LETTER

Proinflammatory Role of *let-7* miRNAs in Experimental Asthma?

Polikepahad *et al*. (1) recently reported that *let-7* microRNAs have proinflammatory roles because inhibition of *let-7a* to *let-7d* alleviated the features of experimental asthma. However, there are serious drawbacks in the study design and interpretations. First, the *in vivo* findings in an IL-13-driven asthma model are exactly opposite to their *in vitro* observations where they found that *let-7* inhibited IL-13. Although they suggest that this discrepancy could be because of secondary and tertiary effects of *let-7* inhibition on the other proinflammatory genes, this is at best speculative and no evidence is provided in support. Second, because there was no change in *let-7* in the asthma model, it is unclear why they chose to inhibit only a few selected *let-7* members, whereas abundant *let-7* members like *let-7f* were not inhibited. This is worrisome because all *let-7* members share the seed region match with IL-13, and a loss of function experiment cannot be properly done unless all members were inhibited. Third, they do not report a more relevant gain-of-function experiment where any of the *let-7* members could have been used to inhibit IL-13 *in vivo*. This is particularly surprising because it would be the logical follow-through of their *in vitro* data. In absence of this critical experiment, we consider their counterintuitive conclusions to be unreliable and possibly due to existence and/or bystander increase in other *let-7* members due to Dicer negative feedback loop (2, 3). Thus the proinflammatory role of Let-7 in asthma is not well justified and further investigations are required to determine the exact role of *let-7* in asthma.

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