Characterization of *Pseudomonas aeruginosa* isolates from patients with endophthalmitis using conventional microbiologic techniques and whole genome sequencing

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**Abstract**

**Purpose:** To demonstrate antibiotic susceptibility and genomic virulence factor profiles of *Pseudomonas aeruginosa* isolates from patients with culture-confirmed endophthalmitis.

**Methods:** Clinical isolates from patients diagnosed with pseudomonas endophthalmitis were included. Laboratory antibiotic susceptibility testing and whole genome sequencing was performed on all isolates.

**Results:** In the current study, 8 patients had vitreous culture-confirmed endophthalmitis due to *P. aeruginosa*. All isolates were multi-drug resistant but sensitive to ceftazidime and each fluoroquinolone tested. Whole genome sequencing revealed a total of 179 unique genes. The most common type of virulence genes included those involved in adherence and the secretion system. Seven of 8 (88%) isolates were of the cytoinvasive phenotype (*exoST*) and no isolates contained *exoU*.

**Conclusions:** *P. aeruginosa* associated endophthalmitis is often multi-drug resistant and demonstrates a variety of virulence factors with those involved in adherence and the secretion system being the most common.

**Keywords:** *Pseudomonas aeruginosa*, Whole genome sequencing, Endophthalmitis

**Background**

Infectious endophthalmitis is a severe sight-threatening entity that can occur post-operatively, following trauma, or coincident with systemic infection. In the Endophthalmitis Vitrectomy Study (EVS) study, 36% of patients with endophthalmitis failed to achieve better than 20/100 visual acuity at 9 to 12 months [1]. Though just 4.1% of isolates in the EVS study were gram-negative organisms, other studies suggest a higher incidence that ranges from 10 to 24% [2–8]. Among gram-negative endophthalmitis cases, *Pseudomonas aeruginosa* is the most commonly isolated organism [3, 9–12] and is associated with a more fulminant clinical course and higher evisceration/enucleation rate compared to its gram-positive counterparts [13–15]. In fact, a recent prospective study by Stevenson et al. reported 30% of patients with gram negative endophthalmitis requiring evisceration or enucleation [8].

In addition to the growing prevalence of multi-drug resistant strains, the virulent nature of pseudomonas is often ascribed to factors expressed by its bacterial DNA [16]. These virulence factors contribute to its ability to induce rapid ocular tissue necrosis [6]. Comparative studies correlating these genotypes with clinical features...
observed in host tissue increase our understanding of pseudomonas pathogenicity [17]. However, there is a paucity of studies which have sought to identify virulence factors implicated in cohorts of pseudomonas keratitis and endophthalmitis [17, 18]. In the current study, whole genome sequencing (WGS) was performed on isolates to identify associated virulence factors in culture-confirmed pseudomonas endophthalmitis.

### Methods

The current study was approved by the Institutional Review Board of the University of Miami School of Medicine Medical Sciences Subcommittee for the Protection of Human Subjects, and was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and later amendments. Clinical and microbiology records were retrospectively reviewed for patients who were evaluated at Bascom Palmer Eye Institute and diagnosed with vitreous culture-confirmed endophthalmitis due to *P. aeruginosa*. Antibiotic susceptibility profiles were identified using standard microbiologic protocols via an automated system, including the VITEK (Automatic Microbial System; Biomerieux Vitek, Hazelwood, Missouri, USA) which provided ‘breakpoint’ MICs (minimal inhibitory concentration values) based on the micro dilution method, the E test (A.B. Biodisk, NA; Remel, Lenexa, Kansas, USA), or disk diffusion (antibiotic-impregnated paper disks; Becton Dickinson, Cockeysville, MD). Whole genome sequencing was performed by COSMOS ID (Rockville, MD) using Illumina and Ion Torrent platforms.

### Results

The current study includes 8 patients diagnosed with vitreous culture-confirmed *P. aeruginosa* endophthalmitis at Bascom Palmer Eye Institute. Clinical data is presented in Table 1. The average age was 74 years (range: 53–84). Four of 8 patients (50%) were men. Endophthalmitis was diagnosed based on clinical findings and confirmed with vitreous cultures obtained via tap or pars plana vitrectomy. Three of 8 cases (38%) were in the setting of recent ocular surgery, which included post-phacoemulsification (*n* = 2) and post-corneal transplant (*n* = 1). Three cases occurred in the setting of corneal ulceration, with one patient exhibiting scleral extension of infection (P1). One case followed an open globe injury with a retained intraocular foreign body. Multiple organisms grew from vitreous cultures in two patients, namely *Staphylococcus aureus* (P5) and *Staphylococcus hominis* (P7).

Average follow-up time for patients in this cohort was 2 years. Clinical presentation, treatment strategy, and visual outcomes are detailed in Table 2. Baseline visual acuity prior to diagnosis of endophthalmitis was not available. Vision at presentation was hand motions or light perception for all patients with documented visual acuity (7 of 8 patients). Final visual outcome ranged from 20/400 to no light perception, with 2 patients ultimately requiring enucleation. Intravitreal tap and injection of antibiotics were used as initial treatment for 5 of 8 cases, while pars plana vitrectomy (PPV) with intraoperative intravitreal injections was performed initially in 2 of 8 cases. For P1 and P4, data was not available regarding initial type of intravitreal antibiotic and for P3, initial treatment choice (PPV vs intravitreal injections) was not indicated in the medical record.

*P. aeruginosa* was identified from the vitreous sample of each patient. Antibiotic sensitivities are summarized in Table 3 and minimum inhibitory concentration values are reported in Supplemental Table 1. All isolates were multi-drug resistant with similar resistance profiles. Sensitivity to ceftazidime was identified across the entire cohort. Vancomycin resistance was not specifically tested, but all isolates were sensitive to the fourth generation cephalosporin, cefepime. Sensitivity to all tested aminoglycosides and fluoroquinolones was seen in all isolates in this cohort, including the newest fluoroquinolone, delafloxacin. Resistance to first- and second-generation cephalosporins, cefazolin and cefoxitin respectively, ampicillin, ampicillin/sulbactam, ceftriaxone, and

### Table 1

| Patient | Sex | Age (yrs) | Clinical setting | Concurrent corneal ulcer | Time after surgery | Additional isolates from vitreous |
|---------|-----|-----------|------------------|--------------------------|-------------------|----------------------------------|
| 1       | F   | 81        | Sclerokeratitis   | Yes                      | –                 | –                                |
| 2       | F   | 69        | Post phacoemulsification | No         | 5 days            | –                                |
| 3       | F   | 80        | UK                | UK                      | UK                | –                                |
| 4       | M   | 71        | Corneal ulcer     | Yes                      | –                 | –                                |
| 5       | M   | 84        | Postoperative phacoemulsification | No     | 5 days            | *Staphylococcus aureus*          |
| 6       | F   | 80        | Post corneal transplant | No         | 8 days            | –                                |
| 7       | M   | 78        | Corneal ulcer     | Yes                      | –                 | *Staphylococcus hominis*         |
| 8       | M   | 53        | Globe rupture with IOFB | No         | –                 | –                                |

Clinical characteristics of patients with *P. aeruginosa* isolated from vitreous cultures in this cohort

Abbreviations: UK unknown, – not applicable, IOFB intraocular foreign body. Detailed clinical records were not available for P3.
nitrofurantoin across all isolates was observed. Seven of 8 (88%) isolates were resistant to sulfamethoxazole/trimethoprim.

All isolates in this study underwent WGS to identify known virulence factors. A total of 1087 virulence genes (179 unique) were identified, with an average of 136 genes per isolate. The number of genes for a particular virulence class in the cohort and per isolate is summarized in Table 4. Genes involved in adherence were among the most prevalent (69 unique genes), followed by those involved in secretion systems (n = 47), anti-phagocytosis (n = 21), and iron uptake (n = 13). Regarding genes implicated in the type III secretion system (T3SS), all isolates harbored exoT and 7 of 8 isolates (88%) were found to have exoS, while no isolates contained exoU.

Isolates were identical with regards to virulence genes known to be involved in protease functions, regulation, biosurfactant, and pigmentation. Among the remaining virulence classes there was a high level of homogeneity with only 22% of genes being represented in less than half of the isolates. All virulence genes identified in this study are listed in Supplemental Table 2.

**Discussion**

The World Health Organization declared *P. aeruginosa* as a critical priority amongst current pathogens urgently in need of new effective antibiotics [19, 20]. A recent study in South India showed a rising resistance to fluoroquinolones, amikacin, and ceftazidime in pseudomonas endophthalmitis, particularly in post-surgical cases [21]. Comparable retrospective studies performed in the United States have not observed a similar increase in resistance yet [14]. In the present study, cultures were

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**Table 2** Presentation, treatment strategies, and outcomes of patients with endophthalmitis caused by *Pseudomonas aeruginosa*

| No. | Baseline VA | Initial VA | Initial Tx | Initial IVTI | Additional Tx (Days after presentation) | Additional IVTI (Days after presentation) | Last VA | Follow-up time |
|-----|-------------|------------|------------|-------------|------------------------------------------|-------------------------------------------|--------|---------------|
| 1   | UK          | LP         | T + I      | Unknown     | PPV (1)                                  | Cfx (2) Ctz (3)                           | NLP    | 2 years       |
| 2   | UK          | LP         | PPV        | Vanc + Ctz (intra-op) | Enucleation | – | Enucleation 7 years |
| 3   | UK          | UK         | UK         | UK          | UK                                       | UK                                       | UK     | UK            |
| 4   | UK          | HM         | T + I      | UK          | Enucleation (6)                          | – | Enucleation 8 months |
| 5   | UK          | LP         | T + I      | Vanc + Ctz + Dex | PPV (4) | Vanc + Dex (4) | Ctz (8) | CF | 3 months |
| 6   | UK          | LP         | T + I      | Vanc + Ctz | PPV (4) | Ctz (2 & 8) Ctz intra-op (4) | LP | 2 days |
| 7   | UK          | LP         | T + I      | Ctz + Vanc | – | Vanc + Dex (2) Vanc + Ctz + Dex (5) | LP | 4 years |
| 8   | UK          | HM         | Globe repair PPV | Vanc + Ctz + Vcz (intra-op) | Retinal detachment repair (4 months) | – | 20/400 | 2 years |

Presentation, treatment strategies, and outcomes of patients with endophthalmitis caused by *Pseudomonas aeruginosa* in this cohort

**Abbreviations**: VA visual acuity, NLP no light perception, LP light perception, HM hand motions, UK unknown, Tx treatment, IVTI intravitreal injection, T + I vitreous tap and intravitreal injection, PPV pars plana vitrectomy, Vanc vancomycin, Ctz ceftazidime, Cfx cefuroxime, Dex dexamethasone, Vcz voriconazole, – not applicable

**Table 3** Antibiotic sensitivities of *Pseudomonas aeruginosa* vitreous isolates

| Antibiotic         | 1   | 2   | 3   | 4   | 5   | 6   | 7   | 8   |
|--------------------|-----|-----|-----|-----|-----|-----|-----|-----|
| Ampicillin         | R   | R   | R   | R   | R   | R   | R   | R   |
| Amp/Sulbactam      | R   | R   | R   | R   | R   | R   | R   | R   |
| Piper/Tazo         | S   | –   | S   | S   | S   | S   | S   | S   |
| Ticar/Clav         | –   | S   | –   | –   | –   | –   | –   | –   |
| Cefazolin          | R   | R   | R   | R   | R   | R   | R   | R   |
| Cefoxitin          | R   | R   | R   | R   | R   | R   | R   | R   |
| Ceftazidime        | S   | S   | S   | S   | S   | S   | S   | S   |
| Ceftriaxone        | R   | R   | R   | R   | R   | R   | R   | R   |
| Ceferpine          | S   | S   | S   | S   | S   | S   | S   | S   |
| Imipenem           | S   | S   | S   | S   | S   | S   | S   | S   |
| Meropenem          | S   | –   | S   | S   | S   | S   | S   | S   |
| Levofloxacin       | S   | S   | S   | S   | S   | S   | S   | S   |
| Ciprofloxacin      | S   | S   | S   | S   | S   | S   | S   | S   |
| Moxifloxacin       | S   | S   | S   | S   | S   | S   | S   | S   |
| Delafloxacin       | S   | S   | S   | S   | S   | S   | S   | S   |
| Gentamicin         | S   | S   | S   | S   | S   | S   | S   | S   |
| Amikacin           | S   | S   | S   | S   | S   | S   | S   | S   |
| Tobramycin         | S   | S   | S   | S   | S   | S   | S   | S   |
| Trimeth/Sulfa      | R   | R   | R   | R   | R   | R   | S   | R   |
| Nitrofurantoin     | R   | R   | R   | R   | R   | R   | R   | R   |

Antibiotic sensitivities of *Pseudomonas aeruginosa* vitreous isolates from patients with endophthalmitis. Sensitivities were calculated with the VITEK-2 automated system, E-test, or disk diffusion testing. S, sensitive; R, resistant; —, not tested

**Abbreviations**: Amp/Sulbactam Ampicillin/Sulbactam, Piper/Tazo Piperacillin/Tazobactam, Ticar/Clav Ticarcillin/Clavulanic acid, Trimeth/Sulfa Trimethoprim/Sulfamethoxazole
performed between 2011 and 2018, with the majority of patients (5 of 8) presenting in 2015 or later. All isolates were sensitive to ceftazidime, which is generally used as a first line intravitreal antibiotic along with vancomycin at this institution. Interestingly, isolates were pan-sensitive to fluoroquinolones tested, including delafloxacin, a newly registered fluoroquinolone not currently used in the treatment of ocular infections [22]. This resistance profile suggests there may be significant geographic variation, which may be better studied in larger cohorts. Specialists should consider local resistance patterns when determining treatment.

*P. aeruginosa* expresses many virulence factors that contribute to its pathogenicity in ocular tissue [18]. In the current study, the most represented virulence factors were those involved in adherence with a total of 69 unique genes of this class identified. Proteins expressed by these genes likely allow pseudomonas to adhere to various intraocular structures. Unique to post operative endophthalmitis, intraocular foreign material, such as a lens implant can serve as a surface for bacteria to attach, and potentially as a nidus for bacteria to grow within a biofilm. Some of the most cited genes implicated in biofilm production include *algD, rhlR, rpoS, and rpoN*, the latter two providing anti-phagocytic capability against host defenses [23–25]. All isolates contained these genes with the exception of *rpoN*. Notably not identified by whole genome sequencing in this cohort were *pslD, pelF*, and *gacS*, genes previously determined to be common amongst biofilm-producing pseudomonas isolates [23, 25]. Genes involved in c-di-GMP regulation are also well-established in the pathophysiology of biofilm production, but were not surveyed in this study, including *siaD, nbdA, dipA, cdrA, PA4781*, or *PA4108* [26]. However, identifying these genes and performing functional assays of clinical isolates in future studies could provide a new avenue for understanding biofilm potential and prevalence in endophthalmitis isolates.

In the current study, all isolates harbored the gene encoding exoenzyme T (exoT). All but one isolate harbored both *exoS* and *exoY*, while *exoU* was not identified. These genes express toxins involved in the T3SS. T3SS is a complex of cellular structures and proteins that allows gram negative organisms to inject proteins directly into host cells, thereby circumventing extracellular obstacles [27]. Exoenzymes are the effector proteins of this system [18]. Generally, strains possessing *exoS* and *exoY* are invasive while strains possessing *exoU* are observed to be cytotoxic in nature. Consistent with previous studies, *exoS* and *exoU* were mutually exclusive, as all strains that contained *exoS*, did not have *exoU* [28–30]. Interestingly, previous reports suggest a predominance of *exoU* strains in isolates from keratitis [28], though even in endophthalmitis arising in the setting of a corneal ulcer in this cohort, this cytotoxic genotype was not present. This may suggest that pseudomonas with a predilection for endophthalmitis may be more commonly of the cytotoxic type (*exoST*). Lastly, the *exoU* genotype is associated with fluoroquinolone resistance in previously studied clinical isolates [31, 32]. The putative correlation of pan-sensitivity to fluoroquinolones and lack of *exoU* genotype in this cohort should be confirmed in larger studies.

To the authors’ knowledge, this is the first report in which WGS was used to characterize pseudomonas

| Virulence class | Total genes | Unique Genes | Class represented in all isolates (yes/no) |
|----------------|-------------|--------------|-----------------------------------------|
|                | No. in cohort | Average per isolate | No. in cohort |                             |
| Adherence      | 410         | 51.3         | 69            | Yes                          |
| Secretion System | 258      | 32.3         | 47            | Yes                          |
| Anti-phagocytosis | 152      | 19.0         | 21            | Yes                          |
| Iron uptake    | 61          | 7.6          | 13            | Yes                          |
| Motility       | 53          | 6.6          | 8             | Yes                          |
| Toxin          | 38          | 4.8          | 5             | Yes                          |
| Regulation     | 32          | 4.0          | 4             | Yes                          |
| Protease       | 24          | 3.0          | 3             | Yes                          |
| Biosurfactant  | 16          | 2.0          | 2             | Yes                          |
| Pigment        | 16          | 2.0          | 2             | Yes                          |
| Exoenzyme      | 8           | 1            | 1             | Yes                          |
| Endotoxin      | 2           | 1            | 1             | No (2/8 isolates)            |
| Other          | 17          | 2.1          | 3             | Yes                          |
| Total          | 1087        | 136          | 179           |                             |

Genes identified among *Pseudomonas aeruginosa* isolates from vitreous cultures of patients with endophthalmitis using whole genome sequencing.
isolates from vitreous cultures of patients with endophthalmitis. As gene expression assays and functional tests were not performed, the authors cannot guarantee that the presence of a virulence gene indicates a role for the respective factor in pseudomonas pathogenesis. Additionally, variability in the clinical context of infection and relative genetic homogeneity between isolates limits the clinical correlations that can be made. Specifically, in this cohort endophthalmitis occurred in the setting of ocular surface disease for 3 patients, post-surgically for 3 patients, and in the setting of trauma for one patient. It is likely that the setting in which infection occurs and the interplay of pseudomonas with host factors play a large role in disease pathogenesis as well [33]. Elucidating this interaction will require a larger cohort. Lastly, in the present study, the genotypic spectrum identified from pseudomonas endophthalmitis isolates were not compared to environmental strains. Such comparisons in future studies would help confirm if particular virulence factors are more common in the setting of endophthalmitis.

Conclusions
In the current study of P. aeruginosa isolates from patients with endophthalmitis, infection occurred in a variety of clinical settings and all organisms were multidrug resistant. Using whole genome sequencing, many unique virulence factors were identified, with those involved in bacterial adherence, the secretion system, and anti-phagocytosis being the most common. This investigation increases current understanding of the pathogenesis of P. aeruginosa endophthalmitis and emphasizes the need for further investigation of these mechanisms.

Supplementary information
Supplementary information accompanies this paper at https://doi.org/10.1186/s12348-020-00216-0.

Additional file 1: Table S1. Antibiotic sensitivity values for individual isolates.

Additional file 2: Table S2. Virulence factor genes identified in cohort.

Abbreviations
P. aeruginosa: Pseudomonas aeruginosa; EVS: Endophthalmitis Vitrectomy Study; WGS: Whole genome sequencing; PPV: Pars plana vitrectomy; T3SS: Type III secretion system

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Disclosures
The authors have no relevant financial disclosures.

Authors’ contributions
JDS and HF wrote the manuscript. MH and JM provided technical assistance with laboratory studies. JD, DRC, AP, AW, NAP, and NAY assisted in data collection and manuscript editing. DM and HF designed the study and interpreted the final results. All authors read and approved the final manuscript.

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Availability of data and materials
The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate
The current study was approved by the Institutional Review Board of the University of Miami School of Medicine Medical Sciences Subcommittee for the Protection of Human Subjects.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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References
1. Results of the Endophthalmitis Vitrectomy Study (1995) A randomized trial of immediate vitrectomy and of intravenous antibiotics for the treatment of postoperative bacterial endophthalmitis. Endophthalmitis Vitrectomy Study Group. Arch Ophthalmol 113:1479–1496
2. Fan JC, Niedere R, von Lany H, Pollinghorne PJ (2008) Infectious endophthalmitis: clinical features, management and visual outcomes. Clin Exp Ophthalmol 36:631–636. https://doi.org/10.1111/j.1442-9071.2008.01813.x
3. Schimmel AM, Miller D, Flynn HW Jr (2013) Endophthalmitis isolates and antibiotic susceptibilities: a 10-year review of culture-proven cases. Am J Ophthalmol 156:50–52 e51. https://doi.org/10.1016/j.ajo.2013.01.027
4. Gupta A, Orlans HO, Horbey SJ, Bowler IC (2014) Microbiology and visual outcomes of culture-positive bacterial endophthalmitis in Oxford, UK. Graefes Arch Clin Exp Ophthalmol 252:1825–1830. https://doi.org/10.1007/s00417-014-2658-7
5. Moloney TP, Park J (2014) Microbiological isolates and antibiotic sensitivities in culture-proven endophthalmitis: a 15-year review. Br J Ophthalmol 98:1492–1497. https://doi.org/10.1136/bjo.2014-059030
6. Dave VP, Pathengay A, Nishant K et al (2017) Clinical presentations, risk factors and outcomes of cefazidime-resistant gram-negative endophthalmitis. Clin Exp Ophthalmol 45:254–260. https://doi.org/10.1111/ceo.12833
7. Liu C, Ji J, Li S et al (2017) Microbiological isolates and antibiotic susceptibilities: a 10-year review of culture-proven endophthalmitis cases. Curr Eye Res 42:443–447. https://doi.org/10.1080/02713683.2016.1188118
8. Stevenson LJ, Dawkins RCH, Sheeley H, McGuiness MB, Hurley AH, Allen PJ (2020) Gram-negative endophthalmitis: a prospective study examining the microbiology, clinical associations and visual outcomes following infection. Clin Exp Ophthalmol. https://doi.org/10.1111/ceo.13768
9. Pathengay A, Flynn HW Jr, Isom RF, Miller D (2012) Endophthalmitis outbreaks following cataract surgery: causative organisms, etiologies, and visual acuity outcomes. J Cataract Refract Surg 38:1278–1282. https://doi. org/10.1016/j.cjrs.2012.04.021
10. Bhamimbunchoo C, Ratanapakorn T, Sinawat S, Sanguansak T, Moontawee K, Yospaiboon Y (2013) Infectious endophthalmitis: review of 420 cases. Clin Ophthalmol 7:247–252. https://doi.org/10.2147/OPTH.S39934
11. Lalitha P, Sengupta S, Ravindran RD et al (2017) A literature review and update on the incidence and microbiology spectrum of postcataract surgery endophthalmitis over past two decades in India. Indian J Ophthalmol 65:673–677. https://doi.org/10.4103/ijo.IJO_509_17
12. Yospaiboon Y, Intarapanich A, Laovirojjanakul W et al (2018) Factors affecting visual outcomes after treatment of infectious endophthalmitis in
northeastern Thailand. Clin Ophthalmol 12:765–772. https://doi.org/10.2147/OPHTHS160758
13. Elfgig CW, Scott IU, Flynn HW Jr, Miller D (2003) Endophthalmitis caused by Pseudomonas aeruginosa. Ophthalmology 110:1714–1717. https://doi.org/10.1016/S0161-6420(03)00572-4
14. Srividhar J, Kuriyan AE, Flynn HW Jr, Miller D (2015) Endophthalmitis caused by Pseudomonas aeruginosa: clinical features, antibiotic susceptibilities, and treatment outcomes. Retina 35:1101–1106. https://doi.org/10.1097/IAE.0000000000000469
15. Falavarjani KG, Amipooya Alemzadeh S, Habibi A, Hadavandkhani A, Askari S, Pourhabibi A (2017) Pseudomonas aeruginosa endophthalmitis: clinical outcomes and antibiotic susceptibilities. Ocul Immunol Inflamm 25:377–381. https://doi.org/10.3109/09273948.2015.1132740
16. Sawa T, Morniyama K, Mihara T, Kainuma A, Kinoshita M, Moriyama K (2020) Molecular epidemiology of clinically high-risk Pseudomonas aeruginosa strains: practical overview. Microbiol Immunol. https://doi.org/10.1111/1348-0421.12776
17. Oka N, Suzuki T, Ishikawa E et al (2015) Relationship of virulence factors and clinical features in keratitis caused by Pseudomonas aeruginosa. Invest Ophthalmol Vis Sci 56:6892–6898. https://doi.org/10.1167/iovs.15-17356
18. Lakshmi Priya J, Prajna L, Mohankumar V (2015) Genotypic and phenotypic characterization of Pseudomonas aeruginosa isolates from post-cataract endophthalmitis patients. Microb Pathog 78:667–73. https://doi.org/10.1016/j.micpath.2014.11.014
19. Geneva: World Health Organization (2019) 2019 antibacterial agents in use: update. Bull World Health Organ 98:151. https://doi.org/10.2471/BLT.20.251751
20. Pan U, Jain A, Gabut J, Kumari B, Sindal MD (2020) Antibiotic sensitivity trends of pseudomonas endophthalmitis in a tertiary eye care center in South India: a 12-year retrospective study. Indian J Ophthalmol 68:627–631. https://doi.org/10.4103/ijo.IJO_1145_19
21. Beyer P, Paulin S (2020) Priority pathogens and the antibiotic pipeline: an update. Bull World Health Organ 98:151. https://doi.org/10.2471/BLT.20.251751
22. Fan KC, Lin J, Yannuzzi NA et al (2020) In vitro susceptibilities of methicillin-susceptible and resistant staphylococci to traditional antibiotics compared to a novel fluoroquinolone. J Ophthalmic Inflamm Infect 10:9. https://doi.org/10.3109/09273948.2020.1801826
23. Anupama R, Sajitha Luu S, Mukherjee A et al (2018) Cross-regulatory network in Pseudomonas aeruginosa biofilm genes and TIO2 anatase induced molecular perturbations in key proteins unraveled by a systems biology approach. Gene 647:289–296
24. Mukherjee S, Moustafa DA, Stergioula V et al (2018) The PqsE and RhlR biofilm-related genes among clinical isolates of Pseudomonas aeruginosa. Proc Natl Acad Sci U S A 115:E9411–E9418
25. Yamaguchi S, Suzuki T, Kobayashi T et al (2014) Genotypic analysis of Pseudomonas aeruginosa isolated from ocular infection. J Infect Chemother 20:407–411. https://doi.org/10.1016/j.jiac.2014.02.007
26. Stewart RM, Wiehlmann L, Ashelford KE et al (2011) Genetic characterization indicates that a specific subpopulation of Pseudomonas aeruginosa is associated with keratitis infections. J Clin Microbiol 49:993–1003. https://doi.org/10.1128/JCM.00236-10
27. Coburn B, Sekirov I, Finlay BB (2007) Type III secretion systems and disease. Clin Microbiol Rev 20:535–549. https://doi.org/10.1128/CMR.00013-07
28. Crousilles A, Maunders E, Bartlett S et al (2015) Which microbial factors really are important in Pseudomonas aeruginosa infections? Future Microbiol 10:1825–1836

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