Interleukin-2–Induced Lung Injury
The Role of Complement


Abstract Pulmonary edema and sepsislike syndrome are grave complications of interleukin-2 (IL-2) therapy. Recent animal studies have suggested IL-2–induced microvascular injury as the underlying mechanism. Since complement factors have been shown to mediate increased vascular permeability in diverse conditions that lead to pulmonary injury and recombinant human IL-2 is known to activate the complement system in patients undergoing IL-2 therapy, we hypothesized that complement factors play a pivotal role in the development of increased vascular permeability after IL-2 treatment. To test this hypothesis, we evaluated the capacity of recombinant soluble human complement receptor type 1 (sCR1, BRL 55730), a new highly specific complement inhibitor, to attenuate IL-2–induced lung injury in the rat. Recombinant human IL-2 (intravenously for 60 minutes) at 10⁴ U per rat (n=4) elevated lung water content (37±6%, P<.05), myeloperoxidase activity (162±49%, P<.05), and serum thromboxane B₂ (30±1 pg/100 μL, P<.01) and had no effect on serum tumor necrosis factor-α. sCR-1 at 30 mg/kg (n=5), but not at 10 mg/kg (n=6), attenuated the elevation of lung water content (18±2%, P<.05) and myeloperoxidase activity (42±9%, P<.05) but failed to alter serum thromboxane B₂ response to IL-2. These data suggest the involvement of complement in the pathogenesis of IL-2–induced pulmonary microvascular injury and point to the potential therapeutic capacity of complement inhibitors in combating this toxic effect of IL-2 therapy. (Circ Res. 1994;74:329-335.)

Key Words • cytokines • anaphylatoxins • pulmonary edema

Interleukin-2 (IL-2) is under investigation as an immunotherapeutic agent used in the treatment of advanced metastatic cancer. The clinical toxicity of the IL-2 regimen includes sepsislike syndrome and pulmonary edema secondary to increased vascular permeability. Although the pathophysiological processes leading to these side effects are still obscure, several mechanisms have been proposed. For example, recent in vitro data have suggested that tissue injury is mediated by lymphokine-activated killer cells activated in response to IL-2. However, several in vivo studies conducted in sheep and rats cast doubt on this possibility, since lung microvascular injury has been demonstrated as early as 2 to 6 hours after IL-2 infusion, a time interval insufficient for lymphokine-activated killer cell generation. Neutrophils, which are early-response inflammatory cells, have been recently implicated in the pulmonary response to acute IL-2 administration. In addition, increased vascular permeability could be consequent to the IL-2–induced production of several humoral inflammatory mediators such as interleukin-1, tumor necrosis factor-α (TNF-α), thromboxane A₂ (TXA₂), and platelet-activating factor (PAF). This possibility draws credence from the observation that IL-2 itself did not induce permeability defects in vitro and that athymic nude mice and leukocyte-depleted mice develop a milder form of lung microvascular injury after IL-2 infusion.

Recently, IL-2 infusion to cancer patients has been shown to induce a dose-dependent activation of the complement system that correlated with the development of microvascular injury (vascular leakage syndrome). Also, complement factors have been shown to play a key role in other pathological conditions that involve endothelial damage and microvascular injury, such as sepsis and adult respiratory distress syndrome. Therefore, we hypothesized that complement might be involved in the mediation of IL-2–induced lung injury.

Recently, the human complement receptor-1 gene has been cloned, and the solubilized truncated extracellular form has been expressed and purified. This 200-kD protein has been shown to be a potent inhibitor of human C3 and C5 convertases in vitro and to potentially inhibit C3a and C4a formation. Soluble complement receptor type 1 (sCR1) has already demonstrated efficacy in the inhibition of complement-mediated tissue injury in vivo, including pulmonary microvascular injury associated with IgG or cobra venom factor–induced complement activation, burn injury, or endotoxin-induced adult respiratory distress syndrome in PAF-primed rats. The present study tested the hypothesis that sCR1 might also mitigate pulmonary vascular injury consequent to IL-2 infusion in rats and to investigate whether this action compromises the capacity of IL-2 to activate T cells in vitro.

Materials and Methods

Drugs

IL-2

Human recombinant IL-2, kindly provided by Hoffman LaRoche Inc, Nutley, NJ, was reconstituted before use with 1 mL sterile 0.9% NaCl per 10⁴ U of IL-2.
Indomethacin

Indomethacin (Sigma Chemical Co, St Louis, Mo) was dissolved in 0.2 mol/L Na₂CO₃ (pH 8) to give a final concentration of 1 or 10 mg/mL. Indomethacin vehicle was prepared by dissolving 0.2 mol/L Na₂CO₃ in 0.9% NaCl at similar volumes.

Animals

Male Sprague-Dawley rats (220 to 350 g) were studied. The rats were kept in groups of three in standard cages with food and water ad libitum at 22°C and a 12-hour light/dark cycle until surgery.

In Vivo Experimental Protocol

A scheme of the experimental protocol is presented in Table 1. Under pentobarbital (30 mg/kg IP) anesthesia, catheters (PE-50) were inserted into a single femoral artery for blood sampling and into both femoral veins for IL-2 and sCR1 infusion. A basal blood sample (0.7 mL exchanged with an equimolar of 0.9% NaCl) was collected for serum thromboxane B₂ (TXB₂), the nonactive metabolite of TXA₂, and TNF-α determination. The animals were randomly assigned to several groups: (1) sCR1 vehicle (at a volume similar to that used in the sCR1 dose of 30 mg/kg) was injected as an intraperitoneal bolus. Ten minutes later, sCR1 vehicle at the same dose and IL-2 at 10⁶ U were infused intravenously (using separate intravenous lines) for 1 hour. Blood samples (for the above-mentioned assays) were collected at 0.5, 2, and 4 hours. At the end of the observation period (4 hours), the left lung was removed and used to determine lung myeloperoxidase (MPO) activity and lung wet and dry weights. (2) A similar protocol was repeated using sCR1 at 10 or 30 mg/kg (50% administered as an initial intraperitoneal bolus and 50% as an intravenous infusion for 1 hour). (3) The first protocol was repeated but with sCR1 and IL-2 vehicles. Additional blood samples (0.15 mL) for serum sCR1 determination were obtained at several time points in animals receiving sCR1 at 30 mg/kg. The IL-2 dose was selected on the basis of previous studies that characterized the pulmonary responses to IL-2.¹⁷ The sCR1 dose was selected on the basis of previous studies in which similar doses attenuated microvascular lung injury produced by endotoxin in PAF-primed rats,²⁶ immune complexes,²⁵ or thermal injury.²⁵,²⁸

Additional protocols were conducted to establish the time course of the pulmonary responses to IL-2 infusion. Protocol 1 was repeated but with lungs removed at 1 (n=6) or 2 (n=6) hours.

Preliminary data showed increased TXB₂ in the serum of IL-2-treated animals. Thus, to further evaluate the role of TXA₂ in the development of IL-2-induced lung injury, the effect of TXA₂ inhibition by indomethacin was studied. To that end, animals were given indomethacin (1 or 10 mg/kg IV, n=5) or vehicle (n=5) 15 minutes before the administration of IL-2. Control animals given indomethacin (10 mg/kg IV) followed by IL-2 vehicle were also evaluated. Blood was sampled for TXB₂ assay as previously described, and lungs were harvested at 4 hours to determine water content.

To confirm that IL-2 activates the complement system, additional rats were given IL-2 (10⁶ U IV) or vehicle (n=4), and blood samples for serum complement hemolytic activity were collected before and at several time points after IL-2 infusion.

In Vitro Experimental Protocol

The activation of T cells by IL-2 was tested using a proliferation assay in IL-2–dependent T-cell lines. The murine IL-2–dependent cytotoxic T-cell line CTLL-2²⁹ was maintained in RPMI 1640 medium supplemented with 10% heat-inactivated fetal bovine serum, 2 mmol/L sodium pyruvate, 10

Table 1. Scheme of the Experimental Protocols

<table>
<thead>
<tr>
<th>Protocol</th>
<th>n</th>
<th>Intraperitoneal Bolus</th>
<th>Intravenous Infusion (+10 minutes)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4</td>
<td>sCR1v</td>
<td>sCR1v + IL-2</td>
</tr>
<tr>
<td>2a</td>
<td>6</td>
<td>5 mg/kg sCR1</td>
<td>5 mg/kg sCR1 + IL-2</td>
</tr>
<tr>
<td>2b</td>
<td>5</td>
<td>15 mg/kg sCR1</td>
<td>15 mg/kg sCR1 + IL-2</td>
</tr>
<tr>
<td>3</td>
<td>6</td>
<td>sCR1v</td>
<td>sCR1v + IL-2v</td>
</tr>
</tbody>
</table>

sCR1v indicates soluble complement receptor type 1 vehicle; sCR1, soluble complement receptor type 1; IL-2, interleukin-2; and IL-2v, interleukin-2 vehicle.

![Fig 1](http://circres.ahajournals.org/)

Fig 1. Bar graphs showing the effect of soluble complement receptor type 1 (sCR1) on lung wet weight (A) and wet minus dry weight (B) response to interleukin-2 (IL-2, 10⁶ U per rat). − indicates absence; +, presence. #P<.05 vs vehicle control group (a) and all other groups (b). Percent change is assessed against the vehicle control groups.
mmol/L HEPES, 50 μmol/L 2-mercaptoethanol, and 50 U/mL recombinant human IL-2 in a humidified 5% CO₂ incubator at 37°C. The proliferation of CTLL-2 cells in response to IL-2 was determined by [³H]thymidine incorporation. Cells were washed three times with culture media without IL-2 and plated in flat-bottom 96-well plates (10⁴ cells per well). Triplicate cultures were preincubated for 1 hour with various amounts of sCR1, and then IL-2 (100 U/mL) was added. After incubation for 22 hours, the cultures were pulsed with 1 μCi [³H]thymidine for 2 hours and harvested onto glass-fiber filter strips by a semiautomatic cell harvester, and the radioactivity incorporated into DNA was measured by liquid scintillation counting.30

The murine IL-2-dependent T helper clone L2 was maintained as described.31 Seven days after exposure to irradiated allogenic spleen cells and 5 U/mL recombinant IL-2, the cells were purified by Ficoll-Hypaque density gradient centrifugation, incubated for 16 hours in culture media without IL-2, and then used in IL-2-induced proliferation assay as described above.

Assays and Techniques

**TNF-α**

Serum levels of TNF-α were measured by a “sandwich” enzyme-linked immunosorbent assay (ELISA)32 using a hamster monoclonal anti-mouse TNF-α (Genzyme Corp, Cambridge, Mass) as the capture antibody and a polyclonal rabbit anti-murine TNF-α (Genzyme) as the detecting antibody. TNF-α levels in rat samples were calculated from a standard curve generated with recombinant murine TNF-α (Genzyme). TNF-α levels determined by ELISA correlated with levels detected by the L-929 bioassay,33 with 1 U of activity in the bioassay corresponding to 5 pg of TNF-α in the ELISA. The ELISA detected levels of TNF-α down to 25 pg/mL.

**TXB₂**

TXB₂ was determined by radioimmunoassay (sensitivity of 5.0 pg/100 μL) as previously described.34

**MPO**

MPO activity in the lung was assayed as described previously35 on the basis of a modification of Bradley’s method36 adapted for rat lung MPO assay.37

**Pulmonary Water Content**

The removed left lung was immediately frozen on dry ice. When defrosted, the lung was weighed to determine wet weight. Dry weight was determined after the lung was dried at 80°C for 36 hours, and the pulmonary water content was calculated by subtracting the lung dry weight from the wet lung weight.

**Serum sCR1 Antihemolytic Activity**

Serum sCR1 levels were assayed using an antihemolytic assay, which measures the inhibition of complement-mediated sheep erythrocyte hemolysis as a function of sCR1 concentration. The assay was previously described in detail.26

**Serum Complement Hemolytic Activity**

Complement activity of rat serum was determined by measuring the ability of the serum to lyse antibody-sensitized sheep red blood cells. In a V-bottom plate, sensitized sheep red blood cells at 1×10⁷ cells per milliliter (Diamedix, Miami, Fl, USA) were incubated with serial dilutions of rat serum using HEPES buffer (0.1% mol/L HEPES, 0.15 mol/L NaCl, and 0.1% bovine serum albumin, pH 7.4) for 60 minutes at 37°C. Cells were pelleted, the supernatants were transferred to a flat-bottom microtiter plate, and the absorbance at 405 nm was measured to determine released hemoglobin. All serum samples were run in duplicate.

**Data Analysis**

Data in text and figures are mean±SEM for the indicated number of animals. ANOVA followed by the Student-Newman-Keuls test for multiple comparisons was used for statistical analysis, with a value of P < .05 considered significant.

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**Fig 2.** Bar graph showing the effect of soluble complement receptor type 1 (sCR1) on lung myeloperoxidase (MPO) response to interleukin-2 (IL-2, 10⁸ U per rat). – indicates absence; +, presence. *P < .05 vs vehicle control group (a) and all other groups (b). Percent change is assessed against the vehicle control group.

**Fig 3.** Graph showing the effect of soluble complement receptor type 1 (sCR1) on serum thromboxane B₂ (TXB₂) response to interleukin-2 (IL-2, 10⁸ U per rat). #P < .01 vs basal value (a) and sCR1 vehicle + IL-2 vehicle group (b). The dashed line represents the sensitivity of the assay (5 pg/100 μL).
TABLE 2. Time Course of Lung Myeloperoxidase and Weight Response to Interleukin-2 Infusion

<table>
<thead>
<tr>
<th>Control</th>
<th>Δ1 h, %</th>
<th>Δ2 h, %</th>
<th>Δ4 h, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>MPO 10±1 U/g wet weight</td>
<td>23±26</td>
<td>13±1</td>
<td>42±9*</td>
</tr>
<tr>
<td>Wet weight 463±28 mg</td>
<td>5±12</td>
<td>-1±7</td>
<td>41±5*</td>
</tr>
<tr>
<td>Dry weight 92±5 mg</td>
<td>2±10</td>
<td>1±6</td>
<td>38±7*</td>
</tr>
<tr>
<td>Wet-dry weight 369±15 mg</td>
<td>5±7</td>
<td>3±6</td>
<td>36±6*</td>
</tr>
</tbody>
</table>

Control indicates values at 4 hours of the soluble complement receptor type 1 vehicle plus interleukin-2 vehicle group; Δ, percent change vs control; and MPO, myeloperoxidase. *P<.05 vs control.

Results

Effect of sCR1 on IL-2-Induced Lung Weight Response

Administration of IL-2 increased basal lung wet (463±28 mg), dry (92±5 mg), and wet minus dry (369±15 mg) weights by 41±5% (P<.05), 38±7% (P<.05), and 36±6% (P<.05), respectively (Fig 1). These results are consistent with previous reports.10,17 sCR1 at 30 mg/kg, but not at 10 mg/kg, attenuated these responses (P<.05, Fig 1).

Effect of sCR1 on IL-2-Induced Lung MPO Response

IL-2 infusion elevated lung MPO activity by 42±9% (P<.05, Fig 2) as compared with vehicle-treated control lungs (10.3±0.6 U/g wet lung weight). These results are in agreement with previous reports.17 sCR1 at 30 mg/kg attenuated lung MPO activity by 74±8% (P<.05, Fig 2), whereas sCR1 at 10 mg/kg failed to alter lung MPO response.

Effect of sCR1 on IL-2-Induced TXB2 and TNF-α Response

Basal serum TXB2 and TNF-α levels were below the sensitivity of the assays used as previously reported.37-40 IL-2 increased serum TXB2 (P<.01, Fig 3) but failed to elevate serum TNF-α (data not shown). sCR1 at all tested doses did not alter the IL-2-induced elevation of serum TXB2 (Fig 3).

Time Course of Lung Weight and MPO Response to IL-2

At 4 hours after infusion, IL-2 elevated lung MPO activity (P<.05, Fig 2), wet weight (P<.05, Fig 1A), and water content (P<.05, Fig 1B); no significant changes were recorded earlier at 1 or 2 hours (Table 2).

Effect of Indomethacin on IL-2-Induced Lung Weight Response

Pretreatment with indomethacin at all tested doses failed to attenuate lung edema induced by IL-2 (Fig 4A). In contrast, indomethacin at 10 mg/kg completely prevented the IL-2-induced elevation of serum TXB2 (Fig 4B). Indomethacin alone did not produce any detectable change in lung weight (Fig 4A).

Serum sCR1

Detectable levels of sCR1 were found in the serum at 30 minutes after sCR1 administration (and before lung injury) (Fig 5). Serum sCR1 levels remained the same throughout the experiment period.

Effect of IL-2 on Serum Complement Hemolytic Activity

IL-2 but not IL-2 vehicle significantly reduced serum complement activity at 2 hours (P<.01) and 4 hours (P<.01) after infusion (Fig 6).

Effect of sCR1 on IL-2-Induced [3H]Thymidine Incorporation to L-2 or CTLL-2 Cells

IL-2 markedly stimulated [3H]thymidine incorporation in both L-2 and CTLL-2 cell lines (Table 3). sCR1 failed to alter this response. Furthermore, sCR1 had no effect of its own on [3H]thymidine incorporation into L-2 or CTLL-2 cells.

Fig 4. Graphs showing the effect of indomethacin (indo) on lung weight (A) and thromboxane B2 (TXB2, B) response to interleukin-2 (IL-2). #P<.05 vs basal value, control, and indo + IL-2 vehicle group (a) and basal value, 10 mg/kg indomethacin + IL-2 group, and 10 mg/kg indomethacin + IL-2 vehicle group (b). The dashed line in panel B represents the sensitivity of the TXB2 assay (5 pg/100 μL).
Discussion

Our demonstration of acute lung microvascular injury characterized by capillary permeability defect and leukosequestration as early as 4 hours after IL-2 infusion correlates well with recent reports from our laboratory and by others7-10,16 and is in accord with observations from clinical studies.3,4,41 In these reports, intravenous infusion of IL-2 to rats and sheep induced microvascular injury within 3 to 6 hours,7-10,16 and IL-2-treated patients developed pulmonary edema associated with acute respiratory failure within minutes of IL-2 administration.3,4,41 In addition, our results indicate that changes in both IL-2–induced permeability defect and leukosequestration begin simultaneously (see Table 2). Taken together, these data suggest that IL-2 induces acute lung microvascular injury and point to the potential role of IL-2 in the mediation of other acute inflammatory responses.

The major finding of the present study is that treatment with sCR1 attenuated the IL-2–induced microvascular injury. Since sCR1 is a highly specific inhibitor of the complement cascade,24 it is conceivable that complement factors play a key role in the pathophysiological processes by which IL-2 induces lung injury. This conclusion is supported by our observation that IL-2 activates serum complement and is complementary to a previous report that demonstrated activation of the complement system during immunotherapy with IL-2 in humans.19 Also, the efficacy of sCR1 to block lung injury produced by IL-2 without affecting the activation of T cells by IL-2 suggests that sCR1 might be effective in combating IL-2 toxicity without compromising the primary therapeutic goal of selected immune stimulation.

The mechanisms by which IL-2 induces complement activation are still obscure. Nevertheless, it is possible that IL-2 might indirectly activate the complement cascade through the production of other inflammatory mediators such as TNF-α or IL-1, which can recruit and activate neutrophils to release proteases42 and toxic oxygen metabolites43 that cleave complement factors. Our finding of elevated lung MPO activity along with a

Table 3. Effect of Soluble Complement Receptor Type 1 on Interleukin-2–Induced [3H]Thymidine Incorporation to L-2 or CTLL-2 Cells

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Experiment 1: CTLL-2, cpm</th>
<th>Experiment 2: CTLL-2, cpm</th>
<th>Experiment 3: L-2, cpm</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-2 + sCR1v</td>
<td>1710</td>
<td>245</td>
<td>211</td>
</tr>
<tr>
<td>IL-2</td>
<td>65 580</td>
<td>29 113</td>
<td>4002</td>
</tr>
<tr>
<td>IL-2 + 0.01 μg/mL sCR1</td>
<td>ND</td>
<td>29 184</td>
<td>4163</td>
</tr>
<tr>
<td>IL-2 + 0.10 μg/mL sCR1</td>
<td>65 136</td>
<td>28 369</td>
<td>6210</td>
</tr>
<tr>
<td>IL-2 + 1.00 μg/mL sCR1</td>
<td>56 752</td>
<td>31 969</td>
<td>5710</td>
</tr>
<tr>
<td>IL-2 + 5.00 μg/mL sCR1</td>
<td>58 383</td>
<td>ND</td>
<td>5341</td>
</tr>
<tr>
<td>IL-2 + 10.00 μg/mL sCR1</td>
<td>66 532</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>IL-2 + 0.01 μg/mL sCR1</td>
<td>ND</td>
<td>252</td>
<td>243</td>
</tr>
<tr>
<td>IL-2 + 0.10 μg/mL sCR1</td>
<td>ND</td>
<td>263</td>
<td>165</td>
</tr>
<tr>
<td>IL-2 + 1.00 μg/mL sCR1</td>
<td>ND</td>
<td>241</td>
<td>201</td>
</tr>
<tr>
<td>IL-2 + 5.00 μg/mL sCR1</td>
<td>ND</td>
<td>ND</td>
<td>225</td>
</tr>
</tbody>
</table>

IL-2v indicates interleukin-2 vehicle; sCR1v, soluble complement receptor type 1 vehicle; IL-2, interleukin-2; sCR1, soluble complement receptor type 1; and ND, not done.

Cells were incubated with IL-2 (100 U/mL) and with various amounts of sCR1 for 22 hours and then pulsed with [3H]thymidine (1 μCi) for 2 hours. Results represent average of triplicates with <10% variability.
previous report demonstrating increased pulmonary neutrophil count in IL-2–treated rats16 strongly supports this possibility. Complement activation might also occur in response to PAF, a potent phospholipid inflammatory mediator (for review see Reference 44), which has been reported to mediate both IL-2–induced lung injury17 and complement-dependent processes such as red cell phagocytosis.45

IL-2 caused leukocyte sequestration, as evidenced by elevated pulmonary MPO activity. This is in accord with recent reports demonstrating leukocyte accumulation in lung tissue16 and increased neutrophil-endothelial adherence in the skeletal muscle microcirculation of IL-2–treated rats.12,46 Currently, no information is available as to the processes leading to IL-2–induced leukocyte adherence and emigration into lung parenchyma. Potential mechanisms are leukocyte and endothelial cell activation by (1) inflammatory mediators such as IL-147 or PAF,44 which are produced in response to IL-2,13,17 and (2) complement anaphylatoxins, which have been shown to carry chemotactic properties and to induce neutrophil aggregation (for review see Reference 48). The latter possibility is supported by our observation that treatment with sCR1 attenuated the IL-2–induced elevation of lung MPO activity; however, our data do not allow us to differentiate between IL-2 action on the leukocytes, endothelium, or both cellular elements.

Although our data support a potential therapeutic role for sCR1 and complement inhibitors in the pulmonary complications of IL-2, it should be noted that inhibition of the complement system, a major component of the host defense mechanism,49 may lead to immune suppression and enhanced susceptibility to infections. Since sCR1 effectively blocks both the alternate and classic pathways of complement activation, it might carry liabilities of complement suppression. However, such a possibility is more likely to be associated with chronic inhibition. In contrast, the therapeutic potential of sCR1 in IL-2–induced lung injury is likely to overshadow any potential immune suppression, because treatment is acute, and serum levels will precipitously decline on cessation of infusion (time to half activation, ~100 minutes).

TXA2, a key prostaglandin mediator of inflammation (for review see Reference 50), was elevated after IL-2 infusion. A similar response, which suggests TXA2 mediation of IL-2–induced lung injury, was previously reported by our group17 and by others.10 In contrast, several observations suggest that TXB2 is not directly involved in the pathogenesis of IL-2–induced lung injury. First, inhibition of TXB2 production by indomethacin failed to attenuate IL-2–induced lung injury. Second, sCR1 attenuated the lung injury produced by IL-2 without affecting the elevated serum TXB2. This phenomenon also suggests that complement is not involved in the processes leading to TXB2 production after IL-2 administration. The source of TXA2 production in response to IL-2 is still obscure. Nevertheless, one potential origin could be activated neutrophils.51 However, the reduction of lung MPO activity by sCR1 without attenuation of the elevated serum TXB2 does not support this possibility. Alternatively, TXA2 could be produced by aggregating platelets in response to IL-2.12 In that respect, platelet activation by IL-2 might result from stimulation by PAF, since rats pretreated with a PAF antagonist failed to elevate serum TXB2 in response to IL-2 infusion.17

In conclusion, the present study suggests that the pulmonary toxicity of IL-2 is mediated in part by complement factors and points to the potential therapeutic capacity of complement inhibitors in combating this grave complication of IL-2 immunotherapy.

References


Interleukin-2-induced lung injury. The role of complement.
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