Author’s response to reviews

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

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**Version:** 2  
**Date:** 6 December 2013

**Author’s response to reviews:** see over
Dear Editor, 

December 6, 2013

Would you please consider our manuscript, entitled "COUP-TFI modifies CXCL12 and CXCR4 expression by activating EGF signaling and stimulates breast cancer cell migration ", for publication in Breast Cancer Research.

Some recent studies have reported that orphan nuclear receptor COUP-TFII is overexpressed in cancer cells of various origin and suggested its role in cancer progression. Nevertheless, very little studies explored the exact roles of COUP-TFI in breast cancer cells. In this study, we report both in vitro and in vivo data indicating that COUP-TFI could be involved in breast cancerization. Considering the importance of CXCL12/CXCR4 signaling in tumor growth and metastasis, delineating molecular events of COUP-TFI-regulation of this signaling axis, in breast cancer cells, is very important. Our results show for the first time the mechanisms by which COUP-TFI selectively and differentially modifies the expression levels of CXCL12/CXCR4 in breast cancer cells. This is correlated with our quantitative analysis of CXCL12/CXCR4 expression profiles obtained from breast tumors and control non-tumor samples. This study is also an original work because while COUP-TFI modifies the balance of CXCL12/CXCR4 expression, it contributes to phenotypical changes of cancer cells, notably it enhances cell migration toward a CXCL12 gradient.

We believe that this work contributes to the comprehension of COUP-TFI roles in breast cancer cell proliferation and migration; and will interest all scientists in the field of molecular actions of nuclear receptors in breast cancer.

We thank you for your time and consideration in handling this manuscript.

Yours sincerely,

F. PAKDEL (PhD)