Does miR-1 Play a Role in Malignant Pleural Mesothelioma Development and Progression?

To the Editor:

We read with interest the article in CHEST (November 2013) by Xu et al.1 The authors reported the identification of miR-1 as a potential marker of mesothelioma and suggested that overexpression of miR-1 may induce apoptosis, thus making it a candidate therapeutic target.

We agree with the authors’ statement that a lack of a consistent normal comparator for malignant pleural mesothelioma studies has hampered efforts to identify consistent changes in microRNA expression across multiple profiling studies, despite these groups presumably using the best normal controls available at the time.2-4 Therefore, the use of unmatched normal pleura as a control series in the present study is a good choice and is likely to be the most appropriate control. However, we believe that there are several problems with the experimental design and presentation of data in this article, and these make it difficult to draw firm conclusions.

First, it is unclear why validation of candidate microRNAs was performed in only four of 26 tumors instead of all tumors subjected to microarray profiling. Normal practice is to technically replicate, using an independent method, in all of the samples assayed by microarray rather than cherry picking. Second, it is unclear why the authors selected only miR-1 for further analysis when other microRNAs from the same family demonstrate greater underexpression, and why they chose to validate known apoptosis genes instead of analyzing the correlation between miR-1 and its (predicted) direct targets. Third, there is a general lack of detail regarding methodology; for example, there is no detail regarding how reverse transcription-quantitative polymerase chain reaction was performed and analyzed and no mention of the amount of pre-microRNA used in functional assays. Finally, it would be helpful if the authors had put their study into context with previous profiling studies, as at least one of their “novel” microRNAs, miR-34b, was the subject of an extensive analysis published in 2011 by Kubo et al.5

Based on the lack of essential details as outlined, it is difficult to judge whether this study has contributed significantly to the field. Rigorous validation both technically and biologically is required to ensure that selected candidates are not false positives and are detectable in various datasets. Sufficient experimental detail is also required to ensure experiments can be easily replicated by independent laboratories and to prevent further confusion in what is already a murky field.

Response

To the Editor:

We appreciate the comments of Ms Wright and colleagues about our recent article.1 Unfortunately, we disagree with their conclusion that our study did not contribute to knowledge about the role of microRNA in mesothelioma.

We did not “cherry pick” our validation samples, but instead selected them because these tissue specimens were plentiful and would not be exhausted. Selected validation, using a subset of microRNA and tissue specimens, of array profiling data is the most reasonable, cost-effective design. This strategy is a well-accepted practice in current literature, including the article by Kubo et al.2

References