Reviewer's report

**Title:** High Serum Concentrations of Autoantibodies to HSP47 in Nonspecific Interstitial Pneumonia Compared with Idiopathic Pulmonary Fibrosis

**Version:** 1  **Date:** 28 April 2008

**Reviewer:** Antje Prasse

**Reviewer's report:**

In the study by Kakugawa et al serum the concentration of HSP47 autoantibodies in patients with COP, UIP and NSIP was analyzed. The authors show a significantly higher level of HSP47 autoantibodies in idiopathic NSIP and hypothesize that these autoantibodies might help to discriminate between different IIP. The studied subject is of interest in itself and the authors are well-known in this field. However, the presented data are meagre and the study cohort small. The data is purely observational and over-interpreted, and it does not support the proclaimed possibility to discriminate between NSIP or not.

1.) The main hypothesis of the article that it might be possible to discriminate NSIP from other IIP by the measurement of serum HSP47 concentrations is, from my point of view, hazardous. The authors over-interpreted their findings by this hypothesis and I highly recommend the re-writing of the manuscript regarding this subject. First of all, the authors should give a scattergram to show the power of discrimination between the distinct disease groups. The actually presented figures do not support the main hypothesis of the article, because there is an overlap of HSP47 sera concentrations in patients with UIP versus NSIP.

2.) Given the fact that idiopathic NSIP is extraordinarily seldom, I wondered how the authors could include a similar amount of patients with UIP/IPF and NSIP in their study. The authors describe that they excluded underlying rheumatic disease by clinical and serologic signs, but what have they tested for? NSIP is most often seen in patients with systemic sclerosis or mixed connective tissue disease, and in these patients an increase of HSP47 has been shown. The authors should discuss the fact that most of the patients with idiopathic NSIP will develop rheumatic disease later on in the disease course. It would be of interest, if patients with UIP and rheumatic disease have increased HSP47 autoantibodies or not (e.g. UIP in line with systemic sclerosis and rheumatoid arthritis). In addition, if the authors would have included data from rheumatic diseases the authors could have argued that patients with NSIP display signs of auto-immunity in contrast to patients with UIP/ IPF.

3.) It would be highly interesting to show whether HSP47 autoantibodies are neutralizing or not. Additional, functional data would improve the manuscript a lot.

4.) The authors should state their criteria, by which they discriminate between
cellular and fibrotic NSIP. In addition, it is difficult for the reader to discriminate between group 2 and group 3 NSIP. Why did they not use fibrotic versus cellular NSIP?