# Development of an Oligonucleotide Probe for Aureobasidium pullulans Based on the Small-Subunit rRNA Gene

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Aureobasidium pullulans, a cosmopolitan yeast-like fungus, colonizes leaf surfaces and has potential as a biocontrol agent of pathogens. To assess the feasibility of rRNA as a target for *A. pullulans*-specific oligonucleotide probes, we compared the nucleotide sequences of the small-subunit rRNA (18S) genes of 12 geographically diverse *A. pullulans* strains. Extreme sequence conservation was observed. The consensus *A. pullulans* sequence was compared with other fungal sequences to identify potential probes. A 21-mer probe which hybridized to the 12 *A. pullulans* strains but not to 98 other fungi, including 82 isolates from the phylloplane, was identified. A 17-mer highly specific for *Cladosporium herbarum* was also identified. These probes have potential in monitoring and quantifying fungi in leaf surface and other microbial communities.

Several direct and indirect methods exist for the detection and quantification of microbes in ecosystems (for reviews, see references 24 and 42). The mainstay of these has been the viable-cell count, typically reported as CFU of the organism of interest per unit area or weight of sample (23, 46). Indirect assessment based on CFU from washings of a substratum has been the preponderant method of assessing terrestrial microbial populations generally and leaves in particular (5, 23). This method is rapid and simple and gives a measure of the culturable population. Its major detractions are that not all viable cells are culturable, the efficiency of removal may be very low or highly variable, and positional (microenvironmental) relationships between the microbe and surface are lost.

Within the last decade, molecular methods which offer precision and high sensitivity to the characterization of populations have revolutionized the detection, identification, and quantification of microbes (8, 30, 45). Indirect applications typically involve DNA or RNA isolation, frequently PCR amplification, and probing with labeled oligonucleotides (25, 30, 45). The small-subunit rRNAs (16S in prokaryotes and 18S in eukaryotes) are commonly used as targets for probes because they are abundant, have enough evolutionary information for inference of close as well as distant phylogenetic relationships, and contain conserved sequences which can be used as primer templates in sequencing (15, 40, 43).

In the direct application, microbial cells are visualized, often in situ, by use of radioactive (<sup>3</sup>H or <sup>35</sup>S) or nonradioactive (digoxigenin, biotin, or fluorochrome) labels. Hybridization with fluorescently labeled, rRNA-targeted probes (fluorescence in situ hybridization [FISH]) (1, 35, 38) has been exploited to study bacteria in various ecosystems, including aquatic habitats (28), sediments (21), biofilms (3), and the rhizosphere (7). To date, successful applications of FISH in fungal microbial ecology have been limited, though it has been used to detect fungal mating type genes (36) and yeasts (13, 20) under laboratory conditions.

Aureobasidium pullulans (de Bary) Arnaud, a yeast-like deuteromycete (4, 19, 27), is of commercial interest primarily because of its extracellular polysaccharide, pullulan (34), and of ecological interest because it colonizes many habitats (18). It is one of the relatively few fungi that grows actively and ubiquitously on living leaves (phylloplane) (4). We are devising molecular methods to detect and quantify *A. pullulans* directly on leaf surfaces. As a first step in developing in situ probes, we describe a 21-mer which hybridizes to the 18S rRNA of *A. pullulans* but not to 16 other fungi and 82 phylloplane fungal isolates tested. Research reported here on the *A. pullulans* probe and related work with a universal probe have been confirmed in preliminary FISH experiments (37, 37a).

### MATERIALS AND METHODS

Fungal strains. The sources, origins, and strain designations of the fungi used for PCR amplification of the 18S rRNA gene in this study are listed in Table 1. In addition to 12 A. pullulans strains, 16 other fungi representing 14 genera were chosen. These fungi were selected on the basis of several considerations. Either sequence information on the 18S rRNA gene was available in the GenBank database, or they were sequenced by us (Table 1). Further criteria for selection were their routine occurrence in the phyllosphere (5, 6, 10) (Alternaria alternata, Cladosporium herbarum, Cladosporium cladosporioides, Cryptococcus laurentii, Rhodotorula rubra, and Sporobolomyces holsaticus) or a taxonomic (19) (Hormonema dematioides) or phylogenetic (12, 16, 32) (Aspergillus nidulans, Neurospora crassa, Penicillium chrysogenum, Penicillium notatum, Podospora anserina, and Colletotrichum gloeosporioides) relationship to A. pullulans. Additionally, 82 phylloplane yeasts, numbered nonconsecutively between L1 and L100, were isolated on potato dextrose agar with 250 mg of chloramphenicol per liter by standard leaf wash methods (6) from apple trees at the Mandt Farm Experiment Station, Madison, Wis., and at the Picnic Point orchard adjacent to the University of Wisconsin campus. Leaves were collected for processing on two dates, 5 and 10 October 1994. Colonies were selected from plates on the basis of their color and comprised members of the two broad categories of phylloplane yeasts: the so-called pink yeasts (mainly Sporobolomyces and Rhodotorula spp.) and white yeasts (mainly Cryptococcus spp.) (10). The isolates were provisionally identified to genus level and, where possible, to species level, primarily with the API 20C Analytical Profile Index (bioMérieux Vitek, Inc., Hazelwood, Mo.) (48). This system includes 19 substrate assimilation tests in cupules, supplemented by morphological and additional biochemical data, including urea utilization; KNO3 assimilation; and fermentation of cellobiose, glucose, maltose, raffinose, and sucrose in Durham tubes (33). With this system, the phylloplane yeast isolates were identified as a Rhodotorula sp., R. glutinus, R. rubra, R. minuta, Cryptococcus laurentii, C. albidus, and Candida parapsilosis.

**Genomic DNA extraction.** Fungal strains were grown on potato dextrose agar (Difco, Detroit, Mich.) at room temperature for 2 to 7 days. Total genomic DNA was extracted from agar plates (47) and diluted 1:50 prior to use.

**PCR amplifications.** Oligonucleotide primers (for details, see the legend to Fig. 1) and probes were synthesized by the  $\beta$ -cyanoethyl phosphoramidite method on a 391 DNA Synthesizer (Applied Biosystems, Foster City, Calif.) and used without further purification.

Reaction mixtures for genomic DNA amplification contained 1.25 U of Taq DNA polymerase (Promega, Madison, Wis.), 0.2 mM deoxynucleoside triphos-

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Ap19 L1-L100 **NRRL 807** 

ATCC 9179

ATCC 6710

NRRL Y-1592

NRRL Y-17285

Strain	Species	Source	Strain	Species	Source						
Ap1 <sup>b</sup>	A. pullulans	NRRL 12779	Aa <sup>b</sup>	Alternaria alternata	NRRL 5255						
$Ap2^{b}$	A. pullulans	ATCC 90393	An	Aspergillus nidulans	FGSC 4						
Ap3 <sup>b</sup>	A. pullulans	NRRL Y2567	Be	Blastocladiella emersonii	ATCC 22665						
$Ap4^{b}$	A. pullulans	ATCC 48168	Cc	Cladosporium cladosporioides	NRRL 20632						
Ap5 <sup>b</sup>	A. pullulans var. melanigenum	ATCC 12536	Ch <sup>b</sup>	Cladosporium herbarum	NRRL 2175						
Ap6 <sup>b</sup>	A. pullulans var. melanigenum	CBS 210.65	Cg	Colletotrichum gloeosporioides	JHA S19-3						
$Ap7^{b}$	A. pullulans var. pullulans	CBS 704.76	$CI^b$	Cryptococcus laurentii	NRRL 2536						
$Ap8^{b}$	A. pullulans var. melanigenum	CBS 584.75	Hd <sup>b</sup>	Hormonema dematioides	CBS 116.29						
Ap12 <sup>b</sup>	A. pullulans var. pullulans	ATCC 11942	Lp	Leucostoma persoonii	ATCC 69911						
Ap13 <sup>b</sup>	A. pullulans	ATCC 28998	Nc	Neurospora crassa	FGSC 2490						
$Ap18^{b}$	A. pullulans	WF1	Ou	Ophiostoma ulmi	JHA 82						

WF2

Apple phylloplane

TABLE 1 Fungal strains from which the 18S rRNA gene was PCR amplified<sup>a</sup>

<sup>a</sup> NRRL, Northern Regional Research Lab, Peoria, Ill.; ATCC, American Type Culture Collection, Rockville, Md.; CBS, Centraalbureau voor Schimmelcultures, Baarn, The Netherlands; FGSC, Fungal Genetics Stock Center, Kansas City, Kans.; WF1 and WF2, field isolates from Madison, Wis.; JHA, J. H. Andrews' collection, Madison, Wis.

 $Pc^b$ 

Pn

Pa

 $\mathrm{Rr}^{b}$ 

Sh

<sup>b</sup> Sequenced in this study.

A. pullulans

phate (dNTP) (Pharmacia, Milwaukee, Wis.), 5 µl of 10× PCR buffer (500 mM KCl, 100 mM Tris-HCl [pH 9.0 at 25°C], and 1.0% Triton X-100 [Promega]), 2.5 mM MgCl<sub>2</sub>, 10% dimethyl sulfoxide (Sigma, St. Louis, Mo.), 10 pmol of primers, and 1 µl of diluted DNA sample. The reaction volume was made up to 50 µl. Occasionally, rRNA genes were amplified directly from spores as described elsewhere (9).

Yeast isolates (total: 82, nonconsecutive)

The PCR cycling conditions were 6 min of initial denaturing at 94°C, 2 min of annealing at 54°C, 40 min of prolonged extension at 72°C, and then 94°C for 1 min, 54°C for 2 min, and 72°C for 5 min for 35 cycles, followed by a 15-min extension at 72°C. Negative controls excluded DNA template and spores. Modification of these conditions, including shorter extension periods, could be employed.

DNA sequencing and sequence analysis. To assess intraspecific sequence conservation, a 578-bp region of 11 A. pullulans strains (Table 1) was PCR amplified (Fig. 1), subcloned into plasmid pCRII (Invitrogen, San Diego, Calif.), and



Primers Probes #282 (NS3): 5'-GCAAGTCTGGTGCCAGCA-3 #283: 5'-AGCCTTGCGACCATACTC-3' #120 (NS1): 5'-GTAGTCATATGCTTGTCT-3' #121 (NS8): 5'-TCCGCAGGTTCACCTACGGA-3' #500: #501:

-TTGTTGGTTTCTAGGACC-3' '-GGTCCTAGAAACCAACAA-3

A: 5'-TTCGTTTAGTTATTATGAATC-3' (#665) B: 5'-GAATTACCGCGGCTGCTG-3' (U519) C: 5'-TTAATCAAAACATCCTT-3' (#614)

FIG. 1. Schematic representation of primer and probe locations in the 18S rRNA gene of A. pullulans Ap2. Primers 282 and 283 generated a 578-bp PCR product; primers 120 and 121 amplified the full length of the 18S rRNA gene; primers 500 and 501 were used for sequencing. Primers 282, 120, and 121 correspond to the conserved primers NS3, NS1, and NS8, respectively, described by White et al. (50); primers 283, 500, and 501 were designed by us on the basis of the 18S rRNA sequence of the A. pullulans strain designated here as Ap2 (32). Probe A (665) is A. pullulans specific; B (U519) is a universal probe based on all known small-subunit rRNA sequences (20, 26); and C (614) is C. herbarum specific.

sequenced by the dideoxy chain termination method (44) with automated dyelabeled ddNTPs on an Applied Biosystems model 373A automated sequencer. Both strands were sequenced. Nucleotide sequences were aligned by the Clustal method (29) with DNASTAR software (Madison, Wis.).

Penicillium chrysogenum

Sporobolomyces holsaticus

Penicillium notatum

Podospora anserina

Rhodotorula rubra

Southern blot and dot blot hybridizations. Following amplification, PCR products were size fractionated on agarose gels containing 1% SeaKem GTG agarose (FMC, Rockland, Maine). Gels were blotted to Nytran (Schleicher & Schuell, Inc., Keene, N.H.) and UV cross-linked (UV Stratalinker 1800; Stratagene Inc., La Jolla, Calif.).

The standard Southern blot protocol of Wallace and Miyada (49) was used with minor modification. Probes were <sup>32</sup>P end labeled with T4 polynucleotide kinases (Promega). Hybridizations and final 15-min washes were adjusted to Td $3^{\circ}$ C or  $Td - 5^{\circ}$ C, where Td = 2(A+T) + 4(G+C). Blots were exposed to Kodak XAR film with or without an amplifying screen for 2 to 72 h.

Dot blots were performed by the procedure described by Meinkoth and Wahl (39) with slight modification. The double-stranded PCR products were denatured in 3 M NaOH at 65°C for 15 min, cooled on ice, neutralized with an equal volume of 2 M ammonium acetate (pH 7.0), and blotted onto Nytran. Following UV cross-linking, prehybridization and hybridization were conducted as described above. To ensure equivalent amounts of PCR target among samples, a probe complementing all known small-subunit rRNA sequences (universal probe) (20, 26) was also used.

Nucleotide sequence accession numbers. The GenBank accession numbers of the nucleotide sequence analyzed in this study include those for Aspergillus fumigatus (M55626), Athelia bombacina (M55638), Aureobasidium pullulans (M55639), Blastocladiella emersonii (M54937), Candida albicans (X534597), Coccidioides immitis (M55627), Colletotrichum gloeosporioides (M55627), Leucostoma persoonii (M83259), Neurospora crassa (X04971), Ophiostoma ulmi (M83261), Penicillium notatum (M556280), and Podospora anserina (X54864). The nucleotide sequences of 11 A. pullulans strains and six other fungi have been deposited with the Genome Sequence Database and assigned accession numbers: Ap1 (L76135), Ap2 (L76136), Ap3 (L76137), Ap4 (L76138), Ap5 (L76139), Ap6 (L76140), Ap7 (L76141), Ap8 (L76142), Ap12 (L76143), Ap13 (L76144), Ap18 (L76145), Aa (L76146), Ch (L76147), Cl (L76152), Hd (L76148), Pc (L76153), and Rr (L76149).

## **RESULTS AND DISCUSSION**

To provide a means of specifically detecting A. pullulans, we designed probes based on the 18S rRNA gene even though it contains fewer variable regions for distinguishing among closely related taxa than does the 28S rRNA gene (41). The 18S rRNA gene has been the molecule of choice in developing molecular phylogenies, and accordingly, most of the sequence information published to date relates to this molecule (41). The taxonomy of A. pullulans is uncertain (19, 27), so sequence conservation among purported "strains" could not be presumed. Accordingly, the nucleotide sequence of 11 strains within a 578-bp variable region (50) of the gene was deter-

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1	GCAAGTCIGGIGCCAGCAGCGGGTAATTCCAGCTCCAATAGCGTATATTAAAGTTGTTGCAGTTAAAAAACTCGTAGTTGAACCTTGGCCCGGCTGG	Ap3
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1	GCAAGTCTQGTQCCAGCAGCQGGTAATTCCAGCTCCAATACCTTATATTAAAGTTYCTYCCAGCTCAAAAAACCTCCTAGATTGAACCTCTCGCCCAGCTCCAATACCTCCCAGCTCCAATACCTCCAGCTCCAATACCTCCAGCTCCAATACCTCCAGCTCCAATACCTCCAGCTCCAATACCTCCAGCTCCAATACCTCCAGCTCCAATACCTCCCAGCTCCAATACCTCCAGCTCCAATACCTCCAGCTCCAATACCTCCAGCTCCAATACCTCCACTCCAATACCTCCAGCTCCAATACCTCCAGCTCCAATACCTCCACTCCAATACCTCCACTCCAATACCTCCACTCCCCACTCCCCACTCCACTCCACTCCACTCCACTCCACCCACTCCCACTCCACTCCACTCCACTCCACTCCAC	Ap6
1		1.7
1	GLAAGTCTGSTGULAGLAGUUGGGTAATTULAGUTULAATAGUGTATATTAAAGTTGFTGLAGFTAAAAAGCTUGTAGTTGAAUUTTUGUUTUGG	Ap/
1	GCAAGTCTGGTGCCAGCCGCGGTAATTCCAGCTCCAATAOOGTATATTAAAGTTGTTGCAGTTAAAAAGCTCGTAGTTGAACCTTGGGCCTGGCTGG	Ap8
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1	GCAAGICTUGTUGCAGCCGCGGGTAATTCCAGCTCCAATADOGTATATTAAAGTTGTTGCAGTTAAAAAGCTCGTAGTTGAACCTTGGGCCTGGCTGG	Ap13
1	GCAAGTCTGGTGCCAGCAGCGGGTAATTCCAGCACCAATAGCGTTATATTAAAGTTCGTGCAGTTAAAAGTTCGTGCTGGTGGTGGTGGTGGCTGGC	Ap18
101	CCGGTCCGCCTCACCGCGTGTACTGGTCCGGCCGGGCCCTTTCCTTCTGGGGAGCCGCATGCCCTTCACTGGGCGTGTCGGGGAACCACGACCTTTTACTTT	Ap1
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TOT	CUSCICCACCICACCICCICCCCCCCCCCCCCCCCCCCCC	Ap6
101	COGTOGCCTCACCGCTGTACTGGTCOGGCCGGTCCTTTCCTT	Ap7
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101		AD0
TOT	CUGICUGCICACGGGIGIGIACIUGICCGGGGGGCCTTTCCTTCTGGGGAGCCCCTGCCCTTCACTGGGGGGGACCACGGCCTTTTACTTT	Ap12
101	COGGICOGCCTCACCCGTGTACTCGTCCGGCCGGCCCTTTCCTTCTCGGCGACCCCCTTCCCGCCGCGCGCG	Ap13
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201		1201
201	GAAAAAATTAGAGIGTICAAABLAGGUUTTIGCIUGAATACATTAGAATAATAGGAATAGGAOGTGOGGTTCTATTTIGTIGGITTCTAGGACCOC	Ap2
201	GAAAAAATTAGAGTGTTCAAAGCAGGCCTTTGCTCGAATACATTAGCATGGAATAATAGAATACGACGTGCGCTTCTATTTTCTTCGTTTCTAGGACCCC	Ap3
201		3-4
201	GAAAAAATTAGAAGIGI ICAAAGGAGGCCTTI GCTCGAATACATTAGAATAGAACGIGCGGTTCTATTTTGTTCGTTTCTAGGACCCC	AP4
201	GAAAAAATTAGAGTGTTCAAAGCAGGCCTTTGCTCGAATACATTAGCATGGAATAATAGAATAGGACGTGCGGTTCTATTTTGTTGGTTTCTAGGACCCC	Ap5
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201		1012
201	GAAAAAATTAGAATGTTCAAAGCCTTTGCTCGAATACATTAGCATGGAATAATAGAATAGGACGTGCGGTTCTATBTTGTTGGTTTCTAGGACCCC	Ap13
201		Ap18
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301 301 301 301 301 301 301 301 301 301	CETANIGATTAATAGGATAGTOGGGGGGATCAGTATTOAATTGTCAGAGGTGAAATTCTTIGGATTTATTGAAGACTAACTACTGCGGAAGCATTGGCG CETANIGATTAATAGGGATAGTOGGGGGCATCAGTATTCAATTGTCAGAGGTGAAATTCTTIGGATTTATTGAAGACTAACTACTGCGAAACCATTGCCA CETANIGATTAATAGGGATAGTOGGGGGCATCAGTATTCAATTGTCAGAGTGAATTCTTIGGATTTATTGAAGACTAACTACTGCGAAACCATTTGCCA CETANIGATTAATAGGGATAGTOGGGGCATCAGTATTCAATTGTCAGGGTGAAATTCTTCGATTTATTGAAGACTAACTA	Ap1 Ap2 Ap3 Ap4 Ap5 Ap6 Ap7 Ap8 Ap12 Ap13 Ap18
301 301 301 301 301 301 301 301 301 301	$\label{eq:constraints} Constraints and the experimental experiments and experiments $	Ap1 Ap2 Ap3 Ap4 Ap5 Ap6 Ap7 Ap8 Ap12 Ap13 Ap18
301 301 301 301 301 301 301 301 301 301	CGTANIGATTANIAGGAINAGTOSGGGGGICAGTATICAATIGICAGAGGIGAANITCITIGGAITTAITGAAGACTAACIACIGGGAAAGCAITTGOCA CGTANIGHTAAITAGGGAINAGTOGGGGGCAICAGTATICAATIGICAGAGGIGAANITCITIGGAITTAITGAAGACTAACIACIGGGAAAGCAITTGOCA CGTANIGHTAAITAGGGAINAGTOGGGGGCAICAGTATICAATIGICAGAGGIGAANITCITIGGAITTAITGAAGACTAACIACIGGAAAGCAITTGOCA CGTANIGAITAAITAGGGAINAGTOGGGGGCAICAGTATICAATIGICAGAGGIGAANITCITIGGAITTAITGAAGACTAACIACIGGCAAAGCAITTGOCA CGTANIGAITAAITAGGGAINAGTOGGGGGCAICAGTATICAATIGICAGAGGIGAANITCITIGGAITTAITGAAGACTAACIACIGCOAAAGCAITTGOCA CGTANIGAITAAITAGGGAINAGTOGGGGGCAICAGTATICAATIGICAGAGGIGAANITCITIGGAITTAITGAAGACTAACIACIGCOAAAGCAITTGOCA CGTANIGAITAAITAGGGAINAGTOGGGGGCAICAGTATICAATIGICAGAGGIGAANITCITIGGAITTAITGAAGACTAACIACIGCOAAAGCAITTGOCA CGTANIGAITAAITAGGGAINAGTOGGGGGCAICAGTATICAATIGICAGAGGIGAANITCITIGGAITTAITGAAGACTAACIACIGCOAAAGCAITTGOCA CGTANIGAITAAITAGGGAINAGTOGGGGGCAICAGTATICAATIGICAGAGGIGAANITCITIGGAITTAITGAAGACTAACIACIGCOAAAGCAITTGOCA CGTANIGAITAAITAGGGAINAGTOGGGGGCAICAGTAICCAATIGACAGAGGIGAANITCITIGGAITTAITGAAGACTAACIACIGCOGAAAGCAITTGOCA CGTANIGAITAAITAGGGAINAGTOGGGGGCAICAGTAITCAATIGICAGAGGIGGAANITCITIGGAITTAITGAAGACTAACIACIGCOGAAAGCAITTGOCA CGTANIGAITAAITAGGGAINAGTOGGGGGCAICAGTAICAATIGACAGAGGIGGAANITCITIGGAITTAITGAAGACTAACIACIGCOGAAAGCAITTGOCA CGTANIGAITAAITAGGGAINAGTOGGGGGCAICAGTAITCAATIGICAGAGGIGGAANITCITIGGAITTAITGAAGACIAACIACIGCOGAAAGCAITTGOCA CGTANIGAITAAITAGGGAINAGTOGGGGGGCAICAGTAITCAATIGICAGAGGIGGAANITCITIGGAITTAITGAAGACIAACIACIGCOGAAAGCAITTGOCA CGTANIGAITAAITAGGGAINAGTOGGGGGGAAACIGAGTAACIACIGCOGAAACAITTGOCA CGTANIGAITAAITAGGGAINAGTOGGGGGAAGACIGAGACTAACIGCOGAAACAITTGOCA CGTANIGAITAAITAGGGAINAGTOGGGGGCAICAGTAITCCAATIGCCAGAGGGAAATICCITIGGAITTAITGAAGACIAACIACIGCOGAAACAITTGOCA CGTANIGAITAAITAGGGAINAGTOGGGGGAAGACTAACIGCOGAACACIACIGCACAACIACIGCACGAAGACTAACIACIGGAAGACTAACIGCIGGAAAGACIAACIACIGCACAACIACIGGAAGACTAACIGCIGGAAAGACTAACIGCIGGAAATICCITGGATTAITGAAGAGCAACAACIACIGGGAAAACIACIGCACAACIGCACAACIACIGGAAAGACTAACIGCIGGAAACIACIGACGAACIACIGCACAACIACIGGAAGACIAACIA	Ap1 Ap2 Ap3 Ap4 Ap5 Ap6 Ap7 Ap8 Ap12 Ap13 Ap18
301 301 301 301 301 301 301 301 301 301	CGTAARGATTAATAGGGATAGTOGGGGGATAGTATTCAATTGTCAGAGGTGAAATTCTTTGGATTTATTGAAGACTAACTA	Ap1 Ap2 Ap3 Ap4 Ap5 Ap6 Ap7 Ap8 Ap12 Ap13 Ap18 Ap1
301 301 301 301 301 301 301 301 301 301	CGTANIGATTANIAGGAINAGTOSGGGGICAGTATICOAGAGGIGAANTICITIGGATTANIGAGACTAACTACTGCGAAAGCAITTGCCA CGTANIGHTANIAGGGAINAGTOGGGGGCAICAGTATICAATTGICAGAGGIGAANTICITIGGAITTANIGAGACTAACTACTGCGAAAGCAITTGCCA CGTANIGHTANIAGGGAINAGTOGGGGGCAICAGTATICAATTGICAGAGGIGAANTICITIGGAITTANIGAGACTAACTACTGCGAAAGCAITTGCCA CGTANIGATTANIAGGGAINAGTOGGGGGCAICAGTATICAATTGICAGAGGIGAANTICITIGGAITTANIGAGACTAACTACTGCGAAAGCAITTGCCA CGTANIGATTANIAGGGAINAGTOGGGGGCAICAGTATICAATTGICAGAGGIGAANTICITIGGAITTANIGAGACTAACTACTGCGAAAGCAITTGCCA CGTANIGATTANIAGGGAINAGTOGGGGGCAICAGTATICCAATGICAGAGGIGAANTICITIGGAITTANIGAGACTAACTACTGCGAAAGCAITTGCCA CGTANIGATTANIAGGGAINAGTOGGGGGCAICAGTATICCAATGICAGAGGIGAANTICITIGGAITTANIGAGACTAACTACTGCCAAACCAITTGCCA CGTANIGATTANIAGGGAINAGTOGGGGGCAICAGTATICCAATGICAGAGGIGAANTICITIGGAITTANIGAGACTAACTACTGCCGAAACCAITTGCCA CGTANIGAITANIAGGGAINAGTOGGGGGCAICAGTAICCAATGICAGAGGIGAANTICITIGGAITTANIGAGACTAACTACTGCCGAAACCAITTGCCA CGTANIGAITANIAGGGAINAGTOGGGGGCAICAGTAICCAAGGGIGAANTICITIGGAITTANIGAGACTAACTACTGCGAAACCAITTGCCA CGTANIGAITTANIAGGGAINAGTOGGGGGCAICAGTAICCAAGGGIGGAANTICITIGGAITTANIGAGACTAACTACTGCGAAACCAITTGCCA CGTANIGAITTANIAGGGAINAGTOGGGGGGCAICAGTAICCAAGGGIGGAANTICITIGGAITTANIGAGACTAACTACTGCGAAACCAITTGCCA CGTANIGAITTANIAGGGAINAGTOGGGGGGCAICAGTAICCAAGGAGGAAATTCCTTGGAITTANIGAAGCTAACTACTGCGAAACCAITTGCCA CGTANIGAITTAATAGGGAINAGTOGGGGGCAICAGTAICCAAGGAGGGAANTICITIGGAITTATIGGAAGCTAACTACTGCGAAACCAITTGCCA CGTAATGAITTAATAGGGAINAGTOGGGGGCAICAGTAICCAAGGAGGGAANTICITIGGAITTATIGGAAGCTAACTACTGCGAAACCAITTGCCA CGTAATGAITTAATAGGGAINAGTOGGAGGGACACGAAGGAGGAAATTCCTGGATTATIGGAAGGCTAACTACTGCGAAACCAITTGCCA CGTAATGAITTAATAAGGGAINAGTOGGAGGACAACGAAGGAGGAAATGCTTGCGAGGGAAGCATACTACTGCGAAGGACTAACTA	Ap1 Ap2 Ap3 Ap4 Ap5 Ap6 Ap7 Ap8 Ap12 Ap13 Ap1 Ap1 Ap2
301 301 301 301 301 301 301 301 301 301	CETANIGATTANIAGGAINAGTOSSOGGETCAGIAITICAATIGICAGAGGIGAANITCITIGGAITIAITIGAAGACTAACIACIGGGAAAGCAITIGGCA CETANIGATIAAITAGGAINAGTOSSOGGAICAGIAITICAATIGICAGAGGIGAANITCITIGGATITAITIGAAGACIAACIACIGGGAAAGCAITIGGCA CETANIGATIAAITAGGAINAGTOSSOGGAICAGIAITICAATIGICAGAGGIGAANITCITIGGATITAITIGAAGACIAACIACIGGAAACAITIGGCA CETANIGATIAAITAGGAINAGTOSSOGGAICAGIAITICAATIGICAGAGGIGAANITCITIGGATITAITIGAAGACIAACIACIGCOAAACAITIGGCA CETANIGATIAAITAGGAINAGTOSSOGGAICAGIAITICAATIGICAGAGGIGAANITCITIGGATITAITIGAAGACIAACIACIGCOAAACAITIGGCA CETANIGATIAAITAGGAINAGTOSSOGGAICAGIAITICAATIGICAGAGGIGAANITCITIGGATITAITIGAAGACIAACIACIGCOAAACAITIGGCA CETANIGATIAAITAGGAINAGTOSSOGGCAICAGIAITICAATIGICAGAGGIGAANITCITIGGATITAITIGAAGCIAACIACIGCOAAACAITIGGCA CETANIGATIAAITAGGAINAGTOSSOGGCAICAGIAITICAATIGICAGAGGIGAANITCITIGGATITAITIGAAGCIAACIACIGCOAAACAITIGGCA CETANIGATIAAITAGGAINAGTOSGOGGAICAGIAITICAATIGICAGAGGIGAANITCITIGGATITAITIGAAGCIAACIACIGCOAAACAITIGGCA CETANIGATIAAITAGGAINAGTOGGAGGCAICAGIAITCAATIGICAGAGGIGAANITCITIGGATITAITIGAAGCIAACIACIGCOAAACAITITGCCA CETANIGATIAAITAGGAINAGTOGGAGGCAICAGIAITCCAITIGICAGAGGIGAANITCITIGGATITAITIGAAGACIAACIACIGCOAAACAITITGCCA CETANIGATIAAITAGGAINAGTOGGAGGCAICAGIAITCCAITIGICAGAGGIGAANITCITIGGATITAITIGAAGCIAACIACIGCOAAACAITITGCCA CETANIGATIAAITAGGAINAGTOGGAGGCAICAGIATICCAITGCCAGAGGIGAANITCITIGGATITAITIGAAGCIAACIACIGCOAAACAITITGCCA CETANIGATIAAITAGGAINAGTOGGAGGCAICAGIATICCAITGCCAGAGGIGGAANITCITIGGATITAITIGAAGCIAACIACIGCOAAACAITITIGCCA CETANIGATIAAITAGGAINAGTOGGAGGACICAGIATCCAITGCCAGAGCIGAAATICITICGAATITAITAGAGCIAACIACIGCOGGAAACIACIGGAGAATICGCOGAACIGAITITCCCA AGGAIGTITICCAITIAAICAGIGAACGAAAGITAGGAGGAICAGAICA	Ap1 Ap2 Ap3 Ap4 Ap5 Ap6 Ap7 Ap8 Ap12 Ap13 Ap18 Ap1 Ap2
301 301 301 301 301 301 301 301 301 301	CGTAARGATTAATAGGGATAGTOGGGGGATTCOATGTOAGAGGIGAAATTCTTOGATTTATTGAAGACTAACTACTGCGGAAGCATTGGCG CGTAARGATTAATAGGGATAGTOGGGGGCACGGTATTCAATTGTCAGGGGGAAATTCTTOGGATTTATTGAAGACTAACTACTGCGAAACCATTGOCG CGTAARGATTAATAGGGATAGTOGGGGGCACGGTATCAATTGTCAGGGTGAATTCTTOGGATTTATTGAAGACTAACTACTGCGAAACCATTGOCG CGTAARGATTAATAGGGATAGTOGGGGGCACGGTATCAATTGTCAGGGTGAATTCTTOGGATTTATTGAAGACTAACTACTGCGAAACCATTGOCG CGTAARGATTAATAGGGATAGTOGGGGGCACGGTAGTGATTCATTGTCAGGGTGAATTCTTOGGATTTATTGAAGACTAACTACTGCGAAACCATTGOCG CGTAARGATTAATAGGGATAGTOGGGGGCACGGTGAGTGCAGGGGGAAATTCTTOGGATTTATTGAAGACTAACTACTGCGAAACCATTGOCG CGTAARGATTAATAGGGATAGTOGGGGGCATCAGTATCCAATTGTCAGGGTGAAATTCTTOGGATTTATTGAAGACTAACTACTGCGAAACCATTGOCG CGTAARGATTAATAGGGATAGTOGGGGGCATCAGTATCCAATTGTCAGGGTGAAATTCTTOGGATTTATTGAAGACTAACTACTGCGAAACCATTGOCG CGTAARGATTAATAGGGATAGTOGGGGGCATCAGTATCCAATTGTCAGAGTGGAATTCTTTGGATTTATTGAAGACTAACTA	Ap1 Ap2 Ap3 Ap4 Ap5 Ap6 Ap7 Ap8 Ap12 Ap13 Ap18 Ap1 Ap2 Ap3
301 301 301 301 301 301 301 301 301 301	CETANIGATTANIAGCAINAGTOSOGGICAGIAITICAATIGICAGAGIGAANITCITIGATITAITIGAAGACTAACIACIGGAAAGCAITIGICA CETANIGAITIANIAGGAINAGTOSOGGICAGIAITICAATIGICAGAGIGAANITCITIGATITAITIGAAGACTAACIACIGGAAAGCAITIGICA CETANIGAITIANIAGGAINAGTOGGIGGACAGIAITICAATIGICAGAGIGAANITCITIGATITAITIGAAGACTAACIACIGCAANCAITIGICA CETANIGAITIANIAGGAINAGTOGGIGGCAICAGIAITICAATIGICAGAGIGAANITCITIGATITAITIGAAGACTAACIACIGCAANCAITIGICA CETANIGAITIANIAGGAINAGTOGGIGGCAICAGIAITICAATIGICAGAGIGAANITCITIGATITAITIGAAGACTAACIACIGCAANCAITIGICA CETANIGAITIANIAGGAINAGTOGGIGGCAICAGIAITICAATIGICAGAGIGAANITCITIGATITAITIGAAGACIAACIACIGCAANCAITIGICA CETANIGAITIANIAGGAINAGTOGGIGGCAICAGIAITICAATIGICAGAGIGAANITCITIGATITAITIGAAGCIAACIACIGCOAANCAITIGOCA CETANIGAITIANIAGGAINAGTOGGIGGCAICAGIAITICAATIGICAGAGIGAANITCITIGATITAITIGAAGCIAACIACIGCOAANCAITIGOCA CETANIGAITIANIAGGAINAGTOGGIGGCAICAGIAITICAATIGICAGAGIGAANITCITIGATITAITIGAAGCIAACIACIGCOAANCAITIGOCA CETANIGAITIANIAGGAINAGTOGGIGGCAICAGIAITICAATIGICAGAGIGAANITCITIGATITAITIGAAGCIAACIACIGCOAANCAITIGOCA CETANIGAITIANIAGGAINAGTOGGIGGCAICAGIAITICAATIGICAGAGIGAANITCITIGATITAITIGAAGCIAACIACIGCOAANCAITIGOCA CETANIGAITIANIAGGAINAGTOGGIGGCAICAGIAITICAAGAGIGAANITCITIGATITAITIGAAGCIAACIACIGCOGAAACAITIGOCA CETANIGAITIANIAGGAINAGTOGGIGGCAICAGIAICACIGAGAGIGAANITCITIGAATITAITIGAAGCIAACIACIGCOGAAACAITIGOCA CETANIGAITIANIAGGAINAGTOGGIGGGCAICAGINCAGAITICATIGCAGAITIATIGAAGACIAACIACIGCOGAAACAITIGOCA CETANIGAITIANIAGGAINAGTOGGIGGCAICAGINCACAINCOGOGIGGAANITCITIGAATITAITIGAAGCIAACIACIGCOGAAACAITIGOCA CETANIGAITIANIAGGAINAGTOGGIGGCAICAGINGACAANCIGCIGAACITAICIACIGACIAACACIACIGCOGAACAAITIGOCA CETANIGAITIAATAGOGAINAGTIAGGIGAAGACIAACAGAICAGAITACOIGGIGAANITCITIGAATITAITIGAAGACIAACTACIGCOGAAACAITIGOCA CETANIGAITITAATAGOGAINAGTIAGGIGAACACAACAACAACAACAACAACAACAACIACIGOCAAACAACIACIGOGGAI CETANIGAITITAATAGOGAAAGITAGGIGAACAACAACAACAACAACAACAACAACAACAACAACAAC	Ap1 Ap2 Ap3 Ap4 Ap5 Ap6 Ap7 Ap8 Ap12 Ap13 Ap18 Ap1 Ap2 Ap3 Ap4
301 301 301 301 301 301 301 301 301 301	CGTAARGATTAATAGGGATAGTGGGGGGGATGGAGGGAGGAATTCTTGGATTATTGAAGGCTAACTACTGCGGAAGCATTGGCG CGTAARGATTAATAGGGATAGTGGGGGGGGGAATTCTGGGGTGAATTCTTGGATTTATTGAAGCTAACTACTGCGAAACCATTGGCG CGTAARGATTAATAGGGATAGTGGGGGGGGAATCGTGGGATTTATTGAAGCTAACTACTGCGAAACCATTGCCG CGTAARGATTAATAGGGATAGTGGGGGGGGAATTCTGGGATTGATT	Apl Ap2 Ap3 Ap4 Ap5 Ap6 Ap7 Ap8 Ap12 Ap13 Ap18 Ap1 Ap2 Ap3 Ap4
301 301 301 301 301 301 301 301 301 301	CGENARGATTANTAGGATAGTO3333GCIECAGTATTOCATROCAGAGGIGAAATTOCTIGGATTATTGAAGACTAACTACTGCGGAAGCATTIGOCA CGENARGATTAATAGGATAGTO3333GCATCAGTATTCAATTGTCAGAGGIGAAATTOCTIGGATTTATTGAAGACTAACTACTGCGAAAGCATTTOCCA CGENARGATTAATAGGGATAGTO3333GCATCAGTATTCAATTGTCAGAGGIGAAATTOCTIGGATTTATTGAAGACTAACTACTGCGAAACGATTTOCCA CGENARGATTAATAGGGATAGTO3333GCATCAGTATTCAATTGTCAGAGGIGAAATTOCTIGGATTTATTGAAGACTAACTACTGCGAAACGATTTOCCA CGENARGATTAATAGGGATAGTO3333GCATCAGTATTCAATTGTCAGAGGIGAAATTOCTIGGATTTATTGAAGACTAACTACTGCGAAACGATTTOCCA CGENARGATTAATAGGGATAGTO3333GCATCAGTATTCAATTGTCAGAGGIGAAATTOCTIGGATTTATTGAAGCTAACTACTGCGAAACGATTTGCCA CGENARGATTAATAGGGATAGTO3333GCATCAGTATTCAATTGTCAGAGGIGAAATTOCTIGGATTTATTGAAGCTAACTACTGCGAAACGATTTGCCA CGENARGATTAATAGGGATAGTO3333GCATCAGTATTCAATTGTCAGAGGIGAAATTOCTIGGATTTATTGAAGCTAACTACTGCGAAACGATTTGCCA CGENARGATTAATAGGGATAGTO3333GCATCAGTATTCAATTGTCAGAGGIGAAATTCTTGGATTTATTGAAGCTAACTACTGCGAAACGATTTGCCA CGENARGATTAATAGGGATAGTO3333GCATCAGTATTCAATTGTCAGAGGIGAAATTCTTGGATTTATTGAAGCTAACTACTGCGAAACGATTTGCCA CGENARGATTAATAGGGATAGTO3333GCATCAGTATCCAATTGCCAGGGIGAAATTCTTGGATTTATTGCAGGCTAACTACTGCGAAACGATTTGCCA CGENARGATTAATAGGATAGTO3333GCATCAGTATTCAATTGTCAGAGGIGAAATTCTTGGATTTATTGCAGGCTAACTACTGCGAAACGATTTGCCA CGENARGATTAATAGGATAGTO3333GCATCAGTATCCAATTGCCAGGGIGAAATTCTTGGATTTATTGCAGGCTAACTACTGCCGAAACGATTTGCCA CGENARGATTAATAGGATAGTO333GCATCAGTAGTAGCAACGACGAACTGCTTAACTACTGCCGAAACGATTTGCCA CGENARGATTAATAGGATAGTGAGGAGAAGTTAGGAGGAGAACGAAC	Apl Ap2 Ap3 Ap4 Ap5 Ap6 Ap7 Ap8 Ap12 Ap13 Ap18 Ap1 Ap2 Ap3 Ap4 Ap5
301 301 301 301 301 301 301 301 301 301	CGTAARGATTAATAGGGATAGTGGGGGGGATTCAATTGTCAAGAGTGGAAATTCTTTGGATTTATTGAAGACTAACTA	Ap1 Ap2 Ap3 Ap4 Ap5 Ap6 Ap7 Ap8 Ap12 Ap13 Ap18 Ap1 Ap2 Ap3 Ap4 Ap5 Ap6
301 301 301 301 301 301 301 301 301 301	CGTANIGATTANIAGGATAGTGAGGGGGTGAATTGCAGAGGGGAATTCTTIGGATTATTGAAGACTAACTACTGCGGAAGCATTGGGG CGTANIGATTAATAGGGATAGTGGGGGGGGATTCGAATTGCAGAGGGGAATTCTTIGGATTTATTGAAGACTAACTACTGCGAAAGCATTTGCCG CGTANIGATTAATAGGGATAGTGGGGGGGCATCAGTATTCAATTGCAGAGGGGAATTCTTIGGATTTATTGAAGACTAACTACTGCGAAAGCATTTGCCA CGTANIGATTAATAGGGATAGTGGGGGGCATCAGTATTCAATTGCAGAGGGGAATTCTTGGATTTATTGAAGACTAACTA	Ap1 Ap2 Ap3 Ap4 Ap5 Ap6 Ap7 Ap8 Ap12 Ap13 Ap18 Ap1 Ap2 Ap3 Ap4 Ap5 Ap1 Ap2 Ap3 Ap4 Ap5 Ap5 Ap6 Ap7
301 301 301 301 301 301 301 301 301 301	CGTAARGATTAATAGGGATAGTOGGGGGGGATTCOATTGTCAGAGGTGAAATTCTTTGGATTTATTGAAGACTAACTA	Ap1 Ap2 Ap3 Ap4 Ap5 Ap6 Ap7 Ap8 Ap12 Ap13 Ap18 Ap1 Ap2 Ap3 Ap4 Ap5 Ap6 Ap7 Ap2 Ap3 Ap4 Ap5 Ap6 Ap7 Ap2 Ap13 Ap4 Ap2 Ap3 Ap4 Ap5 Ap6 Ap7 Ap5 Ap6 Ap7 Ap5 Ap6 Ap7 Ap5 Ap6 Ap7 Ap5 Ap6 Ap7 Ap7 Ap5 Ap6 Ap7 Ap7 Ap5 Ap6 Ap7 Ap7 Ap7 Ap6 Ap7 Ap7 Ap7 Ap7 Ap6 Ap7 Ap7 Ap7 Ap7 Ap7 Ap7 Ap7 Ap7 Ap7 Ap7
301 301 301 301 301 301 301 301 301 301	CGTANIGATTANIAGGAINAGTOGGGGGGICAGTATICOATIGICAGAGGIGAANTICITIGGATTATIGAAGACTAACIACIGGGAAAGCAITIGICG CGTANIGATTANIAGGGAINAGTOGGGGGCAICAGTATICAATIGICAGAGIGAANTICITIGGATTATIGAAGACTAACIACIGGGAAAGCAITIGICG CGTANIGATTANIAGGGAINAGTGGGGGGCAICAGTATICAATIGICAGAGIGAANTICITIGGATTATIGAAGACTAACIACIGGAAAGCAITIGICG CGTANIGATTANIAGGGAINAGTGGGGGCAICAGTATICAATIGICAGAGIGAANTICITIGGATTANITGAAGACTAACIACIGGAAAGCAITIGICG CGTANIGATTANIAGGGAINAGTGGGGGCAICAGTATICAATIGICAGAGIGAANTICITIGGAITTAITIGAAGACTAACIACIGGAAAGCAITIGICG CGTANIGAITAATAGGGAINAGTGGGGGGCAICAGTATICAATIGICAGAGIGAAATICITIGGAITTAITIGAAGACTAACIACIGGAAAGCAITIGICG CGTANIGAITAATAGGGAINAGTGGGGGGCAICAGTATICAATIGICAGAGIGAAATICITIGGAITTAITIGAAGACTAACIACIGGAAAGCAITIGICG CGTANIGAITAATAGGGAINAGTGGGGGGCAICAGTATICAATIGICAGAGIGAAATICITIGGAITTAITIGAAGACTAACIACIGCGAAACGAITIGOCG CGTANIGAITAATAGGGAINAGTGGGGGGGAICAGTATICAATIGICAGAGIGGAANTICITIGGAITTAITIGAAGACTAACIACIGCGAAAGCAITIGOCG CGTANIGAITAATAGGGAINAGTGGGGGGCAICAGTATICAATIGICAGAGIGGAANTICITIGGAITTAITIGAAGACTAACIACIGCGAAAGCAITIGOCG CGTANIGAITAATAGGGAINAGTGGGGGGAICAGTAICCAATIGICAGAGIGGAANTICITIGGAITTAITIGAAGACTAACTACIGCGAAAGCAITIGOCG CGTANIGAITAATAGGGAINGTGGGGGGAICAGTAICGAIGGGGAANTICITIGGAITTAITIGAAGACTAACTACIGCGAAAGCAITIGOCG CGTANIGAITTAATAGGGAINGTGGGGGGAICAGTACGAIGCGGGAANTICITIGGAITTAITIGAAGACTAACTACIGCGAANGCAITTIGOCG CGTANIGAITTAATAGGGAINGTGGGGGAICAGTAICGAIGGGGAANTICITIGGAITTAITIGAAGACTAACTACIGCGAANGCAITTIGOCG CGTANIGAITTAATAGGGAINGTGGGGGAICGAIGGAGAACIGCGAINCOGTGGAIGCTTAACGAACAACTACIGCGGACGAGACGAICGGAIGGGGGG CGAGIGTITTCAITTAATAGGGAINGTAGGGGAICGAAGACGACACGAINCOGTGGAIGCTTAACCATAACCATAGCGGAICGGGAIGGGGGG CGAGAIGTITTCAITTAATAGGGAAAGTTAGGGGAICGAAGACGACACGAINCOGTGGAIGCTTAACCATAACCATAGCGAICGGGAIGGGGGG CGAGAIGTTTCAITTAATAGGGAAAGTTAGGGGAICGAAGACGAACAGAINCOGTGGAIGCTTAACCATAACCATAACCATAGCGAICGGGGGGGA CGAGAIGTTTCAITTAATCAGIGAAAGAAAGTTAGGGGAICGAAGACGAACAGAINCOGTGGAIGGTGTGACATAACCATAACCATAGCGAICGGAICG	Ap1 Ap2 Ap3 Ap4 Ap5 Ap6 Ap7 Ap8 Ap12 Ap13 Ap18 Ap1 Ap2 Ap3 Ap4 Ap5 Ap6 Ap7 Ap8 Ap4 Ap5 Ap6 Ap7 Ap8 Ap4 Ap3 Ap4 Ap3 Ap4 Ap5 Ap5 Ap5 Ap5 Ap5 Ap5 Ap5 Ap5 Ap5 Ap5
301 301 301 301 301 301 301 301 301 301	CETANIGATTANIAGCATAGTOSOGGOGICAGTATTOCATTGTCAGAGGIGAANTCTTOGATTATTGAAGACTAACTACTGCGGAAGCATTGGCG CETANIGATTAATAGGCATAGTOSOGGOCICAGTATTCAATTGTCAGAGGIGAANTCTTOGATTTATTGAAGACTAACTACTGCGAAACCATTGOCA CETANIGATTAATAGGCATAGTOGGOGGOCICAGTATTCAATTGTCAGGGIGAANTCTTOGATTTATTGAAGACTAACTACTGCCGAAACCATTGOCA CETANIGATTAATAGGCATAGTOGGOGGOCICAGTATTCAATTGTCAGGGIGAANTCTTOGATTTATTGAAGACTAACTACTGCCGAAACCATTGOCA CETANIGATTAATAGGCATAGTOGGOGGOCICAGTATTCAATTGTCAGGGIGAANTCTTOGATTTATTGAAGACTAACTACTGCCGAAACCATTGOCA CETANIGATTAATAGGCATAGTOGGOGGOCICAGTATTCAATTGTCAGGGIGGAANTCTTOGATTTATTGAAGACTAACTACTGCCGAAACCATTGOCA CETANIGATTAATAGGCATAGTOGGOGGOCICAGTATCCAATTGTCAGGGIGGAANTCTTOGATTTATTGAAGACTAACTACTGCCGAAACCATTTGOCA CETANIGATTAATAGGCATAGTOGGOGGOCICAGTATCCAATTGICAGGGIGGAANTCTTOGATTTATTGAAGCTAACTACTGCCGAAACCATTTGOCA CETANIGATTAATAGGCATAGTOGGOGGOCICAGTATCCAATTGICAGGGIGGAANTCTTGGATTTATTGAAGCTAACTACTGCCGAAACCATTGOCA CETANIGATTAATAGGCATAGTOGGOGGOCICAGTATCCAATTGICAGGGIGGAANTCTTGGATTTATTGAAGCTAACTACTGCCGAAACCATTTGOCA CETANIGATTAATAGGCATAGTOGGOGGOCICAGTATCCAATTGICAGGGIGGAANTCTTGGATTTATTGAAGCTAACTACTGCCGAAACCATTTGOCA CETANIGATTAATAGGCATAGTOGGOGGOCICAGTATCCAATTGICAGAGGIGGAANTCTTGGATTTATTGAAGCTAACTACTGCCGAAACCATTTGOCA CETANIGATTAATAGGCATAGTOGGOGGOCICAGTATCCAATGCCGAGGGGAANTCTTGGAGTTTATTGAAGCTAACTACTGCCGAAACCATTTGOCA CETANIGATTAATAGGGATAGTOGGOGOCICAGTACGATTCCAATGCCGGGTGAGTTTATTGAAGCTAACTACTGCCGAAACCATTTGOCA CETANIGATTAATAGGGATAGTOGGGGACGGAGGAGGAGGAGGAGAGGA	Ap1 Ap2 Ap3 Ap4 Ap5 Ap6 Ap7 Ap8 Ap12 Ap13 Ap18 Ap1 Ap2 Ap3 Ap4 Ap5 Ap6 Ap7 Ap8 Ap7 Ap8 Ap12 Ap5 Ap6 Ap7 Ap8 Ap14 Ap5 Ap6 Ap7 Ap8 Ap4 Ap5 Ap5 Ap6 Ap7 Ap8 Ap6 Ap7 Ap8 Ap6 Ap7 Ap8 Ap6 Ap7 Ap8 Ap6 Ap7 Ap8 Ap6 Ap7 Ap8 Ap6 Ap7 Ap8 Ap6 Ap7 Ap8 Ap6 Ap7 Ap8 Ap7 Ap8 Ap6 Ap7 Ap8 Ap7 Ap8 Ap6 Ap7 Ap8 Ap7 Ap8 Ap7 Ap8 Ap6 Ap7 Ap8 Ap7 Ap7 Ap8 Ap7 Ap7 Ap8 Ap7 Ap7 Ap8 Ap7 Ap7 Ap7 Ap7 Ap7 Ap7 Ap7 Ap7 Ap7 Ap7
301 301 301 301 301 301 301 301 301 301	CGTANIGATTANIAGGATAGTOSOGGGGTCAGTATTOCATTGCAGAGGGAANTCCTTGGATTATTGAAGACTAACTACTGCGGAAGCATTGGCG CGTANIGATTAATAGGGATAGTOGGGGGCATCAGTATTCAATTGCAGAGGGAANTCCTTGGATTTATTGAAGACTAACTACTGCGAAAGCATTGGCG CGTANIGATTAATAGGGATAGTOGGGGGCATCAGTATCCAATTGCAGAGGGAANTCCTTGGATTTATTGAAGACTAACTACTGCGAAAGCATTGGCG CGTANIGATTAATAGGGATAGTGGGGGGCATCAGTATCCAATTGCAGAGGGAANTCCTTGGATTTATTGAAGACTAACTACTGCGAAAGCATTGGCG CGTANIGATTAATAGGGATAGTGGGGGGCATCAGTATCCAATTGCAGAGGGAANTCCTTGGATTTATTGAAGACTAACTACTGCGAAAGCATTGCCG CGTANIGATTAATAGGGATAGTGGGGGGCATCAGTATCCAATTGCAGAGGGAANTCCTTGGATTTATTGAAGACTAACTACTGCGAAAGCATTGCCG CGTANIGATTAATAGGGATAGTGGGGGGGCATCAGTATCCAATTGCAGAGGGAANTCCTTGGATTTATTGAAGACTAACTACTGCGAAACGATTGCCG CGTANIGATTAATAGGGATAGTGGGGGGGCATCAGTATCCAATTGCAGAGGGAANTCCTTGGATTTATTGAAGACTAACTACTGCGAAACGATTGCCG CGTANIGATTAATAGGGATAGTGGGGGGGGCATCAGTATCCAATTGCAGAGGGGAANTCCTTGGATTTATTGAAGACTAACTACTGCGGAAACGATTGCCG CGTANIGATTAATAGGGATAGTGGGGGGGCATCAGTATCCAATTGCAGAGGGGAANTCCTTGGATTTATTGGAGGCTAACTACTGCGGAAACGATTGCCG CGTANIGATTAATAGGGATAGTGGGGGGGGGGGGCAGGTAGTTGCCGAGGGGGAATTCCTTGGATTTATTGGAGGCTAACTACTGCGGAAACGATTTGCCA CGTANIGATTAATAGGGATAGTGGGGGGGCATCAGTATCCAATGGCAGAGGGGGAANTCCTTGGATTTATTGGAGGCTAACTACTGCCGAAACGATTTGCCA CGTANIGATTAATAGGGATAGTGGGGGGGAATGCGAGGGGGAANTCCTTGGATTTATTGGAGGCTAACTACTGCCGAAACGATTTGCCA CGTANIGATTAATAGGGATAGTGGGGGGGAAGTGGAAGGGGGGAANTCCTTGGATTTATTGGAGGCTAACTACTGCCGGAAACGATTTGCCA CGTANIGATTAATAGGGATAGTGGGGGGGAAGTGGAGGGGGAANTCCTTGGATTTATTGGAGGCTAACTACTGCCGAAGGAATTGCCG CGTAGTGGTTTAATAGGGATAGTGGGAGGAGGAGGAGGAGG	Ap1 Ap2 Ap3 Ap4 Ap5 Ap6 Ap7 Ap8 Ap12 Ap13 Ap18 Ap1 Ap2 Ap3 Ap4 Ap5 Ap7 Ap8 Ap1 Ap2 Ap3 Ap4 Ap5 Ap7 Ap8 Ap12 Ap3 Ap18 Ap1 Ap2 Ap3 Ap10 Ap5 Ap5 Ap5 Ap5 Ap5 Ap5 Ap5 Ap5 Ap5 Ap5
301 301 301 301 301 301 301 301 301 301	CGENARGATTANTAGGATAGTOSOGGGELCAGTATTOCATTGCAGAGGIGAAATTCTTIGATTTATTGAAGACTAACTACTGCGGAAGCATTGGCA CGENARGATTANTAGGATAGTOSOGGGCACAGTATTCAATTGCAGAGGIGAAATTCTTIGATTTATTGAAGACTAACTACTGCGAAACCATTGCCA CGENARGATTAATAGGATAGTOGGGGGCACAGTATTCAATTGCAGAGGIGAAATTCTTIGATTTATTGAAGACTAACTACTGCCAAACCATTGCCA CGENARGATTAATAGGGATAGTGGGGGGCACAGTATCCAATTGCAGAGGIGAAATTCTTIGATTTATTGAAGACTAACTACTGCCGAAACCATTGCCA CGENARGATTAATAGGGATAGTGGGGGGCACAGTACTCAATTGCAGGGIGAAATTCTTIGATTTATTGAAGACTAACTACTGCCGAAACCATTGCCA CGENARGATTAATAGGGATAGTGGGGGGCACAGTACCATTGCAGGGGGAATTCTTIGGATTTATTGAAGACTAACTACTGCCGAAACCATTGCCA CGENARGATTAATAGGGATAGTGGGGGGCACAGTACCATTGCAAGGGGGAATTCTTIGGATTTATTGAAGACTAACTACTGCGAAACCATTGCCA CGENARGATTAATAGGGATAGTGGGGGGGCACAGTACCATTGCAAGGGGGAATTCTTIGGATTTATTGAAGACTAACTACTGCGAAACCATTTGCCA CGENARGATTAATAGGGATAGTGGGGGGGCACAGTACGEATTCCAATGCCAGGGGGAATTCTTGGATTTATTGCAAGCTAACTACTGCGAAACCATTGCCA CGENARGATTAATAGGGATAGTGGGGGGGCACAGTACAGTACTACTGCCAGAGGGGAATTCTTGGATTTATTGCAAGCTAACTACTGCCGAAACCATTGCCA CGENARGATTAATAGGGATAGTGGGGGGGCACAGTACAGTACTGCCAGGGGGAATTCTTGGATTTATTGCAAGCTAACTACTGCCGAAACCATTGCCA CGENARGATTAATAGGGATAGTGGGGGGGCACAGTACAGTACCAGGGGGGAATTCTTGGATTTATTGCAAGCTAACTACTGCCGAAACCATTGCCA CGENARGATTAATAGGGATAGTGGGGGGGCACAGTACAGTACCAGGGGGGAATTCTTGGATTTATTGCAGGCTAACTACTGCCGAAACGATTGCCG CGENARGATTAATGGGATAGTGGGGGGGCACGGATGCGAATGCGGGGGGAATTCTTGGATTTATTGCAGGCTAACTACTGCCGAACGAA	Ap1 Ap2 Ap3 Ap4 Ap5 Ap6 Ap7 Ap8 Ap12 Ap13 Ap18 Ap12 Ap3 Ap4 Ap5 Ap5 Ap5 Ap5 Ap6 Ap5 Ap6 Ap5 Ap6 Ap5 Ap6 Ap5 Ap5 Ap5 Ap5 Ap1 Ap1 Ap3 Ap1 Ap3 Ap5 Ap5 Ap5 Ap5 Ap5 Ap5 Ap5 Ap5 Ap5 Ap5
301 301 301 301 301 301 301 301 301 301	CGTAARGATTAATAGGGATAGTGGGGGGGATGGATATTGCAGAGGGGAAATTCTTGGATTTATTGAAGGCTAACTACTGCGGAAGGATTGGGG CGTAARGATTAATAGGGATAGTGGGGGGGGGGATGGGTATTGCAGAGGGGAAATTCTTGGATTTATTGAAGGCTAACTACTGCGAAAGGATTGGCG CGTAARGATTAATAGGGATAGTGGGGGGGGGGATGGGTATCGATTGCAGAGGGGAATTCTTGGATTTATTGAAGGCTAACTACTGCGAAAGGATTGGCG CGTAARGATTAATAGGGATAGTGGGGGGGCATCAGTATCCAATGGCAGGGGGAAATTCTTGGATTTATTGAAGGCTAACTACTGCGAAAGGATTGCCG CGTAARGATTAATAGGGATAGTGGGGGGCATCAGTATCCAATGGCAGGGGGAAATTCTTGGATTTATTGAAGGCTAACTACTGCGGAAGGATTGCCG CGTAARGATTAATAGGGATAGTGGGGGGCATCAGTATCCAATGGCAGGGGGAAATTCTTGGATTTATTGAAGGCTAACTACTGCGAAAGGATTGCCG CGTAARGATTAATAGGGATAGTGGGGGGCATCAGTATCCAATGGCAGGGGGAAATTCTTGGATTTATTGAAGGCTAACTACTGCGAAACGATTTGCCA CGTAARGATTAATAGGGATAGTGGGGGGGCATCAGTATCCAATGGCAGGGGGAAATTCTTGGATTTATTGAAGGCTAACTACTGCGAAACGATTTGCCA CGTAARGATTAATAGGGATAGTGGGGGGGCATCAGTATCCAATGGCAGGGGGAAATTCTTGGATTTATTGAAGGCTAACTACTGCGGAAGCATTTGCCA CGTAARGATTAATAGGGATAGTGGGGGGGCATCAGTATCCAATGGCAGGGGGAATTCTTGGATTTATTGGAGGCTAACTACTGCGGAAAGCATTTGCCA CGTAARGATTAATAGGGATAGTGGGGGGGCATCAGTATCCAATGGCAGGGGGAATTCTTGGATTTATTGGAGGCTAACTACTGCGGAAAGCATTTGCCA CGTAARGATTAATAGGGATAGTGGGGGGCATCAGTATCCATGGCAGGGGGAATTCTTGGATTTATTGGAGGCTAACTACTGCGGAAAGCATTTGCCA CGTAARGATTAATAGGGATAGTGGGGGGCACGATGGGTGGAATTCTTGGATTTATTGGAGGCTAACCTACTGCGGAAAGCATTTGCCA CGTAARGATTAATAGGGATAGTGGGGGGGAAGTGGGGGGGG	Ap1 Ap2 Ap3 Ap4 Ap5 Ap6 Ap7 Ap8 Ap12 Ap13 Ap13 Ap13 Ap13 Ap1 Ap2 Ap3 Ap4 Ap3 Ap5 Ap6 Ap7 Ap8 Ap12 Ap3 Ap13 Ap13 Ap14 Ap5 Ap5 Ap5 Ap5 Ap5 Ap5 Ap5 Ap5 Ap5 Ap5
301 301 301 301 301 301 301 301 301 301	CGENARGATTANTAGGATAGTGAGGGGAGTAGTGATTGCAGGGGGAATTCTTGGATTTATTGAGGCTAACTACTGCGGAAGCATTGGGG CGENARGATTANTAGGGATAGTGGGGGGGAGTAGTATTCAATTGCAGGGGGAATTCTTGGATTTATTGAGGCTAACTACTGCGAAAGCATTGGCG CGENARGATTAATGGGATAGTGGGGGGGGAATGCGAGGAATTCTTGGATTTATTGAGGCTAACTACTGCGAAACGATTGGCG CGENARGATTAATGGGATAGTGGGGGGGCACGATACTGCAGGGGGAATTCTTGGATTTATTGAGGCTAACTACTGCGAAACGATTGGCG CGENARGATTAATGGGATAGTGGGGGGGCACGATACTGCAGGGGGAATTCTTGGATTTATTGAGGCTAACTACTGCGAAACGATTGGCG CGENARGATTAATGGGATAGTGGGGGGGCACGATACTGCAGGGGGAATTCTTGGATTTATTGAGGCTAACTACTGCGAAACGATTGGCG CGENARGATTAATGGGATAGTGGGGGGGCACGATACTGCAGGGGGGAATTCTTGGATTTATTGAGGCTAACTACTGCGAAACGATTGGC CGENARGATTAATGGGATAGTGGGGGGGCACGATACTGCAGGGGGAATTCTTGGATTTATTGAGGCTAACTACTGCGAAACGATTGGCC CGENARGATTAATGGGATAGTGGGGGGGCACGATACTGCAGGGGGAATTCTTGGATTTATTGAGGCTAACTACTGCGAAACGATTGGCC CGENARGATTAATGGGATAGTGGGGGGGCACGATACTGCAGGGGGAATTCTTGGATTTATTGGAGGCTAACTACTGCGAAACGATTGGCC CGENARGATTAATGGGATAGTGGGGGGGCACGATACTGCAGGGGGAATTCTTGGATTTATTGGAGGCTAACTACTGCGAAACGATTGGCC CGENARGATTAATGGGATAGTGGGGGGGCACGATACGATGCAGGGGGAATTCTTGGATTTATTGGAGGCTAACTACTGCGGAAACGATTGGCC CGENARGATTAATGGGATAGTGGGGGGGCACGGTGGAATTCCTTGGATTTATTGGAGGCTAACTACTGCGGAAACGATTGGCG CGENARGATTAATGGGATAGTGGGGGGCACGGTGGAATTCTTGGATTTATTGGAGGCTAACTACTGCGGAAACGATTGGCG CGENARGATTAATGGGATAGTGGGGGGCACGGTGGAATTGCTTGGATTATTGGAGGCTAACTACTGCGGAAACGATTGGCG CGENARGATTAATGGGATAGTGGGGGGCGACGGCGGGGGGGGGG	Ap1 Ap2 Ap3 Ap4 Ap5 Ap6 Ap7 Ap12 Ap13 Ap18 Ap12 Ap3 Ap4 Ap5 Ap6 Ap6 Ap7 Ap8 Ap5 Ap6 Ap7 Ap8 Ap12 Ap13 Ap18 Ap18
301 301 301 301 301 301 301 301 301 301	CGTAARGATTAATAGGGATAGTGGGGGGGATGGATATTGCAGGGGGGAAATTCTTGGATTTATTGAGGCTAACTACTGCGGAAGGATTGGCG CGTAARGATTAATAGGGATAGTGGGGGGGGGATCGGTATTCAATTGTCAGGGTGGAATTCTTGGATTTATTGAGGCTAACTACTGCGAAAGGATTGGCG CGTAARGATTAATAGGGATAGTGGGGGGCATCAGTATTCAATTGTCAGGGTGGAATTCTTGGATTTATTGAGGCTAACTACTGCGAAAGGATTGGCG CGTAARGATTAATAGGGATAGTGGGGGGCATCAGTATTCAATTGTCAGGGTGGAATTCTTGGATTTATTGAGGCTAACTACTGCGAAAGGATTGGCG CGTAARGATTAATAGGGATAGTGGGGGGCATCAGTATTCAATTGTCAGGGTGGAATTCTTGGATTTATTGAGGCTAACTACTGCGAAAGGATTGGCG CGTAARGATTAATAGGGATAGTGGGGGGCATCAGTATTCAATTGTCAGGGTGGAATTCTTGGATTTATTGAGGCTAACTACTGCGAAAGGATTGCCG CGTAARGATTAATAGGGATAGTGGGGGGGCATCAGTATTCAATTGTCAGGGTGAATTCTTGGATTTATTGAGGCTAACTACTGCGAAACGATTTGCCA CGTAARGATTAATAGGGATAGTGGGGGGGCATCAGTATTCAATTGTCAGGGTGAATTCTTGGATTTATTGAGGCTAACTACTGCCGAAACGATTGCCA CGTAARGATTAATAGGGATAGTGGGGGGGCATCAGTATTCAATTGTCAGGGTGAAATTCTTGGATTTATTGAGGCTAACTACTGCCGAAACGATTGCCA CGTAARGATTAATAGGGATAGTGGGGGGGCATCAGTATTCAATTGTCAGGGTGGAATTCTTGGATTTATTGGAGCTAACTACTGCCGAAACGATTGCCA CGTAARGATTAATAGGGATAGTGGGGGGCATCAGTATTCAATTGTCAGGGTGGAATTCTTGGATTTATTGGAGCTAACTACTGCCGAAACGATTGCCA CGTAARGATTAATAGGGATAGTGGGGGGCATCAGTATTCAATTGTCAGGGGGGAATTCTTGGATTTATTGGAGGCTAACTACTGCCGAAACGATTTGCCA CGTAARGATTAATAGGGATAGTGGGGGGCATCAGTATTGTCAGAGGGGGAATTCTTGGATTTATTGGAGGCTAACTACTGCCGAAACGATTTGCCA CGTAATGGATTAATAGGGATAGTGGGGGGCATCAGTATTGCCGAGGGGGAAATTCTTGGATTATTGGAGGCTAACTACTGCCGAAACGATTTGCCA CGTAATGGATTAATAGGGATAGTGGGGGCGACGGAGGGGGGAAATCCTTGCGATTAATTGGCGACTAACTA	Ap1 Ap2 Ap3 Ap4 Ap5 Ap6 Ap7 Ap8 Ap12 Ap13 Ap18 Ap12 Ap13 Ap18 Ap2 Ap3 Ap2 Ap3 Ap5 Ap6 Ap7 Ap5 Ap6 Ap2 Ap3 Ap5 Ap5 Ap5 Ap5 Ap5 Ap5 Ap5 Ap5 Ap5 Ap5
301 301 301 301 301 301 301 301 301 301	CGTANIGATTANIAGGATAGTO3333GCIPCAGTATTOCATTGTCAGAGGIGAANTCTTIGATTTATTGAGACTAACTACTGCGGAAGCATTGJCCA CGTANIGATTANIAGGATAGTO3333GCATCAGTATTCAATTGTCAGAGGIGAANTCTTIGATTTATTGAGACTAACTACTGCGAAACATTTGCCA CGTANIGATTANIAGGATAGTO3333GCATCAGTATTCAATTGTCAGAGGIGAANTCTTIGATTTATTGAGACTAACTACTGCCAAACATTTGCCA CGTANIGATTANIAGGATAGTO3333GCATCAGTATTCAATTGTCAGAGGIGAANTCTTIGATTTATTGAGACTAACTACTGCCAAACATTTGCCA CGTANIGATTANIAGGATAGTO3333GCATCAGTATTCAATTGTCAGAGGIGAANTCTTIGATTTATTGAGACTAACTACTGCCAAACATTTGCCA CGTANIGATTANIAGGATAGTO3333GCATCAGTATTCAATTGTCAGAGGIGAANTCTTIGATTTATTGAGACTAACTACTGCCAAACATTTGCCA CGTANIGATTANIAGGATAGTO3333GCATCAGTATTCAATTGTCAGAGGIGAANTCTTIGGATTTATTGAGACTAACTACTGCCAAACATTTGCCA CGTANIGATTANIAGGATAGTO3333GCATCAGTATTCAATTGTCAGAGGIGAANTCTTIGGATTTATTGAAGCTAACTACTGCCAAACATTTGCCA CGTANIGATTANIAGGATAGTO3333GCATCAGTATTCAATTGTCAGAGGIGAANTTCTTIGGATTTATTGAAGCTAACTACTGCCGAAACATTTGCCA CGTANIGATTANIAGGATAGTO3333GCATCAGTATTCAATTGTCAGAGGIGAANTTCTTIGGATTTATTGAAGCTAACTACTGCCGAAACANTTGCCA CGTANIGATTANIAGGATAGTO3333GCATCAGTATCCAATTGCCAGAGGIGAANTTCTTIGGATTTATTGAAGCTAACTACTGCCGAAACANTTGCCA CGTANIGATTANIAGGATAGTO3333GCATCAGTATCAATTGCCAGAGGIGAANTTCTTIGGATTTATTGAAGCTAACTACTGCCGAAACANTTGCCA CGTANIGATTAATAGGATAGTO3333GCATCAGTATCAATTGCCAGAGGIGAANTTCTTIGGATTTATTGAAGCTAACTACTGCCGAAACANTTGCCA CGTANIGATTAATAGGATAGTO333GCATCAGTATCCAATTGCCAGAGGIGAANTTCTTIGGATTTATTGAAGCTAACTACTGCCGAAACANTTGCCA CGTANIGATTAATAGGATAGTO333GCATCAGTATCGATGCAGAGGIGAANTTCTTIGGATTTATTGAAGCTAACTACTGCCGAAACANTTGCCA CGTANIGATTAATAGGATAGTGAGGAAGTTAGGGATGAGAGGAGAACTGAACTACTGCGAACTAACT	Ap1 Ap2 Ap3 Ap4 Ap5 Ap6 Ap7 Ap8 Ap12 Ap13 Ap18 Ap13 Ap2 Ap3 Ap2 Ap3 Ap4 Ap5 Ap5 Ap4 Ap5 Ap5 Ap5 Ap5 Ap5 Ap5 Ap5 Ap5 Ap5 Ap5
301 301 301 301 301 301 301 301 301 301	CGTAARGATTAATAGGGATAGTGGGGGGGATTGCAGTGATTGCAGGGGGGAATTCCTTGGATTATTGGAGGCTAACTACTGCGGAAGCATTGGCG CGTAARGATTAATAGGGATAGTGGGGGGGGGATCGGTGTGCGTGGGATTGCTGGGATTAGTGAGGCTAACTACTGCGAAACCATTGCCG CGTAARGATTAATAGGGATAGTGGGGGGGGATCGGTGGAATTCCTTGGATTTATTGGAGGCTAACTACTGCGGAAGCATTGCCG CGTAARGATTAATAGGGATAGTGGGGGGGGATCGGTGGAATTCTTGGATTGATT	Ap1 Ap2 Ap3 Ap4 Ap5 Ap6 Ap7 Ap8 Ap12 Ap13 Ap18 Ap1 Ap2 Ap3 Ap4 Ap5 Ap6 Ap7 Ap8 Ap12 Ap3 Ap4 Ap5 Ap6 Ap7 Ap8 Ap12 Ap3 Ap4 Ap5 Ap6 Ap7 Ap8 Ap13 Ap5 Ap6 Ap7 Ap8 Ap13 Ap5 Ap6 Ap7 Ap8 Ap13 Ap5 Ap6 Ap7 Ap8 Ap13 Ap5 Ap6 Ap7 Ap8 Ap13 Ap5 Ap6 Ap7 Ap8 Ap13 Ap5 Ap6 Ap7 Ap8 Ap13 Ap5 Ap6 Ap7 Ap8 Ap13 Ap5 Ap6 Ap7 Ap8 Ap7 Ap6 Ap7 Ap8 Ap7 Ap7 Ap8 Ap7 Ap7 Ap7 Ap7 Ap7 Ap7 Ap7 Ap7 Ap7 Ap7
301 301 301 301 301 301 301 301 301 301	CGTANIGATTANIAGGATAGTOSOGGGTCAGTATTICAATTGCAGAGGTGAANTCTTIGGATTTATTGAAGACTAACTACTGCGGAAGCATTTGCOG CGTANIGATTAATAGGGATAGTOGGGGGCATCAGTATTCAATTGCAGAGGTGAANTCTTIGGATTTATTGAAGACTAACTACTGCGAAAGCATTTGCCA CGTANIGATTAATAGGGATAGTOGGGGGCATCAGTATTCAATTGCAGAGTGAANTCTTIGGATTTATTGAAGACTAACTACTGCGAAAGCATTTGCCA CGTANIGATTAATAGGGATAGTOGGGGCATCAGTATTCAATTGCAGAGTGAANTCTTIGGATTTATTGAAGACTAACTACTGCGAAAGCATTTGCCA CGTANIGATTAATAGGGATAGTOGGGGCATCAGTATTCAATTGCAGAGTGAANTCTTIGGATTTATTGAAGACTAACTACTGCGAAACGATTGCCA CGTANIGATTAATAGGGATAGTOGGGGCATCAGTATTCAATTGCAGAGTGAANTCTTIGGATTTATTGAAGACTAACTACTGCGAAACGATTGCCA CGTANIGATTAATAGGGATAGTOGGGGCATCAGTATTCAATTGCAGAGTGAANTCTTIGGATTTATTGAAGCTAACTACTGCGAAACGATTGCCA CGTANIGATTAATAGGGATAGTOGGGGGCATCAGTATTCAATTGCAGAGGTGAANTCTTIGGATTTATTGAAGCTAACTACTGCGAAACGATTGCCA CGTANIGATTAATAGGGATAGTOGGGGGCATCAGTATCCAATTGCAGAGGTGAANTCCTTGGATTTATTGAAGCTAACTACTGCGAAACGATTGCCA CGTANIGATTAATAGGGATAGTOGGGGGCATCAGTATCCAATTGCCAGAGGTGAANTCCTTGGATTTATTGAAGCTAACTACTGCGAAACGATTGCCA CGTANIGATTAATAGGGATAGTOGGGGCATCAGTATCCAATTGCCAGAGGTGAANTCCTTGGATTTATTGAAGCTAACTACTGCGAAACGATTGCCA CGTANIGATTAATAGGGATAGTOGGGGCATCAGTATCCAATTGCCAGAGGTGAANTCCTTGGATTTATTGAAGCTAACTACTGCGAAACGATTGCCA CGTANIGATTAATAGGGATAGTOGGGGCATCAGTATCCAATTGCCAGAGGTGAAATTCCTTGGATTTATTGCAGGCTAACCTACTGCCGAAACGATTGCCC CGTANIGATTAATAGGGATAGTOGGGGAAAGTTAGGGGAAATTCGTGGAGTGGA	Ap1 Ap2 Ap3 Ap4 Ap5 Ap6 Ap7 Ap8 Ap12 Ap13 Ap18 Ap12 Ap3 Ap18 Ap12 Ap3 Ap2 Ap3 Ap4 Ap5 Ap6 Ap7 Ap8 Ap12 Ap3 Ap5 Ap5 Ap5 Ap5 Ap5 Ap5 Ap5 Ap5 Ap5 Ap5
301 301 301 301 301 301 301 301 301 301	CETANIGATTANIAGCATAGTOSOGGOGICAGTATTICAATTGICAGAGGIGAANTICTTIGATTTATTGAAGACTAACTACTGIGGAAAGCATTGICG CETANIGATTANIAGGATAGTOGGGGGCACGATATTCAATTGICAGAGGIGAANTICTTIGGATTTATTGAAGACTAACTACTGICGAAAGCATTGICG CETANIGATTAATAGGGATAGTOGGGGGCACAGTATTCAATTGICAGAGGIGAANTICTTIGGATTTATTGAAGACTAACTACTGICGAAACCATTGOCG CETANIGATTAATAGGGATAGTOGGGGGCACCAGTACTGATTGATGICAGAGGATTATTGICAGGAGTAACTACTGICGAAACCATTGOCG CETANIGATTAATAGGGATAGTOGGGGGCACCAGTATTCAATTGICAGGGIGAANTICTTIGGATTTATTGAAGACTAACTACTGOCGAAACCATTGOCG CETANIGATTAATAGGGATAGTOGGGGGCACCAGTATCCATTGICAGGGIGGAATTCTTIGGATTTATTGAAGACTAACTACTGOCGAAACCATTGOCG CETANIGATTAATAGGGATAGTOGGGGGCACCAGTATCCATTGICAGGGIGGAATTCTTIGGATTTATTGAAGACTAACTACTGOCGAAACCATTGOCG CETANIGATTAATAGGGATAGTOGGGGGCACCAGTATCCATTGICAGGGIGGAATTCTTIGGATTTATTGAAGACTAACTACTGOCGAAACCATTGOCG CETANIGATTAATAGGGATAGTOGGGGGCACCAGTATCCATTGICAGGGIGGAATTCTTIGGATTTATTGAAGACTAACTACTGOCGAAACCATTGOCG CETANIGATTAATAGGGATAGTOGGGGGCACGGATATCCATTGICAGGGIGGAATTCTTIGGATTTATTGAAGACTAACTACTGOCGAAACCATTGOCG CETANIGATTAATAGGGATAGTOGGGGGCACAGTACAGTACGAGGIGGAAATTCCTTGGATTTATTGAAGACTAACTACTGOCGAAACCATTGOCG CETANIGATTAATAGGGATAGTOGGGGGCACAGTACAGTACGGIGGAAATTCCTTGGATTTATTGAAGACTAACTACTGOCGAAACCATTGOCG CETANIGATTAATAGGGATAGTOGGGGGCACGGATACAGTACGGTGGAATTCTTGGATTTATTGAAGCTAACTACTGOCGAAACCATTGOCG CETANIGATTAATAGGGATAGTOGGGGGCACGGATACAGTACAGTGCGATTACTTGAAGACTACTGCCGAAACCATTGOCG CETANIGATTAATAGGGATAGTOGGGGACGACGGATCGAATACCTGCGGATTACATGCOCGACTAGGATTGOCG CETANIGATTAATAGGGAAACGTAAGGTAGGGACGACGACGACGACGACGGACG	Ap1 Ap2 Ap3 Ap4 Ap6 Ap6 Ap7 Ap8 Ap12 Ap13 Ap12 Ap13 Ap14 Ap2 Ap13 Ap4 Ap5 Ap6 Ap7 Ap8 Ap13 Ap13 Ap18 Ap13 Ap18 Ap13 Ap18 Ap13 Ap2 Ap13 Ap3 Ap5 Ap5 Ap6 Ap5 Ap5 Ap5 Ap5 Ap5 Ap5 Ap5 Ap5 Ap5 Ap5
301 301 301 301 301 301 301 301 301 301	CGTANIGATTANIAGGAINAGTOGGGGGAINGCAGINITCANTIGCAGAGIGAANITCITIGATTANTGAAGACTAACTACTGCGAAAGCAITTGCG CGTANIGATTANIAGGGAINGCGGGAINGCGAINTCANTIGCAGAGIGAANITCITIGATTANTGAAGACTAACTACTGCGAAAGCAITTGCG CGTANIGATTANIAGGGAINGCGGGGAINCGGAINTCANTIGCAGAGIGAANITCITIGATTANTGAAGACTAACTACTGCGAAAGCAITTGCG CGTANIGATTANIAGGGAINGCGGGGGAINCGGAINTCANTIGCAGAGIGAANITCITIGATTANTGAAGACTAACTACTGCGAAAGCAITTGCG CGTANIGATTANIAGGGAINGCGGGGGAINCGGAINTCANTIGCAGAGIGAANITCITIGATTANTGAAGACTAACTACTGCGAAAGCAITTGCG CGTANIGATTANIAGGGAINGCGGGGGAINCGGAINTCANTIGCAGAGIGAANITCITIGATTANTGAAGACTAACTACTGCGAAAGCAITTGCG CGTANIGATTANIAGGGAINGCGGGGGAINCGGAINTCANTIGCAGAGIGAANITCITIGATTANTGAAGACTAACTACTGCGAAAGCAITTGCC CGTANIGATTANIAGGGAINGCGGGGGAINCGGAINTCANTIGCAGAGIGAANITCITIGATTANTGAAGACTAACTACTGCGAAAGCAITTGCC CGTANIGATTANIAGGGAINGCGGGGGAINCGTANTCANTIGCAGAGIGAANITCITIGGAITTANTGAAGACTAACTACTGCGAAAGCAITTGCC CGTANIGATTANIAGGGAINGCGGGGGAINCGTANCANTGCAGAGIGGAANITCITIGGAITTANTGAAGACTAACTACTGCGAAAGCAITTGCC CGTANIGAITTANIAGGAINGCGGGGGAINGGTAICCANTGCCAGAGIGGAANITCITIGGAITTANTGAAGACTAACTACTGCGAAAGCAITTGCC CGTANIGAITTANIAGGAINGCGGGGGAINGGTAICCANTGCCAGAGIGGAANITCITIGGAITTANTGAAGCTAACTACTGCGAAAGCAITTGCC CGTANIGAITTANIAGGAINGCGGGGGAINGGTGAAGACTACGAINCGCTGGAINTCATGGAINGCCANACTACTGCGAAAGCAITTGCC CGTANIGAITTANIAGGAINGCGGGGAINGGTGGAAGAGIGGAANITCITIGGAITTANTGAAGACTAACTACTGCGAANGCAITTGCC CGTANIGAITTANIAGGAINGTGGGGGAINGGTGGAAGACGAINCGAINCGCGGGGAANITCITIGGAITTANTGAAGACTAACTACTGCGGAINGGGGG CGTANIGAITTANIAGGAINGTGGGAGGAAGTTAGGAINCGAIGCGAAGACGAINCGGTGGAIGCGAINGCGGA CGAIGTTTTCANTANICAGIGAAGGAAGTTAGGAGAINCGAAGACGAINCGGAIGGGAIGGTGAAGCAINCGAINGCGGGGAINGGAIGG AGGAIGTTTTCANTANICAGIGAAGAAGTTAGGAGAINCGAAGACGAINCGAINGCGTGGAIGGGAIGGAINGGGAGG AGGAIGTTTTCANTANICAGIGAAGAAGTTAGGAINCGAAGAAGCAANCGAINCGAINGCGTGAIGGAINGGAIGG AGGAIGTTTTCANTANICAGIGAAGAAGTTAGGAGAINGGAINCGAINCGAINGCGTGGAIGCTTAACCAINACCTANACCTANGCGAINGGAGGG AGGAIGTTTTCANTANACGGAAAGTTAGGAGAINGGAAGAAGAAGGAINCGAINCGAINGCGTGGAIGGAINGGAIGGGAINGGAIGG AGGAIGTTTTCANTAACTAGTGAAGAAGTTAGGAINGGAINGAAGAINCGAINGGGTGGAINGGAINGGAINGGAINGGAIGGAINGGAIGGAINGGAIGG	Ap1 Ap2 Ap3 Ap4 Ap5 Ap6 Ap6 Ap7 Ap12 Ap13 Ap12 Ap13 Ap14 Ap2 Ap3 Ap4 Ap2 Ap3 Ap4 Ap5 Ap6 Ap2 Ap3 Ap4 Ap5 Ap6 Ap1 Ap5 Ap6 Ap5 Ap5 Ap6 Ap5 Ap5 Ap6 Ap5 Ap6 Ap5 Ap6 Ap5 Ap6 Ap5 Ap6 Ap5 Ap6 Ap7 Ap8 Ap1 Ap5 Ap6 Ap7 Ap8 Ap1 Ap1 Ap1 Ap5 Ap6 Ap7 Ap8 Ap1 Ap1 Ap1 Ap1 Ap1 Ap1 Ap1 Ap5 Ap6 Ap7 Ap6 Ap7 Ap8 Ap1 Ap1 Ap1 Ap1 Ap1 Ap1 Ap1 Ap5 Ap6 Ap7 Ap6 Ap7 Ap7 Ap8 Ap1 Ap1 Ap1 Ap1 Ap1 Ap1 Ap2 Ap1 Ap1 Ap2 Ap1 Ap1 Ap2 Ap1 Ap2 Ap1 Ap6 Ap7 Ap7 Ap7 Ap7 Ap7 Ap7 Ap7 Ap7 Ap7 Ap7
301 301 301 301 301 301 301 301 301 301	CGENARGATTANTAGGATAGTOSOGGGICAGTATTOCATTGCAGAGGIGAANTCTTIGATTATTGAAGACTAACTACTGCGGAAGCATTGGCA CGENARGATTANTAGGATAGTOSOGGGICAGTATTCAATTGCAGAGGIGAANTCTTIGATTTATTGAAGACTAACTACTGCGAAAGCATTGGCA CGENARGATTANTAGGATAGTOGGGGGCACAGTATTCAATTGCAGAGGIGAANTCTTIGATTTATTGAAGACTAACTACTGCGAAAGCATTGCCA CGENARGATTANTAGGGATAGTGGGGGGCACAGTATTCAATTGCAGAGGIGAANTCTTIGAGTTTATTGAAGACTAACTACTGCGAAACCATTGCCA CGENARGATTANTAGGGATAGTGGGGGGCATCAGTATTCAATTGCAGGGIGAANTCTTIGAGTTTATTGAAGACTAACTACTGCCGAAACCATTGCCA CGENARGATTANTAGGGATAGTGGGGGGGCATCGETATTCAATTGCAGGGIGAANTCTTIGGATTTATTGAAGACTAACTACTGCGAAACCATTGCCA CGENARGATTANTAGGGATAGTGGGGGGCATCGETATTCAATTGCAGGGIGAANTCTTIGGATTTATTGAAGACTAACTACTGCGAAACCATTGCCA CGENARGATTANTAGGGATAGTGGGGGGCATCGETATTCAATTGCAGGGIGAANTCTTIGGATTTATTGAAGACTAACTACTGCGAAACCATTGCCA CGENARGATTANTAGGGATAGTGGGGGGCATCGETATTCAATTGCAGGIGGAANTCTTIGGATTTATTGAAGACTAACTACTGCGAAACCATTGCCA CGENARGATTANTAGGGATAGTGGGGGGCATCGETATTCAATTGCAGGIGGAANTCCTTGGATTTATTGAAGACTAACTACTGCGAAACCATTGCCA CGENARGATTANTAGGGATAGTGGGGGGCATCGETATCCAATTGCAGGIGGAANTCCTTGGATTTATTGAAGACTAACTACTGCGAAAACCTTGCCG CGENARGATTAATAGGGATAGTGGGGGGCATCGETATCCAATTGCAGGIGGAANTCCTTGGATTTATTGAAGCTAACTACTGCGGAAACCATTGCCA CGENARGATTAATAGGGATAGTGGGGGGCATCGETATCCATTGCAGGIGGAANTCCTTGGATTTATTGAAGCTAACTACTGCGGAAACCTACTGGGGGGGG	Ap1 Ap2 Ap3 Ap4 Ap5 Ap6 Ap6 Ap7 Ap8 Ap12 Ap12 Ap13 Ap12 Ap3 Ap4 Ap5 Ap6 Ap13 Ap4 Ap5 Ap6 Ap13 Ap13 Ap18 Ap13 Ap18 Ap13 Ap18 Ap13 Ap5 Ap5 Ap5 Ap6 Ap5 Ap6 Ap5 Ap6 Ap5 Ap6 Ap5 Ap6 Ap7 Ap8 Ap5 Ap6 Ap7 Ap8 Ap5 Ap6 Ap7 Ap8 Ap7 Ap8 Ap5 Ap6 Ap7 Ap8 Ap7 Ap7 Ap8 Ap7 Ap8 Ap7 Ap8 Ap7 Ap8 Ap7 Ap8 Ap7 Ap8 Ap7 Ap8 Ap7 Ap7 Ap8 Ap7 Ap8 Ap7 Ap7 Ap8 Ap7 Ap7 Ap8 Ap7 Ap7 Ap7 Ap7 Ap7 Ap7 Ap7 Ap7 Ap7 Ap7
301 301 301 301 301 301 301 301 301 301	CGTANIGATTANIAGGAINAGTOGGGGGGICAGTATICOATGOAGAGIGAANTICTIGGATTATIGAAGACTAACTACTGCGGAAGCAITTIGCO CGTANIGHTAAITAGGGAINAGTGGGGGGCAICAGTATICAATGICAGAGGIGAANTICTIGGATTATIGAAGACTAACTACTGCGAAAGCAITTIGCO CGTANIGATTAAITAGGGAINAGTGGGGGGCAICAGTATICAATGICAGAGGIGAANTICTIGGATTATIGAAGACTAACTACTGCGAAAGCAITTIGCO CGTANIGATTAAITAGGGAINAGTGGGGGGCAICAGTATICCAATGICAGAGGIGAANTICTIGGATTATIGAAGACTAACTACTGCGAAAGCAITTIGCO CGTANIGATTAAITAGGGAINAGTGGGGGGCAICAGTATICCAATGICAGAGGIGAANTICTIGGATTATIGAAGACTAACTACTGCGAAAGCAITTIGCO CGTANIGAITAAITAGGGAINAGTGGGGGGCAICAGTATICCAATGICAGAGGIGAANTICTIGGATTTATIGAAGACTAACTACTGCGAAAGCAITTIGCO CGTANIGATTAAITAGGGAINAGTGGGGGGCAICAGTATICCAATGICAGAGGIGAANTICTIGGATTTATIGAAGACTAACTACTGCGAAAGCAITTIGCO CGTANIGATTAAITAGGGAINAGTGGGGGGGCAICAGTATCCAATGICAGAGGIGAANTICTIGGATTTATIGAAGACTAACTACTGCGAAAGCAITTIGCO CGTANIGATTAAITAGGGAINAGTGGGGGGGCAICAGTATCCAATGICAGAGGIGAANTICTIGGATTTATIGAAGACTAACTACTGCGAAAGCAITTIGCO CGTANIGATTAAITAGGGAINAGTGGGGGGGAICAGTATCCAATGICAGAGGIGAANTICTIGGATTTATIGAAGACTAACTACTGCGGAAAGCAITTIGCO CGTANIGATTAAITAGGGAINAGTGGGGGGGAICAGTATCCAATGICAGAGGIGGAANTICTIGGATTTATIGGAAGCTAACTACTGCGGAAAGCAITTIGCO CGTANIGATTAAITAGGGAINAGTGGGGGGAICAGTAICCAATGACTGCGAATGACTACTGCGGAAACCAATTIGCO CGTANIGATTAAITAGGGAINGTGGGGGGAICAGTAICCAATGACGAGCTAACTACTGCGGAAACCAATTIGCO CGTANIGATTAAITAGGGAINGTGGGGGGGAICAGTAICGAIGGGGAANTICTIGGATTTATIGGAAGCTAACTACTGCGGAACGAITTIGCO CGTANIGATTAAITAGGGAINGTGGGGGGGAICAGTAICGAITGACGAGGGGAANTICTIGGATTTATIGGAAGCTAACTACTGCGGAACGAACTGACGAICGAGAICGAAGACGAICGAATTAGGAGGACGAACGAICGAATTAGGAGGAAGCAACTACGAICGACTAACTACTGCGGACTAGGAICGGAIGGGGG CGTAGTTTCCATTAAICAGTGAACGAAGATTAGGGGAICGAAGAGGAICGAATACGAICGAGAICGAATACCATAACCATAACCTAICGCGCACGAGGAICGGAGG AGGAIGTTTTCATTAAICAGTGAACGAAAGTTAGGGGAICGAAGAGCAICGAAIACCATAACCATAACCATAACCATAACCATAGCGAICGGGGGG AGGAIGTTTTCATTAAICAGTGAACGAAAGTTAGGGGAICGAAGAAGCAICGAAICGA	Ap1 Ap2 Ap3 Ap4 Ap5 Ap6 Ap6 Ap7 Ap12 Ap13 Ap14 Ap12 Ap13 Ap14 Ap2 Ap3 Ap4 Ap5 Ap6 Ap7 Ap8 Ap2 Ap3 Ap4 Ap5 Ap6 Ap7 Ap8 Ap5 Ap6 Ap7 Ap8 Ap5 Ap6 Ap7 Ap8 Ap5 Ap7 Ap8 Ap7 Ap7 Ap8 Ap7 Ap8 Ap7 Ap7 Ap8 Ap7 Ap7 Ap8 Ap7 Ap7 Ap8 Ap7 Ap7 Ap8 Ap7 Ap7 Ap8 Ap7 Ap8 Ap7 Ap7 Ap8 Ap7 Ap7 Ap8 Ap7 Ap7 Ap8 Ap7 Ap7 Ap8 Ap7 Ap7 Ap7 Ap8 Ap7 Ap7 Ap7 Ap7 Ap7 Ap7 Ap7 Ap7 Ap7 Ap7
301 301 301 301 301 301 301 301 301 301	CGENARGATTANTAGGATAGTG3G3GGGTGAATTGCAATGCAGAGGGAAATTCTTGGATTATTGAAGACTAACTA	Ap1 Ap2 Ap3 Ap4 Ap5 Ap6 Ap6 Ap12 Ap13 Ap13 Ap13 Ap13 Ap13 Ap13 Ap13 Ap2 Ap3 Ap2 Ap3 Ap5 Ap6 Ap7 Ap8 Ap5 Ap6 Ap7 Ap8 Ap5 Ap5 Ap6 Ap7 Ap8 Ap5 Ap5 Ap6 Ap5 Ap6 Ap5 Ap6 Ap7 Ap8 Ap13 Ap13 Ap13 Ap13 Ap14 Ap5 Ap5 Ap6 Ap5 Ap6 Ap7 Ap8 Ap5 Ap6 Ap7 Ap8 Ap5 Ap6 Ap7 Ap8 Ap5 Ap6 Ap7 Ap8 Ap5 Ap6 Ap7 Ap8 Ap5 Ap6 Ap7 Ap8 Ap5 Ap6 Ap7 Ap8 Ap5 Ap6 Ap7 Ap8 Ap5 Ap6 Ap7 Ap8 Ap5 Ap6 Ap7 Ap8 Ap7 Ap8 Ap7 Ap8 Ap7 Ap8 Ap7 Ap8 Ap7 Ap8 Ap7 Ap8 Ap7 Ap7 Ap8 Ap7 Ap7 Ap8 Ap7 Ap6 Ap7 Ap7 Ap8 Ap7 Ap7 Ap7 Ap7 Ap7 Ap7 Ap7 Ap7 Ap7 Ap7
301       401       401       401       401       401       501       501       501       501       501       501       501       501       501       501	CGTANIGATTAATAGGATAGTGGGGGGGATGGATATTGAATGTCAGGGGGAAATTCTTGGATTATTGAAGGCTAACTACTGCGGAAGGATTGGCG CGTAATGATTAATGGGGATAGTGGGGGGGATGGATATTGAATGTCAGGGGGAAATTCTTGGATTTATTGAAGGCTAACTACTGCGAAAGGATTGGCG CGTAATGATTAATGGGGATAGTGGGGGGGATGGATACTGAATGGGGGGAATTCTTGGATTTATTGAAGGCTAACTACTGCGAAAGGATTGGCG CGTAATGATTAATGGGGATGGGGGGGCATGGATATCCAATGTCAGGGGGAAATTCTTGGATTTATTGAAGGCTAACTACTGCGAAAGGATTGGCG CGTAATGATTAATGGGGATGGGGGGGCATCAGTATCCAATGCAGGGGGAAATTCTTGGATTTATTGAAGGCTAACTACTGCGAAAGGATTGGCG CGTAATGATTAATGGGGATGGGGGGCATCAGTATCCAATGCAGGGGGAAATTCTTGGATTTATTGAAGGCTAACTACTGCGAAAGGATTGCCG CGTAATGATTAATGGGGATGGGGGGGCATCAGTATCCAATGCAGGGGGAATTCTTGGATTTATTGAAGGCTAACTACTGCGAAAGGATTGCCG CGTAATGATTAATGGGGATGGGGGGGCATCAGTATCCAATGCAGGGGGAATTCTTGGATTTATTGAAGGCTAACTACTGCGGAAGCATTTGCCA CGTAATGATTAATGGGGATGGGGGGGCATCAGTATCCAATGCAGGGGGAATTCTTGGATTTATTGAAGGCTAACTACTGCGGAAGCATTTGCCA CGTAATGATTAATGGGGATGGGGGGGCATCAGTATCCAATGCAGGGGGAATTCTTGGATTTATTGAAGCTAACTACTGCGGAAGCATTTGCCA CGTAATGATTAATGGGGATGGGGGGGCATCAGTATCCAATGCAGGGGGAATTCTTGGATTTATTGAAGCTAACTACTGCGGAAGCATTTGCCA CGTAATGATTAATGGGATGGG	Ap1 Ap2 Ap3 Ap4 Ap5 Ap6 Ap7 Ap8 Ap12 Ap13 Ap14 Ap2 Ap13 Ap18 Ap1 Ap2 Ap3 Ap4 Ap5 Ap5 Ap6 Ap7 Ap8 Ap5 Ap6 Ap7 Ap8 Ap1 Ap5 Ap5 Ap5 Ap5 Ap5 Ap5 Ap5 Ap5 Ap5 Ap5
301 301 301 301 301 301 301 301 301 301	CGENARGATTANTAGGATAGTGAGGGGATGGATTGCAGGGGGAATTCTTGGATTATTGAGGCTAACTACTGCGGAAGCATTGGCG GGTANRGATTANTAGGGATAGTGGGGGGGCAGGATTCCAGGGGGAATTCTTGGATTTATTGAGGCTAACTACTGCGAAACGATTGGCG GGTANRGATTANTAGGGATAGTGGGGGGGCAGCAGTATCCAATGCCAGGGGGAATTCTTGGATTTATTGAGGCTAACTACTGCCGAAACGATTGCCA GGTANRGATTANTAGGGATAGTGGGGGGGCATCAGTATCCAATGCCAGGGGGAATTCTTGGATTTATTGAGGCTAACTACTGCCGAAACGATTGCCA GGTANRGATTANTAGGGATAGTGGGGGGCATCAGTATCCAATGCCAGGGGGAATTCTTGGATTTATTGAGGCTAACTACTGCCGAAACGATTGCCA GGTANRGATTANTAGGGATAGTGGGGGGCATCAGTATCCAATGCCAGGGGGAATTCTTGGATTTATTGAGGCTAACTACTGCCGAAACGATTGCCA GGTANRGATTANTAGGGATAGTGGGGGGGCATCAGTATCCAATGCCAGGGGGAATTCTTGGATTTATTGAAGCTAACTACTGCCGAAACGATTGCCA GGTANRGATTAATAGGGATAGTGGGGGGGCATCAGTATCCAATGCCAGGGGGAATTCTTGGATTTATTGAAGCTAACTACTGCCGAAACGATTGCCA GGTANRGATTAATAGGGATAGTGGGGGGGCACGGTAGTGTCCAATGCCAGGGGGAATTCTTGGATTTATTGAAGCTAACTACTGCCGAAACGATTGCCA GGTANRGATTAATAGGGATAGTGGGGGGGCACGGTAGTGTGCGAAGGTGGAATTCTTGGATTTATTGAAGCTAACTACTGCCGAAACGATTGCCA GGTANRGATTAATAGGGATAGTGGGGGGGCACGGTAGGTAGTGCGAGGGGGAATTCTTGGATTTATTGGAGGCTAACTACTGCCGAAACGATTGCCC GGTANRGATTAATAGGGATAGTGGGGGGGCACGGTGGAATTCCTTGGATTTATTGGAGGCTAACTACTGCCGAAACGATTGCCCA GGTAATGGTTAATAGGGATAGTGGGGGGCACGGTGGAATTCCTTGGATTATTGGAGGCTAACTACTGCCGAAACGATTGCCC GGTANRGATTAATAGGGATAGTGGGGGGCACGGATGCGGGGGAATTCCTTGGATTTATTGGAGGCTAACTACTGCCGAAGCGATTGCCC GGTAATGGTTTAATAGGGATAGTGGGGGAGGATGGAGGGGGG	Ap1 Ap2 Ap3 Ap5 Ap6 Ap5 Ap6 Ap13 Ap13 Ap13 Ap18 Ap13 Ap18 Ap13 Ap18 Ap2 Ap3 Ap4 Ap5 Ap6 Ap7 Ap8 Ap13 Ap18 Ap13 Ap18 Ap13 Ap18 Ap13 Ap18 Ap13 Ap5 Ap6 Ap5 Ap6 Ap5 Ap6 Ap7 Ap5 Ap6 Ap7 Ap5 Ap6 Ap7 Ap5 Ap6 Ap7 Ap7 Ap7 Ap7 Ap7 Ap7 Ap7 Ap7 Ap7 Ap7
301       401       401       401       401       401       501       501       501       501       501       501       501       501       501       501       501       501	GENARGATTANTAGGATAGTOGGGGGATAGTATTCAATTGTCAGGGTGAANTCTTTGATTTATTGAGGCTAACTACTGCGGAAGCATTGGCG GENARGATTANTAGGGATAGTGGGGGGCACGATATTCAATTGTCAGGGTGAANTCTTTGATTTATTGAGGCTAACTACTGCGAAAGCATTGCCG GENARGATTAATAGGGATAGTGGGGGGCACGATACTCAATTGTCAGGGTGAATTCTTTGATTTATTGAGGCTAACTACTGCCGAAACCATTGCCC GENARGATTAATAGGGATAGTGGGGGGCACGATACTGATTGCAGGGGGAATTCTTGGATTTATTGAGGCTAACTACTGCCGAAACCATTGCCC GETAARGATTAATAGGGATAGTGGGGGGCACGATACTGATTGCAGGGGGAATTCTTGGATTTATTGAGGCTAACTACTGCCGAAACCATTGCCC GETAARGATTAATAGGGATAGTGGGGGGCACGATATCCAATTGCCAGGGGGAATTCTTGGATTTATTGAGGCTAACTACTGCGAAACCATTGCCC GETAARGATTAATAGGGATAGTGGGGGGCACGATATCCAATTGCCAGGGGGAATTCTTGGATTTATTGAGGCTAACTACTGCGAAACCATTGCCC GETAARGATTAATAGGGATAGTGGGGGGCACGATATCCAATTGCCAGGGGGAATTCTTGGATTTATTGAGGCTAACTACTGCGAAACCATTGCCC GETAARGATTAATAGGGATAGTGGGGGGCACGATATCCAATTGCCAGGGGGAATTCTTGGATTTATTGAAGCTAACTACTGCCGAAACCATTGCCC GETAARGATTAATAGGGATAGTGGGGGGCACGATACGATACTGCCAGGGGGAATTCTTGGATTTATTGAAGCTAACTACTGCCGAAACCATTGCCC GETAARGATTAATAGGGATAGTGGGGGGCACGATATCCAATTGCCAGGGGGAATTCTTGGATTTATTGCAGGCTAACTACTGCCGAAACCATTGCCC GETAARGATTAATAGGGATAGTGGGGGGCACGATACGATACG	Ap1 Ap2 Ap3 Ap4 Ap5 Ap6 Ap7 Ap8 Ap12 Ap13 Ap13 Ap2 Ap13 Ap2 Ap13 Ap2 Ap13 Ap2 Ap13 Ap2 Ap13 Ap4 Ap5 Ap6 Ap7 Ap8 Ap12 Ap2 Ap13 Ap4 Ap5 Ap5 Ap7 Ap8 Ap14 Ap5 Ap7 Ap8 Ap12 Ap13 Ap4 Ap5 Ap7 Ap8 Ap14 Ap5 Ap7 Ap8 Ap7 Ap8 Ap13 Ap4 Ap5 Ap7 Ap8 Ap7 Ap8 Ap7 Ap8 Ap7 Ap8 Ap7 Ap8 Ap7 Ap7 Ap8 Ap7 Ap7 Ap8 Ap7 Ap7 Ap8 Ap7 Ap7 Ap8 Ap7 Ap7 Ap7 Ap8 Ap7 Ap7 Ap7 Ap7 Ap7 Ap7 Ap7 Ap7 Ap7 Ap7
301 301 301 301 301 301 301 301 301 301	CGENARGATTANINGGENAGTOGOGGENCAGIATICOAGGEGAATICTICGATTATTGAAGACTAACTACTICGGAAAGCAITTGOCA CGENARGATTANINGGENAGTGGGGGGCAICAGIATCAATIGTCAGGGGGAATICTICGATTIATTGAAGACTAACTACTIGCGAAAGCAITTGOCA CGENARGATTANINGGGANGGGGGGCAICAGIATCAATIGTCAGGGGGAATICTICGATTIATTGAAGACTAACTACTIGCGAAAGCAITTGOCA CGENARGATTANINGGGGAGGAITGGGGGCAICAGIATCAATIGTCAGGGGGAATICTICGATTIATTGAAGACTAACTACTIGCGAAAGCAITTGOCA CGENARGATTANINGGGANGGTGGGGGCAICAGIATCAATIGTCAGGGGGAATICTICGATTIATTGAAGACTAACTACTIGCGAAAGCAITTGOCA CGENARGATTANINGGGANGGTGGGGGCAICAGIATCAATIGTCAGGGGGAATICTICGATTIATTGAAGACTAACTACTIGCGAAAGCAITTGOCA CGENARGATTANINGGGANGGCAICAGIATCCAATIGTCAGGGGGAATICTICGATTIATTGAAGCTAACTACTIGCGAAAGCAITTGOCA CGENARGATTANINGGGANGGCAICAGIATCCAATIGTCAGGGGGAATICTICGATTIATTGAAGCTAACTACTIGCGAAAGCAITTGOCA CGENARGATTANINGGGANGGCAICAGIATCCAATIGTCAGGGGGAATICCTICGATTIATTGAAGCTAACTACTIGCGAAAGCAITTGOCA CGENARGATTANINGGGANGGCAICAGIATCCAATIGTCAGGGGGAATICCTICGATTIATTGAAGCTAACTACTIGCGAAAGCAITTGOCA CGENARGATTANINGGGANGGCAGGGGAATICGAITGCCAGGGGGAATICCTICGATTIATTGAAGCTAACTACTGCGAAAGCAITTGOCA CGENARGATTANINGGGANGGTGGGGGAATICGAITGCCAGGGGGAATICCTICGATTIATTGAAGCTAACTACTGCGAAAGCAITTGOCA CGENARGATTANINGGGANGGTGGGGGAATICGAGTAGAATICCTICGATTIATTGAAGACTAACTACTGCGAAAGCAITTGOCA CGENARGATTANINGGANGGANGGTGAGGAGAAGCAGAACTAACTACTGCGAAACGAITTGOCA CGENARGATTANINGGANGGTGGGGGAAGTTGGGGGGAATICCTICGATTATTGAAGACTAACTACTGCGGAACGACTGGGGG CGENARGATTANINGGANGGAAGGTGGGGGAAGCAGACGAATACGATGGGAGGACGACTGACT	Ap1 Ap2 Ap3 Ap5 Ap6 Ap5 Ap6 Ap13 Ap13 Ap13 Ap18 Ap13 Ap18 Ap13 Ap18 Ap2 Ap3 Ap4 Ap2 Ap3 Ap4 Ap5 Ap6 Ap7 Ap8 Ap13 Ap18 Ap13 Ap18 Ap13 Ap18 Ap13 Ap18 Ap5 Ap6 Ap5 Ap6 Ap5 Ap6 Ap7 Ap5 Ap6 Ap7 Ap5 Ap6 Ap7 Ap5 Ap6 Ap7 Ap7 Ap7 Ap7 Ap7 Ap7 Ap7 Ap7 Ap7 Ap7
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FIG. 2. Multiple alignment of partial 18S sequences of the 11 *A. pullulans* strains studied. The region shown was amplified with primers 282 (NS3) and 283 (Fig. 1) and corresponds to *A. pullulans* residues 550 to 1128 (GenBank accession number M55639). Residues differing from the consensus sequence are boxed. Strain designations are as specified in Table 1. Y, C or T.

mined (Fig. 1). Multiple alignment of sequences showed conservation among the geographically diverse isolates (Fig. 2). These initial results affirmed the feasibility of developing species-specific oligonucleotide probes based on the 18S rRNA gene.

To design specific probes, the *A. pullulans* 18S sequences were compared with fungal sequences accessible through Gen-Bank or sequenced by us (organisms listed in Table 1 plus *Aspergillus fumigatus, Candida albicans,* and *Coccidioides immitis*). On this basis, several probes were synthesized and tested. The probe designated 665 was complementary to a region near the 5' end of the 18S gene (Fig. 1) and differed by at least one nucleotide from all known fungal sequences (Fig. 3) as of 5 May 1995. Southern blot hybridizations involving previously characterized fungi (Fig. 4) and a dot blot with 82

phylloplane yeast isolates (Fig. 5) clearly demonstrate the specificity of probe 665. The complementary approach of testing probes against DNA extracted from the leaf surface community as a whole could not be performed because *A. pullulans* occurs on every leaf (5, 6). While additional fungi could have been tested individually for hybridization to the probe, we have shown a reasonable presumptive basis for operational specificity based on taxonomic, phylogenetic, and ecological criteria. This implies that the probe should be sufficiently specific at least to discriminate *A. pullulans* from other fungi in the leaf surface habitat.

Another probe, 614, differed by a single nucleotide from the *A. pullulans* and almost all known fungal sequences (Fig. 3). Under the conditions employed, this 17-mer was highly specific for another ubiquitous fungus, *C. herbarum* (Fig. 4). Aerosols

Probe 665:	5'-TTCGTTTAGTTATTATGAATC-3'
Target:	3'-AAGCAAATCAATAATACTTAG-5'
Ap	AAGCAAATCAATAATACTTAG
Cg	AAGC <u>TCTC</u> CAATAATACTTAG
Af	AAGCAA <u>T</u> TCAATAATACT <u>A</u> AG
Ве	AAGC <u>TAT</u> TCAATAATACT <u>T</u> AG
Cc	AAGCAA <u>T</u> TCAATAATACT <u>A</u> AG
Lp	AAGC <u>TCT</u> TCAATAATACTTAG
Ou	AAGC <u>TGT</u> TCAATA <u>G</u> TACTTAG
Pn	AAGCAA <u>T</u> TCAATAATACT <u>A</u> AG
NC	AAGC <u>TCT</u> TCAATAATACTTAG
Pa	AAGC <u>TCTC</u> CAATAATACTTAG
Ci	AAGC <u>TGT</u> TCAATAATACTTAG
Ca	AAGC <u>TTT</u> TCAATAATACTTAG
Probe 614:	5'-TTAATCAAAACATCCTT-3'
Target:	3'-AATTAGTTTTGTAGGAA-5'
Ch	AATTAGTTTTGTAGGAA
Ap	AATTA <u>C</u> TTTTGTAGGAA
Hd	AATTA <u>C</u> TTTTGTAGGAA
Rr	AATTA <u>C</u> TTTTGTAGGAA
Cl	A <u>G</u> TTA <u>C</u> TTTTG <u>C</u> AGGAA
Aa	AATTA <u>C</u> TTTTGTAGGAA
Cg	A <u>T</u> TTA <u>C</u> TTTTGTAGGAA
Af	AATTA <u>C</u> TTTTGTAGGAA
Be	AATTA <u>C</u> TTTTGTAGGAA
Cc	AATTA <u>C</u> TTTTGTAGGAA
Lp	AATTA <u>C</u> TTTTGTAGGAA
Ou	AATTA <u>C</u> TTTTGTAGGAA
Pc	AATTA <u>C</u> TTTTGTAGGAA
Pn	AATTA <u>C</u> TTTTGTAGGAA
NC	AATTACTTTTGTAGGAA
Pa	AATTA <u>C</u> TTTTGTAGGAA
Ca	AATTACTTTTGCAGGAA
Ci	AATTACTTTTGTAGGAA

FIG. 3. 18S rRNA gene sequence alignments, showing probes and target regions. Af, *Aspergillus fumigatus*; Ca, *Candida albicans*; Ci, *Coccidioides immitis* (for other designations, see Table 1). Probe 665 was used for *A. pullulans*; probe 614 was used for *C. herbarum*. Other than the intended targets, database searches of all rRNA sequences (GenBank release no. 87) showed no sequences, as of 5 May 1995, identical to the two probes. Mismatched nucleotides are underlined.

generated during the harvesting of crops are composed mainly of *Cladosporium* spp. and other fungal saprophytes, many of which are allergenic and can cause a health hazard to farmers (17). *C. herbarum* is also a well-known antagonist of plant and human pathogens (22). Thus, probe 614 might be useful in



FIG. 4. Southern blot hybridization of PCR products (full length of 18S rRNA gene, ~1,770 bp) probed with the universal probe U519 (top panel), *A. pullulans*-specific probe 665 (middle), and a 578-bp PCR product probed with C. *herbarum*-specific probe 614 (bottom). Lanes 1 to 12, *A. pullulans* Ap2, Ap12, Ap5, Ap13, Ap4, Ap6, Ap8, Ap7, Ap3, Ap18, Ap19, and Ap1, respectively; lane 13, *H. dematioides*; lane 14, *R. rubra*; lane 15, *S. holsaticus*; lane 16, *C. laurentii*; lane 17, *A. alternata*; lane 18, *C. herbarum*; lane 19, *C. gloeosporioides*; lane 20, *A. nidulans*; lane 21, *B. emersonii*; lane 22, *C. cladosporioides*; lane 23, *L. persoonii*; lane 24, *O. ulmi*; lane 25, *P. chrysogenum*; lane 26, *P. notatum*; lane 27, *N. crassa*; lane 28, *P. anserina*. Sizes of PCR products are shown at the right.

	А	в	С	D	Е	F	G	н		А	в	С	D	Е	F	G	ŀ
1	٠	٠	٠	٠	•	٠	•	•	1								
2	٠	•	٠	٠	•	٠	٠	•	2	•							
3	۲	•	٠	۲	•	•	٠	٠	3	•							
4	۲	•	۲	٠	۲	٠	٠	٠	4	•							
5	٠	٠	•	•	•	•	•	•	5	•							
6	۰	•	٠	٠	•	٠	٠	•	6	•							
7	٠	٠	٠	۲	٠	٠	٠	٠	7	•							
8	٠		٠	•	•	•	•	•	8	•							
9	•	٠	•	٠	•	٠	•	•	9	•							
10		٠	٠	•	•	٠	•	•	10	•							
11	•	•	•	•	•	•	•		11								
12	•	•	•	•	•	•	•		12	•							

FIG. 5. Dot blot hybridization of full length of 18S rRNA PCR product  $(\sim 1,770 \text{ bp})$  with the <sup>32</sup>P-labeled universal probe U519 (left panel) and *A. pullulans*-specific probe 665 (right panel) to *A. pullulans* strains and 82 yeast isolates from the phylloplane (L1 to L100). Column A, rows 1 to 12: Ap2, Ap12, Ap5, Ap13, Ap4, Ap6, Ap8, Ap7, Ap3, Ap18, Ap19, and Ap1, respectively. Column B, rows 1 to 12: L1, L2, L3, L4, L5, L6, L7, L8, L9, L10, L11, and L13, respectively. Column C, rows 1 to 12: L15, L16, L18, L19, L20, L21, L22, L24, L25, L26, L27, and L28, respectively. Column D, rows 1 to 12: L42, L43, L44, L45, L46, L47, L48, L49, L52, L53, L55, and L60, respectively. Column F, rows 1 to 12: L61, L63, L62, L54, L90, L67, L83, L93, L86, L96, L87, and L79, respectively. Column G, rows 1 to 12: L61, L63, L62, L54, L90, L67, L83, L93, L72, L85, L69, L68, L98, L71, L74, L99, and L95, respectively. Column H, rows 1 to 12: L10, L76, L64, L66, L73, L78, L81, L65, L82, and L94, respectively.

studies of the ecology, medical microbiology, or aerobiology of this fungus.

These results support previous studies (2, 31) which demonstrate that a short oligonucleotide with even a single nucleotide mismatch to the target sequence can differentiate strains. Generally, the internal transcribed spacer between the small- and the large-subunit rRNA genes is thought to be less conserved and more diverse than the coding regions (14, 51). However, the internal transcribed spacer is spliced out during rRNA maturation, making it an undesirable target for FISH.

As noted at the outset, the long-term objective in developing this probe system is to monitor and quantify *A. pullulans* cells directly on leaves by in situ hybridization. Our preliminary results with FISH (37, 37a) confirm the probe results in this report. In brief, we have shown that the fluorescently labeled universal and 665 probes detect *A. pullulans* spores and hyphae on microslides or on apple leaves inoculated with the fungus under controlled conditions. All *A. pullulans* strains tested here also produce a positive hybridization signal with the probe in FISH; none of the heterologous fungi assessed here and found to be negative react with probe 665 in situ. Detailed assessments of hybridization conditions, signal-generating systems, and field performance are in progress.

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