Reviewer's report

Title: COUP-TFI modifies CXCL12 and CXCR4 expression by activating EGF signaling and stimulates breast cancer cell migration

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Reviewer: Yeon Sun Seong

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The manuscript titled ‘COUP-TFI modifies CXCL12 and CXCR4 expression by activating EGF signaling and stimulates breast cancer cell migration’ showed the role of COUP-TFI in relation with E2 signaling in metastasis of breast cancer cell by regulating the CXCL12/CXCR4 axis as well as proliferation. The author’s research in this manuscript is solid and a well-designed work and proposes novel mechanism regarding the role of COUP-TF1 in regulation of CXCL12/CXCR4 and finally correlated with the RNA level of COUP-TFI, CXCL12 and CXCR4 in clinical breast cancer tissue samples. The authors showed the increased expression of CXCR4 and decreased expression of CXCL12 at the level of promoter, mRNA transcription and protein expression in tested cell lines. The authors demonstrated the increased migration capability in COUP-TF overexpression cells was related with CXCR4/CXCL12 using chamber migration assay including CXCL12 and antagonist of it. Finally the authors correlated the altered expression of COUP-TFI, CXCR4, 7 and CXCL12 with SBR grade of breast cancer. This research article is well demonstrated and scientifically and medically significant and deserves to be published.

Major Compulsory Revisions

None

Minor Essential Revisions

1. Page 18 – 21, there are numbers of unidentified letters between reference journal name and year of publication in reference.

Ref 2, 3, 5, 6, 9, 11, 12, 13, 15, 19, 20, 21, 22, 24, 26, 27, 28, 29, 30, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42

2. Regarding abbreviation list of EMT in Page 17, line 3, there is no ‘EMT’ description in this manuscript.

3. Page 23, line 25 ‘asterisk’ should be ‘pound’.

4. In Figure 5 A, the Y axis title (Relative migration) should be ‘Relative cell number’.

Discretionary Revisions

1. The authors previously observed the change of E2 responsive genes in COUP-TFI overexpressing stable cell lines using RT-PCR (ref 9). Among them CXCL12/SDF-1 was increased in COUP-TFI constitutive overexpressing MCF-7
cell (MCF-7/CP). In this work the authors used stable cell line similar to previous system. It might be encouraged to check the change of CXCL12 and CXCR4 expression after transient knock down of COUP-TFI by siRNA.

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

**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.