Reviewer’s report

Title: Up-regulated expression of type II very low density lipoprotein receptor correlates with cancer metastasis and has a potential link to beta-catenin in different cancers

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Reviewer: Hideto Yamada

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The authors showed that higher VLDLR II expression levels in tumor tissues were associated with lymph node and distant metastasis in some cancers. They also showed that significant positive correlations were found between VLDLR II and beta-catenin in some cancers, claiming a potential link between VLDLR II and beta-catenin signaling pathway. These results are interesting and the conclusions contain an important message to the broad audiences of BMC Cancer. However, several points below should be appropriately addressed.

Major Comments

1. This study shows that VLDLR II expression in breast cancer is highest, followed by gastric and lung cancer. VLDLR is well known for its role in lipoprotein uptake and metabolism. On the other hand, some researchers have recently indicated the impact of diet and obesity on breast cancer, whereas cancer itself sometimes causes appetite loss, which leads to weight loss. Thus, other features including body weight (or body mass index) and plasma lipid profiles (such as triglycerides, total cholesterol, LDL-cholesterol and HDL-cholesterol) should be mentioned in Table 2, 3 and 4. Is there any relationship between VLDLR II expression and the other clinical features?

2. The importance of VEGF and angiogenesis should be experimentally addressed to strengthen the relationship between VLDLR II expression and distant metastasis. For example, does VEGF expression in cancer tissues correlate with VLDLR II expression and distant metastasis?

Minor comments

3. I am a little confused by the classification regarding TNM stage and Tumor size in Table 2, 3, and 4. For example, at the Tumor size in Table 3, 25 patients have the tumor whose size is no more than two centimeters, which is considered as T1 because T1 in breast cancer means that the tumor is no more than two centimeters and T2 means that the tumor is more than two centimeters. On the other hand, at the TNM stage in Table 3, you state that 24 patients have the tumor considered as T1 or T2. If they were true, the sum of the number of patients having T1 and T2 (24 patients) would be less than the number of patients having T1 only (25 patients). I am curious to know the explanation for this and the way you divided patients with cancer into each subgroup regarding
TNM stage and Tumor size in Table 2-4.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests.