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### Letter to the Editor

## Can pirfenidone prevent paraquat-induced pulmonary fibrosis?—A hypothesis

As you know, paraquat (PQ) poisoning is associated with a high mortality rate, mainly due to respiratory failure. This herbicide preferentially accumulates in the lung and its pulmonary effects are due to the participation of the polyamine transport system that is mostly expressed in the membrane of alveolar cells types 1 and 2 and Clara cells. The main molecular mechanism of PQ toxicity is based on redox cycling and intracellular oxidative stress generation [1–5]. After oxidative destruction, recruitment of the inflammatory cells exacerbates the injury [6]. Based on this mechanism, management and research efforts are directed toward the following: (1) Preventing accumulation of PQ in the lungs (such as decreasing its absorption and enhancing its elimination from the blood by forced diuresis and charcoal hemoperfusion); (2) preventing the generation of reactive oxygen species (ROS) by effective control of iron distribution using desferrioxamine; (3) scavenging ROS with maintenance of effective levels of antioxidants such as N-acetylcysteine and vitamin E; (4) repairing ROS-induced lesions with maintenance of effective levels of glutathione by administration of N-acetylcysteine; and (5) mainly, reducing acute alveolitis and pulmonary fibrosis by administration of anti-inflammatory and immunosuppressive drugs such as dexamethasone, methylprednisolone, cyclophosphamide, and N-acetylcysteine or corticosteroids in severe cases of toxicity [1,4,7–10]. Based on the current core concepts of PQ pathogenesis, it can be hypothesized that pirfenidone (5-methyl-1-phenyl-1H-pyridin-2-one; Pirespa®, Esbriet®), which is currently being approved for treatment of idiopathic pulmonary fibrosis [11], may prevent PQ-induced pulmonary fibrosis in severe cases of PQ intoxication. In addition to its antifibrotic properties, pirfenidone has other activities including anti-inflammatory and antihydroxyl radical activities [11]. Therefore, it seems that this agent theoretically can interrupt the inflammatory process in the course of PQ toxicity. This hypothesis should first be experimentally tested on animals and if it is shown that pirfenidone can prevent the development of PQ-induced pulmonary

fibrosis, a randomized controlled trial should be designed to evaluate the effect of this agent on patients with PQ poisoning.

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Conflict of interest: none.