mechanism of clinical variability associated with *SCN10A*-related diseases remain unclear.

In conclusion, we suggest, for the first time, the association of *SCN10A* variants with isolated congenital harlequin syndrome. These data need to be confirmed by additional cases and further studies on the alterations of channel gating.

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Persistent Lyme disease with cutaneous *Borrelia* biofilm formation

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Dear Editor, Lyme borreliosis, the most common tick-borne infectious disease, is caused by *Borrelia burgdorferi sensu lato* (Bb) and can affect various organs. Erythema migrans (EM) of the skin is the most frequent clinical diagnosis.[1] Sapi *et al.* previously showed that Bb spirochetes accumulate to form cutaneous biofilm aggregates expressing specific markers, including the well-established biofilm marker alginate.[2]

A 54-year-old woman was referred to our clinic with chronic, linear nonpalpable erythemata of the gluteal region (Figure 1a) and the left breast. Additionally, the patient reported fatigue and hip pain. In the preceding months, the patient had been treated for acute EM with doxycycline over 3 weeks. The patient lived in a tick-endemic area in rural Austria and recalled multiple tick bites over the past year. Primary laboratory findings revealed positive Bb-specific IgG antibodies in enzyme immune assay (156 rU mL^{-1}; negative < 16 rU mL^{-1}) and immunoblot (both Euroimmun, Lübeck, Germany) and negative IgM antibodies (4 rU mL^{-1}) in enzyme-linked immunosorbent assay. Histological examination showed typical signs of EM, consisting of a perivascular lymphocytic infiltrate with admixed plasma cells. Polymerase chain reaction (PCR) tested positive for *Borrelia afzelii*. Neuroborreliosis was excluded by the analysis of cerebrospinal fluid. Based on these findings, intravenous ceftriaxone (1 × 4 g) was administered over 4 weeks without symptom improvement. Therapy was switched to cefuroxime (4 × 500 mg) for 4 weeks, without effect. PCR and multilocus sequence typing revealed persistent skin infection with the same *B. afzelii* strain in two body sites (Figure 1c). The lack of response to antibiotics led us to suspect Bb biofilm formation, which we confirmed by antialginate (Thermo Fisher MA5-2757; Thermo Fisher Scientific, Waltham, MA, USA) and anti-Bb immunostaining (Anti-Bb-Flagellin, APC-conjugated, US Biologicals B2570-26F1-APC; United States Biological, Salem, MA, USA) of a lesional skin biopsy (Figure 1d). A diagnosis of therapy-refractory lyme disease (LD) with biofilm formation was made and intensified antibiotic therapy was initiated (intravenous azithromycin 1.5 g single injection and oral cephalexin 1000 mg twice daily for 3 weeks). After treatment, erythema subsided for the first time and joint pain improved. Histological examination of a skin biopsy of the formerly affected area showed an inconspicuous result and a negative Bb PCR.

After 1 month, the patient again reported severe fatigue and joint pain. Diffusely red, urticarial erythema appeared on the thighs (Figure 1b) and the upper left arm. Bb serology and histological examination of the skin lesion were unremarkable with negative Bb PCR. Further investigation revealed serum

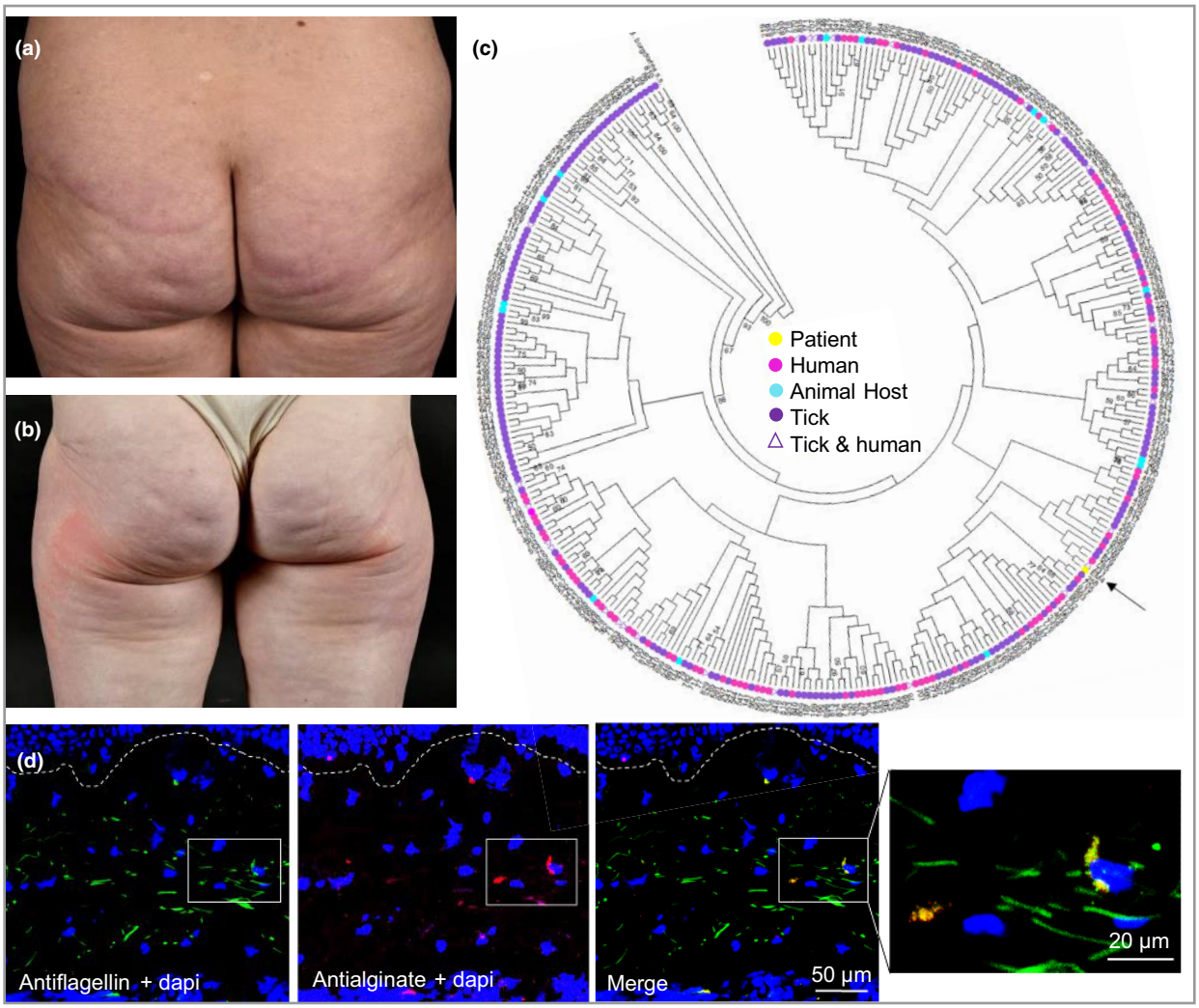

Figure 1 (a) Initial presentation, marginal nonpalpable erythemas in the gluteal region. (B) Late presentation, sharply defined urticarial erythemas. (c) Genetic *Borrelia afzelii* strain characterization. Phylogenetic tree obtained by the neighbour-joining method using the Kimura two-parameter method and 1000 bootstrap replicates. The analysis involved 330 sequences comprising all 328 *B. afzelii* sequence types (ST) from the multilocus sequence typing database and *Borrelia burgdorferi sensu stricto* (ST1) as outgroup. Arrow indicates patient isolate. (d) Alginate-positive Bb biofilm formations in a patient skin biopsy. Immunofluorescence labelling of antialginate positive aggregates (red), Bb-specific antiflagellin (green) and 4′,6-diamidino-2-phenylindole (DAPI) (blue). Yellow signal and arrows indicate overlap. Line indicates dermoepidermal border.

positivity for anticytosolic 5′-nucleotidase 1A (cN1A) antibodies (106 U mL^{-1}), elevated creatine kinase (358 U L^{-1}, range 0–170) and progressive muscle weakness. Magnetic resonance imaging of the hips and shoulders revealed muscular oedema. A diagnosis of atypical post-Lyme syndrome presenting as myositis was made. The patient was treated with lornoxicam and prednisolone (10 mg daily), which stabilized muscle symptoms, but did not improve erythema.

This is the first case in which combined Bb DNA and biofilm detection has led to a diagnosis of persistent LD progressing to myositis. The patient continued to show LD-specific symptoms despite three empirical antibiotic regimens with full adherence. After the detection of biofilm formations, antibiotic therapy with the biofilm-active antibiotic azithromycin proved effective for symptoms of acute LD, but did not prevent complications.

Approximately 10–20% of patients with EM treated with first-line antibiotics (doxycycline and amoxicillin) experience persistent symptoms such as chronic fatigue and joint and muscle pain. When symptoms last 6 months or longer, the condition is referred to as post-treatment LD syndrome (PTLDS).[3] In the course of PTLDS, our patient developed symptoms of myositis including myalgia and muscle weakness. Several cases of LD-related myositis were described and myositis with skin symptoms remains an exceedingly rare presentation of LD.[4] Although the timeline and spatial distribution of symptoms suggest a causal relationship, coincidental myositis cannot be excluded. The pathomechanism of LD-

associated myositis remains unclear and a multifactorial pathogenicity is likely. In addition to immune dysregulation occurring during Bb infection, such as lymphopenia, decreased suppressor cell activity or polygonal B-cell expansion, direct tissue invasion by Bb also appears to play a role. We propose that the formation of bacterial biofilms, which are known to ensure the survival of bacteria under severe conditions, is a contributing factor.[5] Feng *et al.* found that aggregated biofilm-like Bb microcolonies were more tolerant to antibiotics compared with other forms of Bb colonies.[3] In addition, alginate-expressing Bb biofilm formations were previously found in skin biopsies from borrelial lymphocytomas and autopsy tissue sections from the heart, brain, liver and kidney of a patient with LD.[2,6]

In conclusion, the present case illustrates that biofilm formation in EM lesions may lead to persistent Bb infection and, as a consequence, PTLDS. Potential biofilm formation should be considered in therapy-resistant LD in order to apply early calculated antibiotic treatment and prevent the occurrence of late complications.

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Paradoxical psoriasis after exposure to tumour necrosis factor inhibitors in children: a retrospective cohort study

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Dear Editor, Tumour necrosis factor inhibitor (TNFi) use has been associated with the development of paradoxical psoriasiform eruptions in children.[1–8] Here, we describe the prevalence and presentation of TNFi-associated psoriasis in a large cohort of children with chronic nonbacterial osteomyelitis (CNO), juvenile idiopathic arthritis (JIA) or inflammatory bowel disease (IBD) and determine the risk factors in a single tertiary centre. Institutional review board approval (#15732) was obtained. Participants were identified using International Classification of Diseases, 9th revision (ICD-9) codes. Inclusion criteria were (i) age < 18 years, (ii) exposure to TNFi and (iii) at least one follow-up appointment made by a prescribing specialist. The total medication exposure was calculated across all courses of the medication during the observed follow-up for both psoriasis and nonpsoriasis groups; 'time to psoriasis' represented the time from initiation of medication to the onset of psoriasis symptoms. A diagnosis of psoriasis was made by a dermatologist, or by another paediatric specialist in tandem with a dermatologist, after review of supporting clinical findings or photographs. Any psoriasiform lesion that developed during the exposure to TNFi or 60 days after a TNFi was discontinued was considered as an outcome related to TNFi. Statistical analysis was performed using t-tests and χ^2-tests.

A total of 3383 patients (1783 with JIA, 1424 with IBD and 178 with CNO) were identified by an initial ICD code search at Seattle Children's Hospital between 1 January 2005 and 31 July 2015. Among these patients, a total of 1090 patients, including 28 patients with CNO, 621 patients with JIA and 450 patients with IBD, met the inclusion criteria. The age at onset of CNO, JIA and IBD was 11 ± 3.4 years, 8.7 ± 5.2 years and 12.3 ± 3.5 years, respectively. For patients who had a diagnosis of both IBD and JIA, the patients with a prior IBD diagnosis were removed from the JIA cohort.

Psoriasis developed after exposure to TNFi in a total of 31 patients [2.8%, 95% confidence interval (CI) 2.5–3.1], including four of 28 patients with CNO (14%, 95% CI 2.2–25.8), three of 621 patients with JIA (0.5%, 95% CI 0.1–1.0) and 25 of 450 patients with IBD (5.6%, 95% CI 3.8–7.4). One patient developed psoriasis with comorbid CNO and IBD. There was no significant difference in distribution of age, sex, race or family history of psoriasis between the psoriasis and nonpsoriasis subsets as shown in Table 1. Across all three