**Supplementary Methods**

**Proinflammatory cytokine stimulation of fibroblast-like synoviocytes (FLS) and cell proliferation assay**

After washing with PBS, FLS were cultured in 96-well plates at a density of $3 \times 10^3$ cells/well in 100 μl IMDM containing 10% heat-inactivated FBS, penicillin, and streptomycin. After 24 h, 100 ng/ml TNFα (Sigma Aldrich) was added to the culture medium. After 24 h of incubation at 37 °C, 6 mM ITA or PBS was added to the culture medium. After 48 h of incubation, in the tetrazolium/formazan assay, 15 μl of dye solution from the assay kit was added to each well and incubated for another 4 h at 37 °C. Each reaction was terminated using a stop solution from the kit, and the resulting optical density at 570 nm was measured. These proliferation assays were performed in triplicate, and the experiments were performed before the FLS became confluent in the culture dishes. In the BrdU assay, after 48 h of incubation, FLS were added to BrdU and incubated for 2 h. The pyrimidine analog, BrdU, is incorporated in place of thymidine into the DNA of proliferative cells during the labeling period. The incorporated BrdU was then detected using an anti-BrdU antibody conjugated with peroxidase and the data were quantified using a substrate reaction. The absorbance was measured using a Multiskan Ascent plate reader (Thermo Electron) at 370 nm (reference wavelength, 492 nm). The final data were expressed as optical density.

**Supplementary Table and Figure**

**Supplementary Table 1. Characteristics of the patients with rheumatoid arthritis included in this study**

| | |
|---|---|
| No. of women/men | 9/5 |
| Age at operation, years | 66 (60-74) |
| Disease duration, years | 15 (11-24) |
| Serum CRP, mg/dL | 0.43 (0.13-1.50) |
| MMP-3, mg/dL | 143 (71.6-228) |
| RF, units/mL | 20.4 (4.88-93.3) |
| ACPAs, units/mL | 72.7 (10.5-192) |
| Swollen joint count | 2.5 (2.0-4.0) |
| Tender joint count | 3.0 (3.0-7.5) |
| DAS28-ESR | 4.51 (4.16-5.13) |
| HAQ DI score | 1.06 (0.76-1.50) |
| Methotrexate use, no. (%) | 6 (42.9) |
| Biologic agent use, no. (%) | 6 (42.9)* |
| JAK inhibitor use, no. (%) | 1 (7.1)** |

Except where indicated, the values indicate the median (interquartile range). RA, rheumatoid arthritis; CRP, C-reactive protein; MMP-3, matrix metalloproteinase 3; RF, rheumatoid factor; ACPAs, anti-citrullinated protein antibody; DAS28-ESR, Disease Activity Score in 28 joints using erythrocyte sedimentation rate; HAQ-DI, Health Assessment Questionnaire disability index; JAK, Janus kinase.

*Two patients were receiving etanercept (14%), one was receiving golimumab (7.1%), one was receiving abatacept (7.1%), and one was receiving tocilizumab (7.1%).

**One patient was taking baricitinib (7.1%)

**Supplementary Figure 1**

The effect of ITA on the migration of FLS.

FLS were cultured in the absence of TNFα stimulation and treated with ITA or PBS for 48 h.

Migration ratio (%) measured using a scratch assay.

Abbreviations: ITA, itaconate; FLS, fibroblast-like synoviocytes; TNFα, tumor necrosis factor alpha.

**Supplementary Figure 2**

Intracellular levels of metabolites implicated in the TCA cycle from TNFα-stimulated FLS with ITA (n = 3) or PBS (n = 3).

Abbreviations: ITA, itaconate; FLS, fibroblast-like synoviocytes; TNFα, tumor necrosis factor alpha; TCA, tricarboxylic acid; SDH, succinate dehydrogenase.