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Proposal for a unified nomenclature for target site mutations associated with resistance to fungicides

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Abstract

Evolved resistance to fungicides is a major problem limiting our ability to control agricultural, medical and veterinary pathogens and is frequently associated with substitutions in the amino acid sequence of the target protein. The convention for describing amino-acid substitutions is to cite the wild type amino acid, the codon number and the new amino acid, using the one letter amino acid code. It has frequently been observed that orthologous amino acid mutations have been selected in different species by fungicides from the same mode of action class, but the amino acids have different numbers. These differences in numbering arise from the different lengths of the proteins in each species. The purpose of the current paper is to propose a system for unifying the labelling of amino acids in fungicide target proteins. To do this we have produced alignments between fungicide target proteins of relevant species fitted to a well-studied "archetype" species. Orthologous amino acids in all species are then assigned numerical "labels" based on the position of the amino acid in the archetype protein.

Background

Evolved resistance to fungicides is a major problem limiting our ability to control agricultural, medical and veterinary pathogens ^{1, 2}. Research over the last 30 years has often defined the mechanism conferring reduced sensitivity to the fungicide. Many cases of resistance have been ascribed to the activity of efflux pumps ³, or to over-expression of target genes ⁴ but the majority are due, at least partly, to substitutions (or indels) in the amino acid sequence of the target protein.

The convention for describing amino acid substitutions is to cite the wild type amino acid, the codon number and the new amino acid, using the one letter amino acid code (see ⁵ box 6.1 page 138 for a description of the system). A well-known example is the alanine (A) for glycine (G) substitution in the cytochrome b gene at position 143 conferring resistance to strobilurin fungicides, referred to as G143A ⁶. Further alterations can be amino acid deletions designated with a Δ and insertions with an "ins".

Target site amino acid substitutions have been described for seven fungicide groups (named here according to the FRAC convention, ⁷) and their target proteins. These are C3 and cytochrome b (Cytb) (Table 1); G1 and two sterol C14-demethylases (paralogs Cyp51A and Cyp51B), (Tables 2 and 3); B1/B2 and *b*-tubulin, (Table 4); C2 and three of the sub-units of the succinate dehydrogenase complex (SdhB, SdhC and SdhD) (Table 5, 6 and 7); H5 and cellulose synthase A3 (CesA3) (Table 8); E3 and the Os1 family (group III) histidine kinase (Os-1, includes Bos1, BcOS1, Daf1, HK1, HIK1 and NIK1⁸)(Table 9), G3 and the 3-keto reductase (Erg27). Where more than one species has been studied, it has frequently been observed that orthologous amino acid mutations have been associated with resistance to fungicides with the same mode of action.

In cases where the proteins are strongly conserved between species, the mutations have identical numbers. For example, the orthologous Cytb G143A mutation has been found in 22

species (Table 1). However in other cases orthologous mutations have different numbers – e.g. Cyp51B amino acid Y137 in *Zymoseptoria tritici* is orthologous to amino acids numbered from 132 to 145 in different species (Table 3). Similarly, SdhB amino acid H277 in *Pyrenophora teres* is orthologous to amino acids numbered from 249 to 278 (Table 5). These differences in numbers creates unnecessary confusion and obscures the relationships between mutations in different species.

Resistance caused by insertions in promoters and in efflux pumps have a much lower level of homology and so are not considered here.

The Proposal

The differences in numbering arise from the different lengths of the fungicide target protein in each species. The purpose of the current paper is to propose a system for unifying the labelling of mutant amino acids in fungicide target proteins. We propose that orthologous amino acids (i.e. ones presumed to be descended from the same amino acid in the common ancestor of these species) are given the same number in all species regardless of the actual position. The advantages of a unified system is that it would be easier to memorise common changes, to determine whether the changes were novel or were repetitions of what has already been seen in other species and to link changes to particular active ingredients. Orthologous mutations would be assigned the same 'mutation label'.

We distinguish between 'mutation labels' which refers to the orthology between proteins from different species, from 'amino acid numbering', which remains the order of the amino acids in each protein in each species. To avoid confusion, we propose that mutation labels should be italicised and mutation numbers should use regular lettering.

In several cases, amino acid substitutions have been found in the target protein but have not been definitively associated with any change in sensitivity either *in vitro* or in the field. It may be that the mutation underlying the amino acid substitution is a random event and of no obvious relevance. Definitively linking a mutation to a sensitivity change can be technically very demanding. If resistance to the same class of fungicide is linked to mutations affecting orthologous codons in different species, this is strong, if still circumstantial, evidence of the importance of the mutation. Unifying the mutant labelling system will make it much easier to identify important codon changes. This would assist the prioritisation of research aiming to functionally characterise mutations.

Options for producing the alignments

We have produced a set of draft alignments of each target protein for which resistance to multiple species has been reported (Figures 1 to 9) and tables of putatively orthologous amino acids in other species where fungicide resistance has been reported (Tables 1 to 9). The species included in these tables and alignments have been referred to by their European and Mediterranean Plant Protection Organization (EPPO) codes⁹ as listed in Table 10.

The alignments for *b*-tubulin and Cytb are essentially co-linear in fungi studied to date and hence there are no changes to be made on the current nomenclature. For the other genes, we have considered four possible methods to generate the alignment. The alignment could be;

1. Fitted to the longest gene in the gene set.

2. Fitted to a strict consensus alignment.

3. Fitted to the gene from the species that is currently the most researched species for the fungicide resistance concerned.

4. Fitted to the gene from the species that was the first species for the fungicide resistance concerned.

The aim is to create a set of alignments that would be stable into the foreseeable future and would invoke the least relabelling of mutations that have already been described and published. We favour method 3 (basing the alignment on the species with the most currently-described resistance mutations), but also taking into account method 1 (using the longer gene) when alternative species are candidates. We propose that Cyp51A is fitted to ASPEFU (Aspergillus fumigatus), Cyp51B and Cytb are fitted to SEPTRI (Zymoseptoria tritici), b-tubulin to ASPEND (Aspergillus nidulans), the SDH proteins to PYRNTE (Pyrenophora teres), CesA3 to PHYTIN (Phytophthora infestans) and Os-1 to BOTCIN (Botrytis cinerea). For Erg27, mutations associated with resistance have currently been described only in BOTCIN and thus we propose this species as the archetype. The alignments have been summarised and fungicide resistance associated mutations are given in the Tables. By way of example, in Cyp51B the mutation Y136F in ERYSGH would be given the label Y137F. In CANDAL (Candida albicans) the orthologous amino acid is Y132 and has been mutated to both F and H. The Y132H mutation would therefore be given the label Y137H. V151 in SEPTRI is clearly demonstrated to be orthologous to I145F in PHAKPA (Phakopsora pachyrhizi). This mutation would be labelled *I151F* in PHAKPA and *V151F* in SEPTRI. The other proposed relabellings are listed in Tables 1 to 9.

By examining the species that have amino acids mutations with common labels, we can infer that positions 137, 148, 461, 467, 483 and 524 in Cyp51B are especially important in conferring resistance to triazole fungicides. This is consistent with numerous functional studies ^{10, 11}. We expect that the alignments should assist the identification of key amino acids in target proteins of newer fungicide classes.

The proposal in practice

The system must also allow for mutations to be discovered in new species. The parameters used to make the alignments are described below and can be applied to an alignment between the new species and the archetype. We envisage regularly updating the alignments based on new published knowledge.

A potential problem with the system we propose might occur if an amino acid in a newly described mutant gene corresponded to a gap in the archetype protein's sequence. In such a case, the mutation could be labelled as X50.2Y if it concerned the second extra amino acid after number 50 in the archetype sequence. To our knowledge, no examples of mutations of

such poorly conserved amino acids causing resistance have been described, but the possibility remains.

We hope that future studies will refer to the archetype by indicating that the mutation X123Y in the target protein associated with resistance corresponds to the archetype X145Y and refer to this paper or a related web page for support.

We suggest that other target genes from medically important fungi (e.g. the FKS1/2 genes that are targets of Echinocandins) and from herbicide- and insecticide- resistant weeds and insects might also benefit from this approach.

We commend this scheme to the community and seek comment and support. And we urge Journal editors to encourage authors to use this new system.

Note on the alignments

Amino acid sequences were downloaded from NCBI GenBank and annotated with reported amino acid substitutions^{8, 12-15}, using Geneious 6.1.8 software (Biomatters). Alignments of sequences were generated using ClustalW¹⁶ algorithm with Blosum scoring matrix, gap opening penalty 10, gap extension penalty 0.5, free end gaps.

The alignments are available as .doc file and as fasta files as supplementary data,

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Figure Legends

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Figure 1. Amino acid sequence alignment of the Cytb family. Sequences are named by species EPPO code and NCBI gene accession number. Residues highlighted in yellow in the archetype sequence from *Zymoseptoria tritici* denote amino acid substitutions associated with fungicide resistance at an orthologous position in any of the sequences. Numerical mutation labels shown above the alignment are based on the position number of the amino acid in the archetype protein.

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Figure 2. Amino acid sequence alignment of the Cyp51A family. Sequences are named by species EPPO code and NCBI gene accession number. Residues highlighted in yellow in the archetype sequence from *Aspergillus fumigatus* (Cyp51A) denote amino acid substitutions associated with fungicide resistance at an orthologous position in any of the sequences. Numerical mutation labels shown above the alignment are based on the position number of the amino acid in the archetype protein.

	1	ų.	17 19		10
1. SEPTTR - AY253234	HGLLQEVLAQ	FDAQ FG	QTS LWR	LVGLGFLAPSTL	AILINVLSQLLF
2. ASPEFL - KOC13803 8. CANDAL - AF163860	MGILAVILDS MAIVET	VCERCS	GINYFLSL	LSTVALLSILVV SVTQQISILLGV	SVVINVLROLLF PFVYNLVWOYLY
4. CERCBE - HM778021 6. ERYSCH - AJ578761	NG IS ES EMEP	FINH FG YLQ PLL	QLGFGI	LV LLAS TTFFLL ALASGILS LLL	SVVVNVLROVLF LTFLNVLKQLLF
8. ERYSUT - AJ575751 7. FLENF - AF225614	MSAIIPO	YQQLLGQVAQFF	PPWFAALPTS L	VAIAVVG IPAL	TIGTNALGOTCT
8. MYCOFI - XP 007929752	NGLLQDAAAL	FDAOFG	OKSTGT OTATWKI	LYPLGFSIFFAV	SVLLNVLROLLF
10. PHAKPA - KG741476 11. PUCCRT - FJ878683	MSSVIGS MSSVIGS	LLEPIG		DIIISLISILII VLIYLVLAVVS DIACHTSLIIII	IIS IN IFDOLAI
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2. CANDAL - AF153950 4. CERCSE - HM778021	SLRXDRAPLV ROPKNEPPLV	FYWIPWFGSAAS FHFVPIIGSTIS	YGOOPYEFFES Ygidpykfffs	RORYGDVFSFN RERYGDVFTF1	llök intvylöp Llökk tivclöt
5. ERYSGH - AJ578761 6. ERYSGT - AJ578751	KNP-NEPPIV KNP-NEPPIV	FAWIPIIGSTIS FAWIPIIGSTIS	YGMN PYR FFHB. YGMN PYR FFHB.	CARYGNIFTFI CARYGNIFTFI	LLGKKTTVYLGR LLGKKTTVYLGR
7. FILENF - AF225014 8. MONIFC - AF470621	AN P-NEPPVV	FHYLPHFGSAAI	YGIDPYRFFFD	CRAKYGDVFTFI	LIGKETTVYLGR
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2. ASPEFL - KOC13803 3. CANDAL - AF163860	KGNDFILNGK KGHEFVFNAK	LR DV CAEEV YS P LS DV SAEDAYKH	LTTPVFGRHVV LTTPVFGRGVI	Y DC PN AK LMEÖK Y DC PN SR LMEÖK	K FVKFGLTS DAL K FAKFALTTDS F
4. CERCBE - HM778021 6. ERYSOH - AJ578761	KGNDFILNGK	LR DVNAEEIYSP LR DVNAEEIYTV	LTTPVFGKDVV LTTPVFGTDVV	y dc fnsk lmeök Y dc fnsk lmeök	KFVKFGLTSAAL KFMKAALTTEAF
8. ERYSGT - AJ578781 7. FILBNF - AF225914	QGNNFILNGK KGNNLSLGGK	lr dvn abev ysv Isovsabeay th	LTTPVFGTDVV LTTPVFGKGVV	ydc pnsk lmeok Ydc pnemlmook	KFMKAALTTEAF KFIKSGLTTESL
8. MONIFC - AF470821 9. MYCOFI - XP_007929752	KGNDFILNGK	EKDLNABEI YTV IKDVNABEI YSP	LTTPVFGKDVV	rdcfnsklmeok Kdcfnsklmeok	KFMKIGLSTKAF KFVKYGLTSSAL
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	100	D176 N1788	104	- Time	8200T
1. SEPTTR - AY253234 2. ASPEEL - KOC13803	QSYVTLIAAE RSYVELITEE	TROFFDRNN PEK VEDEVOKSS	KFASTSGTIDL	PPALAELTIYTA CETTAEITIYTA	SR <mark>S LOGKEVREG</mark>
3. CANDAL - AF153950 4. CERCSE - HM778021	KRYVPXIREY QSYVTLITEE	iln y fv tdes fr trof fsknn per	LE LE THOVANVI REASTSGT LDL	NKTOPEITIFTA PPAFAELTIYTA	SRSLFGDEMRRI SRSLOGKEVRSK
5. ERYSGH - AJ578781 6. ERYSGT - AJ578751	RSYVPIIONE RSYVPIIONE	VKŠFIEKCD VESFINKCD	dfræskg i in i Dfræseg i in i	DAVNAEITIYTA AAVNAEITIYTA	SBTLOGKEVRDR SBTLOGKEVRDR
7. FILENF - AF225914 8. MONIFC - AF470621	OSYPPMITSE RSYVPIIOME	cedfftkevgi— Venfmerss——	S POR PS ATLDL AFREQUESTANI	LKANSELIILTA PPAMAEITIYTA	SRTLOCKEVRES Shtlockevrdr
8. MYCCF1 - XP_0079287922 10. PHAKPA - KC741479	RXYVGIIVRE	ATSYLEDALFC-	SPNVKSVTKDVI SPNVKSVTKDVI	IDITS SITICTA	SRSLOGREVRER AATLOGREVREG BATLOCREVREG
11. PUGLICI - FAI/9883 12. SACCCE - AA868433 13. UNCINE - AAC49812	KSYVPLIARE HSYVTIIONE	VYKYFROSKNFR VERYTNNCV	LNERTIGTIDU	NVTOPENTIFTA	SRSLIGEENRAK SRSLIGEENRAK
	sia	50 50	50	-	așe.
1. SEPTTR - AY253234	FDSS FADLYS	YLDMGFTFINFM	LFWAPLPONRE	DYAQKKMS ETY	MSIIQRARES
2. ASPEFL - KOC13803 8. CANDAL - AF163860	FDS TFAELYR FDRS FAQLYS	DLDMGFAPINFM DLDKGFTPINFV	L PWA PLPHNRKI F F NLPLPHYWRI	R DAAOKRMTETY R DAAOKK IS ATY	MEIIKERREAG- MKEIKSRRERG-
4. CERCBE - HM778021 6. ERYSGH - AJ578761	FDSSLAVLYR	YLDMĞFTPINFM DLDMĞFTPINFM	LFWAPLPONRRI LHWAPLPHNRAI	R DYAĞKKMTETY R DHAĞRTVAK IY	MSIIKORREAGD MEIINSRRTOK-
8. ERYSOT - AJ578751 7. FLENF - AF225914	FDSELAVLYH LNGOFAKIYE	DLDMGFTPINFM DLDGGFTPLNFM	LHWAPLPHNRAI FFNLPLPSYKRI	R DHAOR TVAK I Y R DEAQKAMS DFY	MEIINSARTOK- LKIMENARKGE-
8. MONIFC - AF470821 9. MYCOFI - XP 007928762	FDISFADLYR	DLDMGFBFINFM DLDMGFTFINFM DLDGGFTBLNFV	LINAPLPINKA LINAPLPONKA FUNI.DLDSVDDI	K DRAOK TVAD TI K DRAOKKMAEV Y L DKAOVSMINEY	TAIIKERREKĜE
11. PUCCRT - FJ879653 12. SACOCE - AABRAA33	LNKS FAOLYH LDTDFAYLYS	DLDGGFTPLHFA	FPN LPLPS YRRI FPN LPLEN YRRI	KDRAÖLAMRN FY KDHAÖKATSGTY	MNIIKKRREDD- MSLIKKRRKNN-
18. UNCINE - AAC10012	FDSS FAALYR	DLDMGFTPINFT	FYWAPLPNNRA	COHAORTVARTY	MNIIQARREEK-
	elo.	NZRAH	E300 H	03Y A3110 0312	A
1. SEPTTR - AY253234 2. ABPEFL - KOC13803	-KTGEREEDM SKKDSEDM	IHNLN <u>O</u> – CKYKD VKNLMS – CMYKD	GNAIPDK <mark>EIAE</mark> GTPV PDBEIAEI	Inial LMAGORS	SSATESWITLRL 959 TAAWIVLEL
2. CANDAL - AF153950 4. CERCSE - HM775021	DIDPNRDL KTSENGREDM	IDSLLIESTYKD INNLMS-CTYKD	SVEMTDOEIAN STPIPDREVAE	LLIGILMGGOHT MIALLMAGOHS	9A9 T9AWFLLEL 939 T93WIFLRL
5. ERYSGH - AJ578781 6. ERYSGT - AJ578751	-ETDDSNLDI -ETDNSNLDI	MNQLMR-SSYKD MNQLMR-SSYKD	STPV PDKEIAH STPV PDKEIAH	INIALLMAGOHS	93939 TWIMLWL 93939 TWIMLWL
7. FILENF - AF225014 8. MONIFC - AF470621		I MELOS - CRYRN MEOLMR - SSYRD	SV PLSDRDIAE ST PV PDKEIAN	INIALLMAGOHT	33ATSSWTLLHL 9595ISWIMIRL
5. MTLART - AP_007560752 10. PHAKPA - KC741475 11. FUCCET - FJOTSES	RECOLEDM	LDVLO?-OHYKD	SRALSDREIAH	INIAV LMAGOHT	SAATG?WLLTEL SAATGSWLLTEL
12. BACCCE - AAB68433 13. UNCINE - AAC49812	DIO-DRDL -RSGENKHDI	ids lärns tyrd Mnelmr – Styrd	VENTDOEIAN TPVPDREIAE	LLIGV LMGGOHT	SAATSAWILLEL SSSTSSWIMLWL
		sții	ap.	sia	572 AST012 PARM
1. SEPTTR - AY253234	AARPOTODEL	LQEOKDMLGVNA	DGSIRELTY	ANLSKLTLLNOV	VRETLRIBAPVE
2. ASPEFL - KOC13803 8. CANDAL - AF163860	AAS PEITEEL GERPELODVI	YOEOLRILGHD- YOEVVELLKEKG	MPPLTY	EN LOK LDLHAKV	IKETLRIHAPIH IKETLRMHMPLH
4. CERCBE - HM778021 6. ERY80H - AJ578761	ATRRDIĞDEL AARPDITEEL	VÖEOK DVLGVNE YÖEÖLELLGSE-	DGSIKELTY LPPLKY	en lök ltilsöv Edlök ls lhönv	VKETLRIHAPIH LKEVIRIHAPIH
8. ERY80T - AJ578781 7. FILBNF - AF225914	AARPDITEEL	YOEOLEILGSE- YÖEÖKOKLGNPD	GTFRDYRY	EDLSKLTLHONV EDLKELPIMDSI	VKEVLRLHAPIH IRETLRMHAPIH
8. MONIFC - AF470821 9. MYCOFI - XP 007928762	ASRPDIQUEL	LOBOLEVLGAD- LOBOKDVLGVNA	LPDLKY DGSIKELTY 28CVLEDL2	ADISKLTLHONI ADISKLPLINOV VDRLOTELINOV	IKETIRLEAPIE
10. FRANZA - KU/414/0 11. PUCCRT - FJ878688 12. SACOCE - AABEA411	ASRPDIVALL	ROEOIDLFGKPG YEEONRVI.D	TDDOELDPLD	LERVÓSPLMIAC	IKEVIRIBPEIB
18. UNCINE - AAC40812	AARPDIMEEL	YEEQLRIFGSER	PFPFLQY	DISKIQLHONV	LKEVIRLEAPIE
article is protected	by copyrig	ht. All rights	reserved.	MIT GHIZA	Hiso
1. SEPTTR - AY253234	SILREVESPM	PIEG	TAYVIPTTETL	LAAPGTTSRNDE	HEPDCLEWEPER.
S ANGER MORAGENE	STTPAUENT	DURC	TOVITOPOTOT	SCOTTO COTT	UTDODITINT

Article Accepted **Figure 3.** Amino acid sequence alignment of the Cyp51B family. Sequences are named by species EPPO code and NCBI gene accession number. Residues highlighted in yellow in the archetype sequence from *Zymoseptoria tritici* denote amino acid substitutions associated with fungicide resistance at an orthologous position in any of the sequences. Numerical mutation labels shown above the alignment are based on the position number of the amino acid in the archetype protein.

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	1 19 Hely	ap	*	4p	YECHE	вþ
1. ASPEND berA bela-tubulin - M17519	MRB IVELOTGOCG	NO IIGAAPWO/FI	SCHEGLDCSGV	INGTSOLOL	BRNNYTFEAS	GRETVERAV
BOTRCI - 296253 CERCBE - AY856373	MREIVELOTGOCC MREIVELOTGOCC	NO IGAAFNOTI NO IGAAFNOTI	SCREENDCSGV SCREENDCSGV	YNCTEDL <u>OL</u> YNCTEDLOL	ERMINTENEAS ERMINTENEAS	GREEVERAV GREEVERAV
. COCHHE - AB000071 . GIBBELI bets 1-tubulin - U27303	MREIVELOTGOCC MREIVELOTGOCC	NO TGAAFNOTT NO TGAAFNOTT	CERCIPCSOV CERCIPCSOV	YNGTEDL <u>O</u> L YNGTEBLOL	ERMINY TENEAS ERMSYNENERS	CREEVERAV GREEVERAV
GIBBFU beta 2-tubulin - KF771161	MREIVHVOVGOCG	NOVESSENOT V	SCENCY DOSOS	YNSTDDOOR	BRIDVIFARAT	RDRYVPRAV
8. HELMSO - Y10670			ACTECT DSSGT		ERMINY TENEAS	CHRFVPRAV
10. LEPTINO - 368022	MREIVILOTOCCO	C TGAARNOTT	GREAT DOBUT	THE TEDLOL	ERMINYTENEAS	DIRFVPRAV
2. NONLA - AY346/46	MREIVELOTGOCO	C TEAAFNOTT	GREAT DESCY	TABLEL	ERMINYTENEAS	DENYVERAV
14. PENIAU - JN112033						PRAV
10. PENIT - K9072770	MREIVHLOTOOCG	CICAAPTOTT	SOKECIAD CDOC	TAGTADLOL	ERMNYTENEAS	ODRYVPRAV
10. RHYNSE - X81046	MREIVELOTOCCO	CICAAPIOTI	GEHCILDOSOV	YNGTEDLOL	ERLAVIENEAS	DERIVERAV
20. SCLEBC - XM 001564764	MREIVHLOTOOCG	CICAAPIOTI	IGERCILDOSOV		ERMNY TENEAD	DRYVPRAV
ET. WENTIN - NO/301	78			00- TIMATERCIĞIS	110 1	Lag
	M	·1·	-1- -	1.	1.	
ASPEND benA bela-lubuln - M17519	INDIALPOTT	Mercelered	NEWTODSCAUR	NNARGHYTE	CARLWDNVVDV	VRREAEGCD
. BOTRCI - 259253 . CERCSE - AY355373	IAVDIASCO, DOWR	MGPFGQLFRPD MGPKGQLFRPD	NEVEGOSGAGN	NTRAK GHYTE NTRAK GHYTE	GYETADÖATDA CYETADÖATDA	VRREAEGCE
. COCHHE - AB009971 1. GIBBRU bala 1-tubulin - U27202	IAVDIASCON DOWR	MGPFGÖLFRPD MGPFGÖLFRPD	NEVEGÖSGAGN NEVEGÖSGAGN	NTRAK GHYTE NTRAK GHYTE	GAELVDÖVLDV GAELVDÖVLDV	VRREAEGOD
5. GIBBFU bala 2-tubulin - KF771181 7. GIBBZE bala 2-tubulin - FJ214853	LVDLEPGPODATE LVDLESGPODATE	MGPLGÖLFRPD MGPLGÖLFRPD	TEVACE SACE	NTRAK GH Y TE NTRAK GH Y TE	GAELVEËAIDV GAELVEEAIDV	VREEVENING
A. HELMSO - 110570 A. HYPMOC - 112255	IAVDIASPOT DOWR	ngpfgglfrpd Sgffgglfrpd	NEVEGOSCACH	NTRAK GHYTE NTRAK GHYTE	GYETADÖATDA CYETADÖATDA	VRREAEGCD
10. LEPTNO - 300922 11. MONIFC - AY263676	IAVDIASSO, DOVIS IAVDIASSO, DOVIS	MGPFGÖLFRPD MGPFGÖLFRPD	NEVEGOSGAGN NEVEGOSGAGN	NTRAKGHY TE NTRAKGHY TE	Cyetadöattaa Cyetadöattaa	VRREREGCE
12. MONILA - AY349149 12. NEUSCR - M13630	IAVDIASSON DOWR	MGPFGQLFRPD MGPFGQLFRPD	NEVEGOSGAGN NEVEGOSGAGN	NNARGHYTE NNARGHYTE	Cyetadöarda Cyetadöarda	VRREAEGCD
14. PENIALI - JN112033 18. PENIEX - KG042886	1470) AS 2677 102 VIS 1470) AS 2677 102 VIS	sgefgelfred Sgefgelfred	NEVEGOSGAGN NEVEGOSGAGN	NTRAKGHY IYE NTRAKGHY IYE	GAELVDÖVLDV GAELVDÖVLDV	VRREALGOD
IB. PENIT - KG072779 17. PYRP8R - KC342227	IAVIDASService WR IAVIDASService WR	sgefgelfred Mgefgglfred	NEVEGOSGAGN NEVEGOSGAGN	NTRAKGHY IYE NTRAKGHY IYE	GAELVDÖVLDV GAELVDÖVLDV	VRREALGOD
18. RHYNSE - X81046 19. SCLEHO - KF765483	IAVIDASSON IDAVIS IAVIDASSON IDAVIS	MGPFGQLFRPD MGPFGQLFRPD	NEVEGOSGAGN NEVEGOSGAGN	NINAR GHYTE NINAR GHYTE	GAELNDÖVLDV GAELNDÖVLDV	VRREAEGCD
20. SCLESC - X04_001894794 21. VENTIN - M97361	IAVDIASPOTT DAVE	MGPFGQLFRPD MGPFGQLFRPD	NEVEGOSGAGN	n nailigh y te Nnailigh y te	<u>CVETADÖATTA</u> A CVETADÖATTAA	VRREAEGCD
	140 140 Q134K	- Alian	100 A105	170 F107	sea	190
ASPEND bank beta-tubulin - M17518	CLOGEOITHBLGG	GINGRIGHTER T	A REPRESENTATION OF A	i i i i i i i i i i i i i i i i i i i	PRVIDTVVRPX	RATISVECL
BOTRCI - 200203	CLOSEDITESLOG	GTORONOTLLI	an an air an an air	ATTSVVPS	PAVEDTWVEPY	NATLEVEOL
COCHHE - AB008871	CLOSEDITESLOG			MATYSVVPS	PRUSDITUTEPY	MATLSIBOL
. GIBBRU bota 2-tubulin - KF771181	HLOGFOLTHSLOG		a ann an taith an tha an taith	ATTSVNDS	PRVEDTVVEPY	NATISLNCL
A HELMSO - Y10070	CLOSEDITESLOG CLOSEDITESLOG	GIT CEASENG TTATAT	n an an that a shirt an Than the shirt of the shirt of the	RATTSVADS	PRVSDTUVEPY	NATLSVBOL
0. LEPTINO - 650822 1. MONIEC - AV283678	CLOSEDITESLOG CLOSEDITESLOG		n an an the set of the	REVUE TAN	PRVSDTUVEPY	NATLSIBOL
2. MONILA - AY349149 3. NEUSCR - M13630	CLOSEDITESLOG CLOSEDITESLOG		a semerikanan yang biraka Roman kanan yang biraka	MATTSVVPS TATYSVVPS	PRUSERTUVEPY	NATLSVHOL
14. PENIAU - JN112033 16. PENIEX - KG042000	CLOSED ITESLOG CLOSED ITESLOG		r som skoket i se birder skomstander i se birder	at isvups At isvups	PRVEDTVVEPY	MATLEVBOL
10. PENIT - KGO72778 17. PYRP8R - KC342227	CLOSED ITESLOG CLOSED ITESLOG	G TACALONIS/TALAT	e homme file de la graf déseñ de e homme file de la graf déseñ de	NATISVVRS NATISVVRS	PROFESSION PROFESSION	NATISVBOL NATISIBOL
18. RHYNSE - X81046 18. ISCLEHO - KF715483	CLOSED ITESLOG CLOSED ITESLOG	G TACALONICATATAT G TACALONICATATAT	elementickel y distrikte elementickel y distrikte	NATISVVRS NATISVVRS	PROFESSION PROFESSION	NATISIBOL NATISVBOL
20. SCLESC - XM 001504794 21. VENTIN - M97951	CLOSEDITESLOG CLOSEDITESLOG	G TYPE CENTER TATE	a sama da da da se bira da Sama da da da se bira da	MATTSVVPS MATTSVVPS	PRVEDTVVEPY	MATLEVHOL
	200	\$10	220	210	240	200
	E199DRG F209Y				L240	
ASPEND benA bala-lubulin - M17319	VERSIETECIDAE	ALYDI CMRTLK	LSNPSTGULRH	LVSAVMSCV	TTOIRFPOIL	SDLERGAVN
2 CERCULE - AY855373	VENSIETTCIDE	ALYDICMRULK		LVSAVMSGV	TTCLRFPGULN	SDLEXLAVA
GIBBEL Sein 1-Lubulle - U27303	VENSIETTCIDE	ALYDICMRULK	LSINPSTOPLANT	LVSAVMSGV	TTCLRFPGULN	SDIRGIAN
. GIB8ZE bela 24bulin - FJ214863	VENSIETFCIDAR	ALYDIYERTLK		LISTVMAGY	TTCFRFFGILN	SDIERLAVA
L HELMOD - 110070 L HYPMOD - 112255	VENSIETTOTIA	ALYDICMETER	LPNPATADLNY	LVSAVMSGV	TTCLRFPGILN	SDIEGLAVA
1. MONEFC - AY253576	VENSIEVTCIDUE	ALYDICMRULK		LVSAVMSGV	TTCLRFPGULN	SDIARAWA
12. NEUSCR - M13530	VENSIEVENIE	ALYDICMRULK		LVSAVMSGV	TVSLRFPGULN	SDIAMANA
16. PENEX - KGO42888	VERSIENT	ALYDICMRULK		LVSAVMSGV	TISLEFPOILN	SDIERLAVA
17. PYRPBR - KC342227	VENSIEVECTION	ALYDICMRULK		LVSAVMSGV	TTCLRFPGULN	SDIRGLAVA
IR SCLEHO - KF785483	VENSIONAL	ALYDICMRTLK	LENPSTONIA	LVSAVMSGV	TTCLRFPGULN	SDIASALAVA
AL BULLERC - AM_W/IGHANH M. VENTIN - M97961	VENSIETFCIDUE	ALYDICARTLE	INNEST GEARE	LVSAVMSGV	TICLEPCIA	SOLINGLAVA
	200 2 N2671.	70 2 4	200	əç	ala ala	ako
ACCENT has a bain that the MATTING		Fabrada va			135100 00000	TOBATTOOT
BOTRCI - 200203		APLISACAIS	FRAVIVPELTO	DER DERNING	ANSIE REGRIL	TCSALFRON
incide is protected by copy	ught Al ng	hts reserve	GAVTVPELTO		aasdernoryl Aasdernoryl	TCSRIYRGE TCSRYYRGE
. GIBBFU bela 1-lubulin - U27303 . GIBBFU bela 2-lubulin - KF771181		APL TSRCAES	FRAVSVPELTO FOELTVPELAO	DE DERNIN	aasdersigry1/	TCBAITRGE
	TURNERS INTO A 1	TAPT. TOP STOP	REAL PROPERTY AND INCOME.	DIFONENTS.	A & A DATA NUMBER T	COMPTER TODO

Article Accepted **Figure 4.** Amino acid sequence alignment of the *b*-tubulin family. Sequences are named by species EPPO code and NCBI gene accession number. Residues highlighted in yellow in the archetype sequence from *Aspergillus nidulans* (benA) denote amino acid substitutions associated with fungicide resistance at an orthologous position in any of the sequences. Numerical mutation labels shown above the alignment are based on the position number of the amino acid in the archetype protein.

	ין ו		25	-		
1. PYRNTE - XM_002302613	MACTRALTRIA	T-KR LAVR P-AV	FORG FASVNDVI	EARDPIERTAE	IVPDAARPT	I PESK TS TVQ
2. ALTEAL - K.M28282 8. ALTESO - KC517311 4. BOTRCI - AY728919 6. CORYCA - A8546736	MAS IRAFTRIA MAS IRAFTRIA MAAIRTGARSA MACTRAFARIA	T – OR TAVR P – AV TS DLV PVR P – AV RA IFAASR P – – J T – TR TAVR PAAV	FSRG FASVNDVI FSRG FASVNDVI JR TOMR TMAŠVI FTRG FASV TDT <i>i</i>	HARDPISK TAR HAREPISK IAR DSSVPE AAREPVSKVAR	k lapdasrs p K lapdasrs p S PTVS PSRPV K IV PDPARKV	tprskts tiq Vprskts tvp BSASKTS tvk Vprsqts tvk
7. EUROOR - XM_001627434	MAAIRSTSRIN	AS SEPLER P-AV	FARS YATV DA-			AAQ
0. SCLESC - XM 001504527 10. SEPTTR - XM 003060706 11. USTIMA - XM_011388576	MAS IR TS AR CA MAIR LA MSLENVENGLA	RS IFAASR FJ TRR FAF- LI TALR PSVI	FR TOMR TMASY FRRGMATT IE-I SESRVAAFSTT	DSOTAVIX ETKEPISATARI AA	S PT IS PSRPV ALS ASRPP ARLA	BPASK TS TVK IKRTK TS TVK TPTSDNVG
	9	碑	nș I	1 90	110	ः युव
1. PYRNTE - XM_008902513	E PS PSKDAK TR	TFHIYR WN PDEE	TSKPKNOS YTLI	DLNK TG PMML DI	ALIRIKNEVD	PTLTFRRSCR
2. ALTEAL - K.M.20202 3. ALTE&O - KC517311 4. BOTRCI - AY720616 5. COTRCI - AY720616 5. COTRCI - AB548738 6. DEVYER - MC150400	E PE PSKDAK TR E PE PSKDAK TR E PAADSESL IR D PO PDKDAK TR	TIHLYR M PDER THLYR M PDER TINLYR M PDER THLYR M PDER	TSRPAN SYNT TSRPAN SYNT TSRPAN SYNT TSRPAN SYNT	DLNK TG PMML D DLNK TG PMML D DLNK TG PMML D DLNK TG PMML D	ALIR IN EV D ALIR IN EV D ALIR IN EV D ALIR IN ELD	PTLTFRRSCR PTLTFRRSCR PTLTFRRSCR PTLTFRRSCR
7. EUROOR - XM 001827454 8. PODOXA - AB547416	DPN PS ETPR TR	TTHIYR WN PDOP	TERPENOS YS LI	DLNIK TG FMML DJ	ALIRIKNEMD	PTLTFRRSCR
8. BCLESC - XM 001594527 10. BEPTTR - XM 003550705 11. USTIMA - XM 011388576	EPETDSNSLIR EPOMDADAETR SSGEPOHIR	TFHIYRWN PDEE TFHIYRWN PDOE GFRIYRWN PDRE	ASK PROS VILL TORPROS VILL SERPRINS VILL	dlar të panel di Dlar të panel di Dlar të pavel di Dlar të pavel di	ALIRIKNEV D ALIRIKNEV D ALIRIKNEID	PTLIFRRSCR PTLIFRRSCR PTLIFRRSCR
	158	148	-	198	175	-
1. PYRNTE - XM_008802818	EGICGSCAMBI	DEVNTLACICE	PT DT TK ESR I YI	PL PHMYVVKDIA	PONTLFYRO	YRSVE PYLOR
2. ALTEAL - KM28282 3. ALTESO - KC517311 4. BÖTRCI - AY728618 5. CORYCA - A8548735 8. DHJYBR - HÖ155460 7. EUROOR - XAL 001827434 8. DODYBR - MÖ155460	EGICGSCAMNI EGICGSCAMNI EGICGSCAMNI EGICGSCAMNI CAMNI EGICGSCAMNI	DGVNTLACLCRI DGVNTLACLCRI DGVNTLACLCRI DGVNTLACLCRI DGVNTLACLCRI DGVNTLACLCRI	PT DT TK EƏR IYI PT DT TK EƏR IYI PR DARH ETK IYI PT DT TK EƏR IYI PT DT AK EƏR IYI PT DT AK EƏR IYI	PL PHMYVVKDIA PL PHMYVVKDIA PL PH TYVVKDIA PL PHMY IVKDIA PL PHMYVVKDIA PL PH TYVVKDIA	/ PDMTLFYKO / PDMTLFYKO / PDLTOFYKO / PDMTLFYKO / PDMTLFYKO / PDLTOFYKO	Yrəve pylor Yrəve pylor Yrəve pylor Yrəve pylor Yrəve pylor Yrəve pylor
B. SCLESC - X04_001594527 10. SEPTTR - X04_002860706 11. USTIMA - X04_011388575	EGICGSCAMNI EGICGSCAMNI EGICGSCAMNI	DGVNTLACLCRI DGVNTLACLCRI DGVNTLACLCRI	PR DARE ETK IYI PT DT AK ETR IYI DK QN D'TK IYI	PL PH TYVVKD IV PL PH TYVVKDIA PL PHMY IVKDIA	/ PDLTOFYKO / PDMTOFYKO / PDLTOFYKO	YKA IK PYLOH YKA IK PYLOR YRA IE PFLKS
	196	sie	219 2	PI 221 P230 N235	2ju	: 2 1 0
1. PYRNTE - XM 002202512	TTAAPDGREER	ÓSKEDEKK LÓGI	YECILCACCST		LGPAVLIOS	YRWIACSRDE
2. ALTEAL - KM20202 8. ALTEBO - KC517311 4. BOTRCI - AY720018 6. CORYCA - AB545735 8. DIDYBR - HC158460 7. EUROOR - XAL 001827434 8. PODXXA - AB547416	TTAAPDGREIR STAAPDGREIR TDPAPEGREYR DTPAPDGREYR TTPSPDGREYR ETKTEDGLEYR	OSKEIRKE LDGI OSKEIRKE LDGI OSKEIRKE LDGI OSKEIRKE LDGI OTKEIRRE LDGI OS PEIRKE LDGI	YICILCACCST YICILCACCST YICILCACCST YICILCACCST YICILCACCST YICILCACCST YICILCACCST			YRW LADS RDE YRW LADS RDE YRW LADS RDE YRW LADS RDE YRW LADS RDE YRW LADS RDE YRW LADS RDE
6. SCLEBC - XM 001564527 10. SEPTTR - XM 003960706 11. USTIMA - XM_011366576	TDPAPGGKEYI DTAPPDGKENR NNTPSEG-EEI	oskeirkk logi Osvalrkk logi Os peerr logi	YECILCACCST YECILCACCST YECILCACCST	SCPS TWEESELS SCPS TWEESELS SCPS TWEEODL	LC PAULICS LC PAVLICS LC PAVLICS	YRWLADSRDO YRWINDSRDE YRWMADSRDD
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1. PYRNTE - XM_003302513	KRAERODALNN	SMSLYRCETIL	CSRTCPEGINP	ALAIAE IKKS M	AFT	
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Figure 5. Amino acid sequence alignment of the SdhB family. Sequences are named by species EPPO code and NCBI gene accession number. Residues highlighted in yellow in the archetype sequence from *Pyrenophora teres* f. sp. *teres* denote amino acid substitutions associated with fungicide

resistance at an orthologous position in any of the sequences. Numerical mutation labels shown above the alignment are based on the position number of the amino acid in the archetype protein.



Figure 6. Amino acid sequence alignment of the SdhC family. Sequences are named by species EPPO code and NCBI gene accession number. Residues highlighted in yellow in the archetype sequence from *Pyrenophora teres* f. sp. *teres* denote amino acid substitutions associated with fungicide resistance at an orthologous position in any of the sequences. Numerical mutation labels shown above the alignment are based on the position number of the amino acid in the archetype protein.



Figure 7. Amino acid sequence alignment of the SdhD family. Sequences are named by species EPPO code and NCBI gene accession number. Residues highlighted in yellow in the archetype sequence from *Pyrenophora teres* f. sp. *teres* denote amino acid substitutions associated with fungicide resistance at an orthologous position in any of the sequences. Numerical mutation labels shown above the alignment are based on the position number of the amino acid in the archetype protein.

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Figure 8. Amino acid sequence alignment of the CesA3 family. Sequences are named by species EPPO code and NCBI gene accession number. Residues highlighted in yellow in the archetype sequence from *Phytophthora infestans* denote amino acid substitutions associated with fungicide resistance at an orthologous position in any of the sequences. Numerical mutation labels shown above the alignment are based on the position number of the amino acid in the archetype protein

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	8. ALTELO - DO987538 4. PLEOAL - EU711371 1. BOTRCI - AF435964 2. ALTEBI - AY70002 8. ALTELO - DO987589 4. PLEOAL - EU711371	VDNVEGKWK VDNVEGKWK VDNVEGKWK M NEVQRVAKD LAVKRVARD LAVKRVARD LAVKRVARD	DLTNNY DLTNNY DLTNNY VGVDGKN VGVDGKN VGVDGKN VGVDGKN YGVDGKN	ITMAON L ITMAON L ITMAON L ITMAON L IGGOADV IGGOADV IGGOADV IGGOADV IGGOADV 7%	TLOVRSI TLOVRSI TLOVRSI TLOVRSI RDIDGRW RDIDGRW RDIDGRW	SEVIQAI SEVIQAI SEVIQAI M KEITTDV KEITTDV KEITTDV KEITTDV KEITTDV	AKGDMSR AKGDMSR AKGDMSR WP0 N TMANN L N TMAON L N TMAON L 730	KIEVAAA RVHVDAB RVHVDAB TTQVRAF TSQVRAF TSQVRAF TSQVRAF	EIRLLKDT EIRLLKDT EIRLLKDT DITNAATI SDITNAAME SDITNAAME SDITNAAME	TINNAVDRLDE VN DAVMRLDE VN DAVMRLDE VN DMVMRLDE VN DV VN DVV	NS NS NS AS AS AS
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	8. ALTELO - DOGR7538 4. PLEOAL - EU711571 1. BOTRCI - AF435594 2. ALTELI - A7435994 4. PLEOAL - EU711571 1. BOTRCI - AF435984 2. ALTELI - DOGR7528 4. PLEOAL - EU711571	VDNVEGKWK VDNVEGKWK VDNVEGKWK WDNVEGKWK W NEVQRVAKD LAVKRVARD LAVKRVARD LAVKRVARD LAVKRVARD GEMDELKRK GEMDELKRK GEMDELKRK GEMDELKRK	DLTNNY DLTNNY DLTNNY VGYDGKN VGYDGKN YGYDGKN YGYDGKN YGYDGKN TNQMYS INQMYS INQMYS	TMAONL TMAONL TMAONL ITMAONL 4GGQADV 4GGQADV 4GGQADV 7% LRDSIQ 5LRESIQ 5LRESIQ 5LRESIQ	TLOVRSI TLOVRSI TLOVRSI TLOVRSI RDIDGRW RDIDGRW RDIDGRW RNTLARE RNTLARE RNTAARE	KEITTDV KEITTDV KEITTDV KEITTDV KEITTDV KEITTDV AAELANK AAELANK	AKGDMSR AKGDMSR WWO NTMANNL NTMAONL NTMAONL 770 TKSEFLA TKSEFLA TKSEFLA WWO	KIEVAAAA RVHVDAE RVHVDAE RVHVDAE TTQVRAF TSQVRAF TSQVRAF TSQVRAF SQVRAF NMSHEIR NMSHEIR NMSHEIR NMSHEIR NMSHEIR	EIRLLKDT EIRLLKDT EIRLLKDT DITNAAT DITNAAME DITNAAME DITNAAME DITNAAME CPMNGIIGD CPMNGIIG PPMNGIIG	VNDAVARLDE VNDAVARLDE	NS NS NS AS AS AS AS AS AS HA HA
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Figure 9. Amino acid sequence alignment of the OS-1 family. Sequences are named by species EPPO code and NCBI gene accession number. Residues highlighted in yellow in the archetype sequence from *Botrytis cinerea* denote amino acid substitutions associated with fungicide resistance at an orthologous position in any of the sequences. Numerical mutation labels shown above the alignment are based on the position number of the amino acid in the archetype protein.

Table 1 CytB

Position number based on alignment to reference sequence from *Zymoseptoria tritici* (NCBI gene accession number AY247413).

Amino acid substitution(s)	Homologous position in
in archetype	other species
F129L	F129L in PHAKPA
	F129L in PLASVI
	F129L in PYRIOR
	F129L in PYRNTE
	F129L in PYRNTR
	F129L in RHIZSO
G137	G137R in PYRNTR
G143A	G143A in ALTEAL
	G143A in ALTELY
	G143A in ALTESO
	G143A in ALTETO
	G143A in BOTRCI
	G143A in CERCBE
	G143A in COLLGR
	G143A in ERYSGT
	G143A in LEPTNO
	G143A in MICDMA
	G143A in MONGNI
	G143A in MYCOFI
	G143A in MYCORA
	G143A in PLASVI
	G143A in PLEOAL
	G143A in PODOFU
	G143A in PSPECU
	G143A in PYRIOR
	G143A in PYRNTR
	G143A in RHIZSO
	G143A in VENTIN

Table 2 Cyp51A

Position number based on alignment to reference sequence from *Aspergillus fumigatus* (Cyp51A) (NCBI gene accession number AF338659).

Amino acid substitution(s)	Homologous position in
in archetype	other species
N22D	NA
S52T	NA
G54E/K/R/V/W	G54W in ASPEPA
Y68	Y132N in ASPEFL
Q88H	NA
L98H	NA
V101F	NA
Y121F	Y136F in AJELCP
N125I	NA
K133	K197N in ASPEFL
G138C/R/S	NA
Q141H	NA
H147Y	NA
P216L	NA
F219S	NA
M220K/I/T/V	NA
D280	D282E in ASPEFL
M286	M288L in ASPEFL
T289A	NA
S297T	NA
P394L	NA
Y431C	NA
G432S	NA
G434C	NA
T440A	NA
G448S	NA
T470	T469S in ASPEFL
Y491H	NA
F495I	NA

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Table 3 Cyp51B

Position number based on alignment to reference sequence from *Zymoseptoria tritici* (NCBI gene accession number AY253234).

Amino acid substitution(s)	Homologous position in
in archetype	other species
Т66	A61V in CANDAL
C80	S79T in ERYSGT
D107V	NA
L126	F120L in PHAKPA
D134G	NA
V136A/C/G	NA
Y137F	Y132F/H in CANDAL
	Y132F/H in PHAKPA
	Y134F in PUCCRT
	Y136F in ERYSGH
	Y136F in ERYSGT
	Y136F in MONIFC
	Y136F in MYCOFI
	Y136F in UNCINE
	Y140F/H in SACCCE
	Y145F in FILBNF
M145L	NA
K148	K142R in PHAKPA
	K143E in CANDAL
	K147Q in ERYSGH
V151	I145F in PHAKPA
D176	K175N in ERYSGT
N178S	NA
S208T	NA
N284H	NA
E300	E297K in CERCBE
H303Y	NA
A311G	A313G in MYCOFI
G312A	NA
1333	I330T in CERCBE
A379G	A381G in MYCOFI
I381V	NA
P391	P394S in CERCBE
A410T	S405F in CANDAL
G412A	NA
H430	H399P in ASPEFL
A453	D411N in ASPEFL
Y459C/D/N/S/P/Δ	Y461D in MYCOFI
G460D/Δ	G462A in MYCOFI
Y461D/H/S	F449S in CANDAL
	Y463D/H/N in MYCOFI
G476	G464S in CANDAL
	G484S in FILBNF

R479	R467K in CANDAL
1483	I471T in CANDAL
	I475T in PHAKPA
V490L	NA
T496	T454P in ASPEFL
G510C	NA
S524T	S508T in PYRPBR
	S509T in ERYSGH

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Table 4 *b*-Tubulin

Position number based on alignment to reference sequence from *Aspergillus nidulans* (benA) (NCBI gene accession number M17519).

Amino acid substitution(s)	Homologous position in other
in archetype	species
H6L/Y	H6Y in LEPTNO
	H6Y in MONIFC
Y50N/S	Y50N in GIBBFU β_1 -tubulin
	Y50C in GIBBZE β_2 -tubulin
	Y50C in HYPMOD
M73	Q73R in GIBBZE β_2 -tubulin
Q134K	NA
A165V	NA
F167	F167Y in CERCBE
	F167Y in COCHHE
	F167Y in GIBBZE β_2 -tubulin
	F167Y in NEUSCR
	F167Y in PENIEX
E198D/K/Q	E198A/G/K/V in BOTRCI
	E198A in CERCBE
	E198V in GIBBFU β_2 -tubulin
	E198K/L/Q in GIBBZE β_2 -tubulin
	E198A/Q in HELMSO
	E198A/K in MONIFC
	E198G in NEUSCR
	E198A/K in PENIAU
	E198A/K/V in PENIEX
	E198K in PENIIT
	E198A/G in PYRPBR
	E198G/K in RHYNSE
	E198A/K in SCLEHO
	E198A in SCLESC
	E198A/K in VENTIN
F200Y	F200Y in BOTRCI
	F200Y in GIBBFU β_2 -tubulin
	F200Y in GIBBZE β_2 -tubulin
	F200Y in PENIAU
	F200Y in PENIIT
	F200Y in RHYNSE
	F200Y in VENTIN
L240	L240F in MONILA
	L240F in PYRPBR
	L240F in VENTIN
M257L	NA

Table 5 SdhB

Position number based on alignment to reference sequence from *Pyrenophora teres* f. sp. *teres* (NCBI gene accession number XM_003302513).

Amino acid substitution(s)	Homologous position in other
in archetype	species
P230	P225F/L/T in BOTRCI
N235	N225I/T in SEPTTR
	N230I in BOTRCI
H277Y	H249L/N/Y in EUROOR
	H257L in USTIMA
	H267L/R/Y in SEPTTR
	H273Y in SCLESC
	H272L/R/V/Y in BOTRCI
	H277R/Y in ALTEAL
	H277R/Y in ALTESO
	H277R/Y in DIDYBR
	H278R/Y in CORYCA
	H->Y in PODOXA ^a
1279	I269V in SEPTTR

^aAmino acid position number for this substitution is unknown as only 176-bp fragment of SdhB gene has been sequenced in both sensitive and resistant isolates

Table 6 SdhC

Position number based on alignment to reference sequence from *Pyrenophora teres* f. sp. *teres* (NCBI gene accession number XM_003302752).

Amino acid substitution(s)	Homologous position in other species
T68	T79I/N in SEPTTR
W69	W80S in SEPTTR
\$73	S73P in CORYCA
	A84V in SEPTTR
	A85V in BOTRCI
N75S	N86K/S in SEPTTR
T78	T90I in EUROOR
G79R	G90R in SEPTTR
H134R	H134R in ALTEAL
	H146R in SCLESC
S135R	NA
H141	H152R in SEPTTR

Table 7 SdhD

Position number based on alignment to reference sequence from *Pyrenophora teres* f. sp. *teres* (NCBI gene accession number XM_003297196).

Amino acid substitution(s)	Homologous position in
in archetype	other species
S118	S89P in CORYCA
D124E/N	NA
H134R	H132R in BOTRCI
	H132R in SCLESC
	H133R in ALTEAL
	H133R in ALTESO
G138	G109V in CORYCA
D145G	D124E in EUROOR
	D129E in SEPTTR

Table 8 CesA3

Position number based on alignment to reference sequence from *Phytophthora infestans* (NCBI gene accession number EF563995).

Amino acid substitution(s)	Homologous position in
in archetype	other species
Q1077	Q1077K in PHYTCP
G1105A/V	G1105S/V in PLASVI
	G1105V/W in PSPECU
V1109L	V1109L/M in PHYTCP
	V1109L in PHYTDR

Table 9 OS-1

Position number based on alignment to reference sequence from *Botrytis cinerea* (Bos1) (NCBI gene accession number AF435964).

Amino acid substitution(s)	Homologous position in
in archetype	other species
F250	F267L in PLEOAL
1273	L290S in PLEOAL
1365N/R/S	NA
V368F	NA
Q369H/P	NA
N373S	NA
G403	G420D in ALTELO
T447S	NA
E738	E753K in ALTEBI
T750	T765R in PLEOAL
Q762	Q777R in PLEOAL

Abbreviation (EPPO code)	Name of pathogen
AJELCP	Ajellomyces capsulatus
ALTEAL	Alternaria alternata
ALTEBI	Alternaria brassicicola
ALTELO	Alternaria longipes
ALTELY	Alternaria arborescens
ALTESO	Alternaria solani
ALTETO	Alternaria tomato
ASPEFL	Aspergillus flavus
ASPEFU	Aspergillus fumigatus
ASPEND	Emericella nidulans
ASPEPA	Aspergillus parasiticus
BOTRCI	Botryotinia fuckeliana
CANDAL	Candida albicans
COCHHE	Cochliobolus heterostrophus
COLLGR	Glomerella graminicola
CORYCA	Corynespora cassiicola
CERCBE	Cercospora beticola
DIDYBR	Stagonosporopsis cucurbitacearum
ERYSGH	Blumeria graminis f. sp. hordei
ERYSGT	Blumeria graminis f. sp. tritici
EUROOR	Eurotium oryzae
FILBNF	Filobasidiella neoformans
GIBBFU	Gibberella fujikuroi
GIBBZE	Gibberella zeae
HELMSO	Helminthosporium solani
HYPMOD	Hypomyces odoratus
LEPTNO	Parastagonospora nodorum
MONGNI	Monographella nivalis
MONIFC	Monilinia fructicola
MONILA	Monilinia laxa
MICDMA	Microdochium majus
MYCOFI	Mycosphaerella fijiensis
MYCORA	Didymella rabiei
NEUSCR	Neurospora crassa
PENIAU	Penicillium aurantiogriseum
PENIEX	Penicillium expansum
PENIIT	Penicillium italicum
РНАКРА	Phakopsora pachyrhizi
РНҮТСР	Phytophthora capsici
PHYTDR	Phytophthora drechsleri
PHYTIN	Phytophthora infestans
PLASVI	Plasmopara viticola
PLEOAL	Pleospora allii
PODOFU	Podosphaera fusca
PODOXA	Podosphaera xanthii
PSPECU	Pseudoperonospora cubensis
PUCCRT	Puccinia triticina
PYRIOR	Maananorthe orvzae

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PYRNTE	Pyrenophora teres
PYRNTR	Pyrenophora tritici-repentis
PYRPBR	Pyrenopeziza brassicae
RHIZSO	Thanatephorus cucumeris
RHYNSE	Rhynchosporium secalis
SACCCE	Saccharomyces cerevisiae
SCLEHO	Sclerotinia homoeocarpa
SCLESC	Sclerotinia sclerotiorum
SEPTTR	Zymoseptoria tritici
UNCINE	Erysiphe necator
USTIMA	Ustilago maydis
VENTIN	Venturia inaequalis

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