Reviewer’s report

Title: Reevaluation of the 22-1-1 antibody and its putative antigen, EBAG9/RCAS1, as a tumor marker

Version: 2 Date: 24 March 2005

Reviewer: SATOSHI INOUE

Reviewer’s report:

Major Compulsory Revision

Basically, the authors do not attend to the critical point that was criticized by this reviewer. Although the authors well understand that the 22-1-1 epitope is distinct from the protein encoded by RCAS1 cDNA and it was Nakashima et al. who showed that RCAS1 is a tumor-associated antigen recognized by the 22-1-1 antibody, it is not fair that the authors still use the term EBAG9 in this manuscript. The authors misunderstand that EBAG9 cDNA was identified later than RCAS1 cDNA, the former was originally reported in 1998 (Watanabe et al., Mol Cell Biol 18: 442, 1998) in comparison with the latter in 1999. Actually, Nakashima et al. refer to the EBAG9 paper in their Nature Medicine article. After the publication by Nakashima et al. and the following immunohistochemical studies using the 22-1-1 antibody, it has been most a general consensus that RCAS1 is an apoptosis-promoting and immunosuppressive antigen especially in tumor immunity. We think that the strong message of this manuscript is the contradiction against the definition by Nakashima et al. in terms of RCAS1 as the 22-1-1 epitope, which has been evaluated by a tumor-specific marker. Their intention can be well observed in Figure 6 as they showed that the finding by Nakashima et al. regarding an apoptosis-inducible function of RCAS1 was not confirmed by their hands. Based on this viewpoint, it is RCAS1 that should be compared with the 22-1-1 antigen even Nakashima et al. accidentally isolated the RCAS1 cDNA that was identical to EBAG9 cDNA through an expression cloning using the 22-1-1 antibody. In other words, the term RCAS1 itself includes entity that the molecule is a cell surface tumor-associated antigen that suppresses immune responses through inducing apoptosis, where as the term EBAG9 definitely does not.

Overall, the publication of this manuscript may further confuse the broad readers of this journal unless the authors do not change their claim. The authors should use the term “RCAS1” in title, abstract and text. The “RCAS1” itself should be reevaluated.

What next?: Reject because scientifically unsound

Level of interest: An article of limited interest

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:

I declare that I have no competing interests.