they are likely to be single-gene diseases. Low serum DNase activity in these patients would be consistent with the idea that factors other than *DNASE I* mutations alone affect serum DNase activity, since the odds of an individual inheriting 2 rare gene mutations would be exceedingly low. Four such patients (3 complete C4 and 1 complete C1r deficient) were studied. The number of patients studied is small, reflecting the very low frequency of homozygous C4 and C1r mutations in the population. The results show that serum DNase activity in patients with SLE due to genetic defects in the classical pathway of complement is not significantly different from that in the usual SLE patients (Figure 1). Both groups had serum DNase activity that was significantly diminished compared with that of healthy controls.

We agree with Dr. Balada and colleagues that defects in the ability to clear extracellular DNA likely contribute to the etiopathogenesis of SLE. While mutations in *DNASE I* could be an occasional, but rare, cause of SLE in humans, the etiology of the low serum DNase activity in SLE is undoubtedly complex. Thus far, the data suggest that in most SLE patients this phenomenon cannot be explained solely by *DNASE I* mutations alone. *DNASE I* transcript levels could be influenced by alternative splicing (9) or messenger RNA stability (10) (although there was no evidence of differences in splicing in our earlier study [1]). There is the potential for epistatic interaction with other genes or, alternatively, enzyme activity could be modulated by posttranslational events such as glycosylation, or by microenvironments particular to specific tissues (6,11). Further investigation will be required to determine if any of these processes downstream from gene transcription are affected in SLE patients, or if defects in other endonucleases are present.

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Call for a trial of Lyprinol, an over-the-counter 5-lipoxygenase inhibitor: comment on the article by Kowal-Bielecka et al

To the Editor:

In their discussion of dermal overexpression of 5-lipoxygenase (5-LOX) in systemic sclerosis (SSc), Kowal-Bielecka et al (1) remind us that disease-modifying therapies for SSc are far from satisfactory. With the demise of benoxaprofen and zileuton, there is not very much to offer in the way of 5-LOX inhibitors. Nonspecific antioxidants (e.g., nordihydroguiaretic acid) have been studied in asthma, without too much success. Each of the alternative strategies for reducing the deleterious effects of leukotrienes, namely curtailing the supply of arachidonate, the 5-LOX substrate, (with corticosteroids) or antagonizing leukotriene receptors (e.g., with montelukast, zafirlukast), presents problems of side effects or specificity.

An alternative 5-LOX inhibitor is Lyprinol, an over-the-counter nutritional supplement that is a lipid extract from the green-lipped mussel (*Perna canaliculus*). These mussels are farmed in pristine waters (Marlborough Sounds) in New Zealand's South Island. Studies to date indicate that Lyprinol is a 5-LOX inhibitor (2,3), has antiarthritic activity without gastric side effects in rats and humans (2,4), and is effective in asthma (5). Particularly valuable is its synergy with low-dose

corticosteroids (e.g., prednisone, dexamethasone) in ameliorating asthma (6) or experimental fibrosis in rats (7). It would seem timely to conduct a trial of Lyprinol in a few patients with SSc, perhaps in combination with a steroid.

The mussel from which Lyprinol is derived has been a traditional staple of the diet of the New Zealand Maori people. Advantages of using the lipid extract, Lyprinol, a ×20 mussel concentrate, are that it is prepared from fresh-frozen, stabilized mussels, it is salt-free, and nonallergenic, and it has no solvent residues (liquified carbon dioxide is being used under supercritical conditions to extract it). There currently are distributors of Lyprinol in the US.

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Reply

To the Editor:

We thank Dr. Whitehouse for his comments on our study. The up-regulation of 5-LOX in skin biopsy specimens from SSc patients compared with those from healthy controls, along with reports about positive effects of LOX inhibitors in fibrotic animal models, led us to the conclusion that inhibition of the 5-LOX pathway might be a treatment option in SSc. This hypothesis is further supported by recent data from our laboratories showing that leukotriene B_4, a product of the 5-LOX pathway, is also up-regulated in bronchoalveolar lavage fluids from patients with SSc. Thus, treatment with inhibitors of the 5-LOX pathway not only might have favorable effects on the progression of skin fibrosis but also might influence the pathogenesis of scleroderma lung disease.

In general, the biologic action of leukotrienes can be blocked by selective inhibitors of 5-LOX (e.g., zileuton), leukotriene receptor antagonists (e.g., montelukast and zafirlukast), inhibitors of the 5-LOX activating protein (e.g., MK-591), and newly developed dual inhibitors, which are able to block both cyclooxygenase and LOX pathways. Lyprinol is not a specific 5-LOX inhibitor but has been suggested to exert its antiinflammatory action in part via inhibition of the 5-LOX pathways.

Several points should be considered before trials with 5-LOX inhibitors are started in patients with SSc. As outlined in our report, there was considerable basal synthesis of 5-LOX in the skin of healthy controls, indicating that this pathway might be involved in physiologic processes. In addition, the SSc group was heterogeneous in that many patients showed a strong up-regulation of 5-LOX, while some others showed expression of 5-LOX in the range of that of the healthy controls. Because only the former group is likely to benefit from inhibition of 5-LOX, these patients should be selected for early trials. Certainly, the American College of Rheumatology guidelines for clinical trials in SSc should be considered (White B, Bauer EA, Goldsmith LA, Hochberg MC, Katz LM, Korn JH, et al. Guidelines for clinical trials in systemic sclerosis [scleroderma]. I. Disease-modifying interventions. Arthritis Rheum 1995;38:351–60).

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Congenital fascial dystrophy, a new scleroderma-like genetic disease with limitation of joint mobility: comment on the clinical image presented by Di Rocco

To the Editor:

Congenital fascial dystrophy, described by Di Rocco as stiff skin syndrome (1), is a scleroderma-like syndrome that is virtually unknown to rheumatologists, even though patients with this condition are usually receiving treatment at rheumatology institutions. This autosomal recessive disease is often identified as scleroderma or sclerodermatomyositis because of indurations of the soft tissues, contractures, and limitation of joint mobility. Because of such misidentification, patients may be subjected to aggressive and harmful therapy.

In 1971, Esterly and McKusick (2) described stiff skin syndrome, a condition recognized as a localized connective tissue disorder or limited mucopolysaccharidosis without mucopolysaccharidurıa. Subsequently, highly heterogeneous disease processes and various scleroderma-like dysmorphic syndromes were reported under this name (3–6). In single cases, Alcian blue deposits were observed between collagen fibers (2,7–9), which favored some relationship with mucopolysaccharidosis.

Our group has reported cases in which patients display stony-hard generalized indurations of the soft tissues, with no visceral involvement and no immunologic or vascular abnormalities (10,11). Frequently, these changes are already noticeable on the buttocks and thighs during the first year of life, with progressive involvement of the trunk and limbs. Because of contractures of the limbs, patients have characteristic tiptoe