the heart showed signs of ischaemia but no evidence of myocardial infarction or viral myocarditis (fig 1). No pulmonary emboli were noted, although diffuse alveolar damage consistent with adult respiratory distress syndrome was observed. All cultures for bacteria and fungi, including lung and blood, did not grow organisms. The rest of the autopsy was unremarkable.

Our patient exhibited some evidence of myocardial and/or pulmonary dysfunction before the initiation of IL 1 blockade. It is possible that her AOSD-associated cardiac disease progressed despite excellent control of her other symptoms. Alternatively, experience with TNF inhibitors suggests that cardiac events can occur despite clinical improvement in the underlying inflammatory disease. Concluding that a similar adverse event profile accompanies IL 1 inhibition is speculative, and we cannot be certain that anakinra played a part in this patient's cardiac events. However, the course of this patient suggests that systematic collection of data to assess possible associations between IL 1 blockade and cardiac complications is important.

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A triple altered collagen II peptide with consecutive substitutions of TCR contacting residues inhibits collagen-induced arthritis

Zhong-Qiang Yao, Ru Li, Zhan-Guo Li

The collagen type II (CII) 263–272 peptide is a predominant T and B cell antigenic peptide in rheumatoid arthritis.¹ Crystallographic data showed that 263F and 264K of CII263–272 are mainly responsible for binding with HLA-DR, and that 267Q and 270K were the major T cell receptor (TCR)-contact residues.^{2–3} We have shown that the CII altered peptide ligand (APL) with individual or consecutive substitutions of the TCR-contact amino acids could inhibit T cell activation induced by wild-type CII peptide in the context of HLA-DRB1, among which the most potent T cell activation suppressor is sub268–270, in which the amino acids of wild-type CII263–272 at positions 268, 269 and 270 were substituted with glycine or alanine (FKGEQAGAGE, substitutions underlined).^{4–5} Collagen-induced arthritis (CIA) is induced by wild-type CII in susceptible rodent strains. It has been regarded as the best rheumatoid arthritis model.⁶ In this study, we examined whether sub268–270 could show inhibitory effect in CIA.

Arthritis was induced in female Lewis rats weighing 120–140 g. Each rat was injected intradermally with 200 μ g bovine CII emulsified with Freund's incomplete adjuvant. A booster immunisation with 100 μ g emulsified CII was given 7 days later.⁶ The treatment with APL was initiated 24 h after arthritis onset. APL (sub268–270) at a dose of 90 μ g was given intravenously once a week, with a total of three injections. The irrelevant peptide (EGKPGQEGKF) and phosphate-buffered saline applied at the same dose were used as irrelevant

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Figure 1 Inhibition of arthritis in rats with collagen induced arthritis by treatment with APL sub268–270. The arthritis score in sub268–270 treated rats was much lower than that of phosphate buffered saline and irrelevant peptide from day 6 to day 21 ($n=8$, $p<0.01$). PBS, phosphate-buffered saline.

Table 1 The effect of sub268–270 on radiological and pathological lesions of CIA

Groups	sub268–270	Irrelevant peptide	PBS
Radiological score	1.32 (0.49)*	2.63 (0.51)	2.69 (0.53)
Pathological score	1.38 (0.53)*	2.94 (0.63)	3.06 (0.65)

CIA, collagen-induced arthritis; PBS, phosphate-buffered saline.
Data were expressed as mean (SD). * $p < 0.01$

and blank control, respectively. Arthritis scores of all four paws were made by two independent observers, with a scale of 0–4 for each paw: 0 = no change, 1 = swelling and erythema of the digit, 2 = mild swelling and erythema of the limb, 3 = gross swelling and erythema of the limb, 4 = gross deformity and inability to use the limb.⁷ Radiographic films of both hind paws were taken at the 21st day of treatment and subjected to radiographic scoring by two independent radiologists according to the degree of cartilage and bone erosions: 0 = no obvious abnormality, 1 = tissue swelling and oedema, 2 = joint space narrowing, and 3 = bone erosion and osteophyte formation.⁸ After killing the rats on treatment day 21, both ankle joints of rats with CIA were detached, embedded in paraffin, stained with haematoxylin–eosin, and pathological scores were made by two independent pathologists according to the following scale: 0 = normal synovium, 1 = synovial membrane hypertrophy and inflammatory cell infiltrates, 2 = pannus formation and cartilage erosion, 3 = major erosion of cartilage and subchondral bone, and 4 = loss of joint integrity and ankylosis.⁹ These assessments were performed by two independent people who were blinded to groups of the animals. These measures might reduce the selection bias to the least level.

As shown in figure 1, the APL did not reduce the baseline arthritis ($p > 0.05$). However, from day 6 to day 21, sub268–270 effectively reduced the inflammation in CIA as compared with irrelevant peptide and blank control ($p < 0.01$). Radiological bone erosion and pathological lesions were the hallmark of rheumatoid arthritis/CIA. As shown in table 1, APL treatment significantly decreased the radiological score of CIA, implying its bone-protection potential ($p < 0.01$). APL decreased the pathological score of CIA, suggesting its role in inhibition of pathological lesions ($p < 0.01$).

In conclusion, APL sub268–270 could effectively reduce the joint inflammation and also decrease the joint injuries in CIA. These results suggest that this APL might be potentially useful in HLA-DRB1-positive patients with rheumatoid arthritis.

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Association of poly(ADP-ribose) polymerase 1 and a novel candidate locus, *LOC127086*, with systemic lupus erythematosus

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Genetic predisposition probably plays an important part in the pathogenesis of systemic lupus erythematosus (SLE). Several loci have been suggested to be related to SLE, among which is the 1q41–42 region on chromosome 1.¹

This region is homologous to the *Sle1* region in an SLE mouse model.² One of the genes on this region is the poly(ADP-ribose) polymerase 1 (*PARP1*) gene, which has been associated with SLE in several studies. This gene encodes a nuclear enzyme