# Genome sequence of a virulent and hypermucoviscous-like Klebsiella michiganensis clinical isolate

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## Abstract

**Objectives:**The hypermucoviscous-like phenotype has been described in Klebsiella pneumoniae species complex (KpSC) and was described as a contributor of increased virulence. This study described the characterization and whole-genome sequencing of an antibiotic susceptible and hypermucoviscous-like Klebsiella michiganensis 9273 clinical isolate.

**Data description:**Here, we report the genome sequence of a K. michiganensis clinical isolate obtained from a urinary tract infection exhibiting the hypermucoviscous-like phenotype. The draft genome sequence consisted of 145 contigs and ~ 6.6 Mb genome size. The annotation revealed 6648 coding DNA sequences and 56 tRNA genes. The strain belongs to the sequence type (ST) 50, and the OXY-1 beta-lactam resistance gene, aph(3')-Ia gene for aminoglycoside resistance and multidrug efflux pumps were identified. The fyuA siderophore receptor of yersiniabactin siderophore was identified. Increased virulence was observed in Galleria mellonella larvae model and increased capsule production was determined by uronic acid quantification. The clinical implications of this phenotype are unknown, but the patient outcome might worsen compared to susceptible- or MDR-classical K. michiganensis isolates.

**Keywords:**Capsule; Hypermucoviscous phenotype; Klebsiella michiganensis; String test; Virulence.

Performance of the 2016 ACR-EULAR myositis response criteria in juvenile dermatomyositis therapeutic trials and consensus profiles

## Abstract

**Objectives:**The 2016 ACR-EULAR Response Criteria for JDM was developed as a composite measure with differential weights of six core set measures (CSMs) to calculate a Total Improvement Score (TIS). We assessed the contribution of each CSM, representation of muscle-related and patient-reported CSMs towards improvement, and frequency of CSM worsening across myositis response criteria (MRC) categories in validation of MRC.

**Methods:**Data from JDM patients in the Rituximab in Myositis trial (n = 48), PRINTO JDM trial (n = 139), and consensus patient profiles (n = 273) were included. Observed vs expected CSM contributions were compared using Sign test. Characteristics of MRC categories were compared by Wilcoxon tests with Bonferroni adjustment. Spearman correlation of changes in TIS and individual CSMs were examined. Agreement between physician-assessed change and MRC categories was evaluated by weighted Cohen's kappa.

**Results:**Of 457 JDM patients with IMACS CSMs and 380 with PRINTO CSMs, 9-13% had minimal, 19-23% had moderate and 41-50% had major improvement. The number of improved and absolute percentage change of CSMs increased by MRC improvement level. Patients with minimal improvement by MRC had a median of 0-1 CSM worsened, and those with moderate/major improvement had a median of zero worsening CSMs. Of patients improved by MRC, 94-95% had improvement in muscle strength and 93-95% had improvement in ≥1 patient-reported CSM. IMACS and PRINTO CSMs performed similarly. Physician-rated change and MRC improvement categories had moderate-to-substantial agreement (Kappa 0.5-0.7).

**Conclusion:**The ACR-EULAR MRC perform consistently across multiple studies, supporting its further use as an efficacy end point in JDM trials.

**Keywords:**JDM; clinical trial; myositis; outcome assessment; outcome measure; response criteria.

Incidence of Small Intestinal Bacterial Overgrowth and Symptoms After 7 Days of Proton Pump Inhibitor Use: A Study on Healthy Volunteers

## Abstract

**Introduction:**Proton pump inhibitors (PPIs) are commonly prescribed drugs. Chronic PPI use has recently been associated with the risk for developing small intestinal bacterial overgrowth (SIBO). It is not known whether the short-term prescription of a PPI can trigger SIBO. Therefore, the aim of the present study was to evaluate the incidence of SIBO and gastrointestinal symptoms after 7 days of PPI use.

**Materials and methods:**A prospective, pilot, open-label study was conducted on asymptomatic healthy volunteers. The incidence of SIBO was evaluated at the baseline and after administration of 40 mg of pantoprazole once a day for 7 days, through a glucose breath test. In addition, the presence of gastrointestinal symptoms, the number of bowel movements, and the consistency of stools, according to the Bristol scale, were assessed.

**Results:**Thirty-eight healthy subjects (71.1% women, mean age 25.18 ± 6.5 years) were analyzed. The incidence of SIBO after 7 days of PPI administration was 7.8% (95% CI 1.6-21.3%). The patients that developed SIBO had a greater prevalence of bloating (p = 0.0002) and flatulence (p = 0.004) after 7 days of treatment.

**Conclusions:**Our study showed that a short-term 7-day PPI course produced SIBO in 7.8% of healthy subjects. Although, inappropriate use of PPIs should be discouraged, but since more than 90% of subjects who received PPIs for one week did not develop SIBO, the advantages of PPI administration seem to outweigh the disadvantages.

**Keywords:**Glucose hydrogen breath test; Proton pump inhibitor; Small intestinal bacterial overgrowth.

YKL-40 serum levels are predicted by inflammatory state, age and diagnosis of idiopathic inflammatory myopathies

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## Abstract

YKL-40 increase according to the aging process, and its functions have been associated with tissue remodeling and systemic inflammation. In Rheumatoid Arthritis (RA) it has been proposed as a possible biomarker of activity and severity, however; in the field of idiopathic inflammatory myopathies (IIM) the role of YKL-40 in IIM is not clear. Thus, we aimed to evaluate if there is an association between the serum levels and muscle tissue expression of YKL-40 with age, IIM phenotype, muscle strength and myositis disease activity. The main finding was that age is the most important variable that affects the YKL-40 serum levels. In muscle biopsy, we observed that YKL-40 is mainly expressed in infiltrating lymphoid cells than in muscle tissue. Using ANCOVA according to the b-coefficients, YKL-40 serum levels are predicted by inflammatory state, age, and IIM diagnosis.

Case Reports

# IgA-dominant postinfectious glomerulonephritis: a case report

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## Abstract

**Introduction:**Acute postinfectious glomerulonephritis (APIGN) is an immunological glomerular disease that is an important health issue in developing countries. The incidence remains high in developing countries with a male-to-female ratio of 2:1 and age predominantly above 50 years. In this case study, we present a patient with a history of *Staphylococcus epidermidis* infection, a past medical history of diabetes mellitus, and histopathological findings of APIGN with Immunoglobulin A (IgA) deposition.

**Methods:**A 58-year-old male presented to the emergency room with a 6-day history of severe low back pain. Three days later, the patient developed fever, chills, abdominal pain in the upper quadrant and a subsequent lower limb cellulitis. Various immunological tests, imaging studies, and kidney biopsy were performed to arrive at a diagnosis.

**Results:**Following the diagnosis and treatment of Cholangitis and *Staphylococcus epidermidis*, further investigation led to a diagnosis of IgA-dominant APIGN. IgA-dominant APIGN was treated with antibiotics, renin-angiotensin-aldosterone system inhibitors and steroids, and the patient was discharged from the hospital.

**Conclusion:**In developing countries, APIGN is a relatively common presentation of kidney damage due to acute kidney injury and nephritic syndrome. IgA-dominant APIGN is a rare but increasingly recognized morphological variant in which IgA is the sole or dominant immunoglobulin. This unique presentation and multidisciplinary approach for diagnosing and treating IgA-dominant APIGN need to be considered and understood by healthcare professionals to better help these patients. Further investigation is needed to understand the best treatment of this IgA-dominant APIGN presentation and its prognosis.

**Keywords:**acute kidney injury; case report; immunoglobulin A; kidney biopsy; postinfectious glomerulonephritis.

Retinoblastoma Outcomes in the Americas: a prospective analysis of 491 children with retinoblastoma from 23 American countries

## Abstract

**Purpose:**Globally, disparities exist in retinoblastoma treatment outcomes between high- and low-income countries, but independent analysis of American countries is lacking. We report outcomes of American retinoblastoma patients and explore factors associated with survival and globe salvage.

**Design:**Subanalysis of prospective cohort study data.

**Methods:**Multicenter analysis at 57 American treatment centers in 23 countries of varying economic levels (low income=LIC, lower-middle=LMIC, upper-middle=UMIC, high=HIC) of 491 treatment-naïve retinoblastoma patients diagnosed in 2017 and followed through 2020. Survival and globe salvage rates analyzed with Kaplan-Meier analysis and Cox proportional hazard models.

**Results:**Of patients, 8 (1.6%), 58 (11.8%), 235 (47.9%) and 190 (38.7%) were from LIC, LMIC, UMIC and HIC, respectively. Three-year survival rates in LICs were 60.0% (95% CI, 12.6-88.2) compared to 99.2% (94.6-99.9) in HICs. Death was less likely in patients older than four years (vs. four or younger, HR=0.45 [95% CI, 0.27 - 0.78], P=0.048). Patients with more advanced tumors (e.g., cT3 vs. cT1, HR= 4.65 × 109 [95% CI, 1.25 × 109 - 1.72 × 1010], P<0.001) and females (vs. males, HR=1.98 [1.27-3.10], P=0.04) were more likely to die. Three-year globe salvage rates were 13.3% (95% CI, 5.1-25.6) in LMICs and 46.2% (38.8-53.3) in HICs. At three years, 70.1% of cT1 eyes (95% CI, 54.5-81.2) versus 8.9% of cT3 eyes (5.5-13.3) were salvaged. Advanced tumor stage was associated with higher enucleation risk (e.g., cT3 vs. cT1, SHR=4.98 [95% CI, 2.36-10.5), P<0.001).

**Conclusions:**Disparities exist in survival and globe salvage in American countries based on economic level and tumor stage demonstrating a need for childhood cancer programs.

**Keywords:**Americas; Enucleation; Prospective; Retinoblastoma; Survival; disparities; globe salvage; treatment.

Palliative care in CADASIL: diagnosis is only the first step

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