



SDI Review Form 1.6

Journal Name:	Journal of Cancer and Tumor International
Manuscript Number:	2015_JCTI_18131
Title of the Manuscript:	MiRNA and target oncogenes in Triple negative breast cancer; major players in age and ethnic related neoplastic events
Type of the Article	Review Article

General guideline for Peer Review process:

This journal's peer review policy states that **NO** manuscript should be rejected only on the basis of '**lack of Novelty**', provided the manuscript is scientifically robust and technically sound.

To know the complete guideline for Peer Review process, reviewers are requested to visit this link:

(<http://www.sciencedomain.org/page.php?id=sdi-general-editorial-policy#Peer-Review-Guideline>)



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PART 1: Review Comments

	Reviewer's comment	Author's comment (if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)
Compulsory REVISION comments		Author owes a great deal of gratitude to the reviewer for his/her contributions to this article.
Minor REVISION comments	1/ Do the results up to now support a definite framework for clinical development of microRNAs inhibitors-based therapeutic strategy in this still incurable disease? 2/ Do familial cases prevent us from observing a direct effect of microRNAs (for example miR-342 on BRCA1)? 3/ Please have a look to the following link. It appears to include very helpful information enabling authors to improve their discussion and conclusions: http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0087039	No. However future research, based on previous studies, may provide that "definite framework". 2. Yes, because most of the cases are BRCA1-mutants 3 Done. Lines 273-288: ID4 is a transcription factor of the helix-loop-helix protein family whose expression is inversely correlated with that of ER. ID4 is expressed in breast cancer, especially triple negative breast cancers [105] and can negatively regulate BRCA1 expression. Increased expression of ID proteins has been reported in several cancer types [106-108] and has been found associated with loss of differentiation, enhanced malignancy and aggressive clinical behavior [109,110]. ID4 is involved in mammalian embryogenesis, angiogenesis and in the maintenance of cancer stem cells [111-113]. Additionally, increased ID4 expression is associated with the ability of breast cancer cells to exhibit anchorage-independent growth, while its depletion determined their morphological change to large and flat epithelial phenotypes



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		[114]. The finding that ID4 is a negative regulator of the tumor suppressor gene BRCA1 [114-116] supports an oncogenic function of ID4. In breast cancer, miR-342 which has been speculated to have a role in reducing the expression of BRCA1 [117] is associated with better prognosis [118,119]. The reports of Crippa et al. [117] showed an inverse correlation between ID4 and miR-342 as well as between ID4 and BRCA1 expression. According to their reports, overexpression of miR-342 in breast cancer cells (as seen in MDA-MB-231 breast cancer cell line) reduced ID4 and increased BRCA1 expression, supporting a possible role of this mechanism in breast cancer. Thus, inhibiting miRNA target oncogenes may provide definite framework for clinical breast cancer therapy. Conclusion This present review has provided insight into the roles of miRNA expressions and their validated targets in TNBC in relation to metastases and overall survival rate. More so, it has provided knowledge of the risk factors, especially the BRCA1 mutation, KRAS and ID4 oncogenes, and the place of Epithelial-to-Mesenchymal Transition (EMT) in the pathogenesis of TNBC. The discovery of miRNAs which function by modulation of some target oncogenes have created future possible therapeutic frameworks for TNBC, this is due to fact that certain target oncogenes have been successfully altered through inhibitory systematic pathways. These insights may provide future novel diagnostic tools and effective management scheme for all breast cancer subtypes. However, more studies are required to unveil the causes of high prevalence of TNBC in the affected age and ethnic groups.
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<u>Optional/General</u> comments	Excellent review covering extensively this particular field of research. Authors are advised to include a few sentences in discussion and in conclusions as far as future therapeutic strategies are concerned in relation to miRNAs	Ok.
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