al*. 2016) (Lin et *al.* 2016)
S768I/F/K/Y	NA	
G770A/I/L/P/V	G700V in PHYTCP	
N837I/F/Y	NA	
G839W	G769W in PHYTCP	
P861H	NA	
L863F/W	NA	
I877F/Y	NA	

Phenamcril

Resistance to phenamacril has been linked to changes on the myosin-5 subunit**.** No myosin-5 gene sequence has yet been published for FUSAAZ, but the following mutations have been reported: A135T, V151M, P204S, I434M, A577T, R580G/H, I581F, S418R, I424R, A577G, K216E/R, S217P/L, E420G/D. The *Fusarium graminearum* sequence is chosen as reference.

Table 7 Myosin-5 - Position number based on alignment to reference sequence from *Fusarium graminearum* (NCBI gene accession number XP_011317208)

Amino acid substitution(s) in archetype	Homologous position in other species	Reference
K216E	K216E/R in FUSAAZ	(Zheng et *al.* 2015, Li et *al.* 2016)
S217L/P	S217L/P in FUSAAZ	
S418R	S418R in FUSAAZ	
E420G	E420G/D in FUSAAZ	
M786V	NA	

No new mutations in b-tubulin, Cyp51A, CesA3 or Os-1 have come to light.

ACKNOWLEDGEMENTS

Research in the authors' laboratory is supported by the Centre for Crop and Disease Management (Curtin University and the Grains Research and Development Corporation) and the Australian Grain and Wine Association.

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Table 8 Abbreviations of Species Names

Abbreviation (EPPO code)	**Name of pathogen**
ALTEAL	*Alternaria alternata*
ALTETO	*Alternaria tenuissima*
BOTRCI	*Botrytis cinerea*
BOTREL	*Botrytis elliptica*
FUSAAZ	*Fusarium asiaticum*
GIBBZE	*Fusarium graminearum*
MYCOFI	*Mycosphaerella fijiensis*
PSDCHA	*Oculimacula acuformis*
PSDCHE	*Oculimacula yallundae*
PENIDI	*Penicillium digitatum*
PHYTCP	*Phytophthora capsici*
PHYTIN	*Phytophthora infestans*
PLEOAL	*Stemphylium vesicarium*
PYRPBR	*Pyrenopeziza brassicae*
RAMUCC	*Ramularia collo-cygni*
SEPTTR	*Zymoseptoria tritici*
UNCINE	*Erysiphe necator*
VENTIN	*Venturia inaequalis*

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