Reviewer’s report

Title: Neoadjuvant administration of Semliki Forest virus expressing interleukin-12 combined with attenuated Salmonella eradicates breast cancer metastasis and achieves long-term survival in immunocompetent mice

Version: 2
Date: 19 May 2015
Reviewer: Walter Storkus

Reviewer’s report:

Kramer and colleagues report that an intratumoral IL-12 gene therapy using a recombinant, cytopathic SFV delivery vector along with Salmonella Typhimurium LVR01 neoadjuvant is synergistically effective in preventing disseminated disease after surgical resection of primary treated disease in a murine orthotopic breast cancer (4T1) model. More than 90% of mice treated with the combined approach exhibited long-term survival benefits and protective resistance against tumor rechallenge. Operationally, the most robust treatment results were obtained when the IL-12 gene therapy preceded administration of the LVR01 neoadjuvant. The report is generally well-written and the “clinical” studies appropriately designed, performed and interpreted.

The major weakness reflects the minimal immune monitoring performed in this report (i.e. only total numbers of T cell subsets in the lymph nodes of treated animals). One would anticipate that durable systemic protection afforded by the effective combined therapy would be linked to higher levels of Type-1 anti-4T1 T effector (and/or central memory) cells and that the ineffective therapies would promote lower levels of such responses. At present, we have no sense of tumor-specific T cell endpoints “on trial” which severely limits enthusiasm for the take home message for this immunotherapy approach and its potential for translation into the clinic.

(Minor) The Introduction is nearly 4 pages in length and should be consolidated to about 2 pages by focusing on the most crucial background points.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests.