Author’s response to reviews

Title: Development of an enzyme-linked immunosorbent assay for the detection of human calretinin in plasma and serum of mesothelioma patients

Authors:
Irina Raiko (raiko@ipa-dguv.de)
Ingrid Sander (sander@ipa-dguv.de)
Daniel G Weber (weber@ipa-dguv.de)
Monika Rauf-Heimsoth (raulf@ipa-dguv.de)
Adrian Gillissen (adrian.gillissen@web.de)
Jens Kollmeier (jens.kollmeier@helios-kliniken.de)
Arnaud Scherpereel (arnaud.scherpereel@chru-lille.fr)
Thomas Brüning (bruening@ipa-dguv.de)
Georg Johnen (johnen@ipa-dguv.de)

Version: 2 Date: 16 April 2010

Author's response to reviews:

Referee 1 (Ettore Seregni):
The sole but important point of critique was the small number of mesothelioma patients in our study to support our conclusions.

We have therefore more than doubled the number of mesothelioma samples (from 18 to 42) and added another control group of 35 asbestos-exposed individuals (besides the 97 healthy controls). We were able to confirm our initial results and the median of the tumor samples even increased slightly. The differences of the medians of the three groups are all statistically significant. We have modified our conclusions accordingly.

Referee 2 (Okio Hino):
The referee recommended “… more study to prove clinical usefulness”.

Therefore, we have increased the number of samples from mesothelioma patients from 18 to 42 and added a second control group (35 asbestos-exposed individuals without malignant disease, besides the 97 healthy controls). A differentiation of asbestos-exposed tumor-free persons (including those with benign diseases such as pleural plaques or asbestosis) and tumor patients would be of clinical relevance when screening a high-risk population of exposed persons. The differences of the medians of the three groups are all statistically significant. We also added a new figure that shows the performance of the assay regarding mesothelioma subtypes, indicating that there are no differences between epithelioid and biphasic mesothelioma. Because most of the other serum markers predominantly detect the epithelioid subtype, this might be a useful feature for clinical application. The number of mesothelioma cases might still be relatively small. However, the main purpose of the study was to describe
the development of the assay and to perform an initial assessment of the new marker. Only a much larger study with more cases and additional controls (benign pleural and lung diseases, tumors of the lung and other organs etc.) would be able to further assess the new ELISA regarding, e.g., tumor stage, histotype and differential diagnosis.