Reviewer's report

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

**Version:** 2  **Date:** 10 May 2005

**Reviewer:** Claus Belka

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The open question is related to the history of the protein RCAS1 the protein EBAG9 and the 22.1.1 antigen. Using the 22.1.1 antigen the cDNAs for both of the above mentioned proteins were cloned and were found to be identical. However the 22.1.1 antigen is likely to be something different. The reviewer now suggest rejection of the paper by the Rehm group based the fact that they used more or less exclusively the term EBAG9 when analysing the relationship between EBAG9/RCAS1 and the 22.1.1 antigen.

As editorial board member I have now been asked to sort all arguments and come to a final recommendation:

1.) The available literature suggests clearly that the terms EBAG9/RCAS1 are used synonymously and refers to the same protein.

   This fact is obviously known by the reviewer since in one of his recent paper he says: “Estrogen receptor-binding fragment-associated gene 9 (EBAG9) has been identified as a primary estrogen-responsive gene from MCF-7 human breast cancer cells [] EBAG9 is identical with RCAS1 (receptor-binding cancer antigen expressed on SiSo cells), which has been reported as a cancer cell surface antigen implicated in immune escape []” Int J Cancer. 2003 EBAG9/RCAS1 expression and its prognostic significance in prostatic cancer. Takahashi S, Urano T, Tsuchiya F, Fujimura T, Kitamura T, Ouchi Y, Muramatsu M, Inoue S.

   Thus, it is the free choice of the author which term he prefers. The fact that a reviewer suggested to use the term RCAS1 rather EBAG9 is not adequate to reject a paper as “scientifically unsound”. Furthermore, the reviewer himselfs recently published a paper on the same protein using the term EBAG9 and found a protein distribution pattern at least similar to the pattern shown by the Rehm group. (Ogushi T, Takahashi S, Takeuchi T, Urano T, Horie-Inoue K, Kumagai J, Kitamura T, Ouchi Y, Muramatsu M, Inoue S. Estrogen receptor-binding fragment-associated antigen 9 is a tumor-promoting and prognostic factor for renal cell carcinoma. Cancer Res. 2005 May 1;65(9):3700-6).

2.) The original question raised by the authors in how far the 22.1.1 antigen is related to the EBAG9/RCAS1 story is adequately addressed. They provide definitively enough evidence showing that EBAG9 and 22.1.1 are not related. Furthermore their suggestion that data derived from experiments using antibodies against the 22.1.1 antigen based on the assumption that 22.1.1 is RCAS1/EBAG9 should be critically revisited is clearly valuable for a wider group of scientists.

   Taken together, the only criticism raised by the reviewer 1 is the fact that he does not agree with the use of the term EBAG9. For me, no other clear scientific reasons are given which are of suitable weight to reject this paper.

   Thus I would finally recommend a rapid acceptance of this paper in order to avoid further delays.