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RNA editing alters microRNA targeting in human breast cancer

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RNA editing by RNA specific adenosine deaminase (ADAR) is increasingly being found to alter microRNA (miR) regulations. Editing of miR transcripts can affect their processing as well as what mRNAs they target. Further, editing of target mRNAs can also affect their complementarily to miRs. Notably, ADAR editing is often increased in malignancy with the effect of these RNA changes largely unclear. In addition, reports have also identified many miRs to be differentially expressed in cancer though the majority of their targets are also undefined. Here we propose that modulating the targets of miRs via mRNA editing can play a direct role in the pathology of many carcinomas. In order to more accurately characterize the relationship between these two regulatory processes this study examined RNA editing events within mRNAs sequences of two breast cancer cell lines (MCF-7 and MDA-MB-231) and determined whether or not these edits modulate miR associations. Computational analyses of RNA-Seq data from the two cell lines identified over 250,000 edit sites within mRNAs, many of which were located in 3' UTR regions. When these locations were screened against the list of currently annotated miRs we discovered that editing caused a subset (~5%) to have significant alterations to mRNA complementarity. One miR in particular, miR-140-3p has been shown to be abhorrently expressed in many breast cancers. Interestingly, we found that mRNA editing made this specific miR able to target the apoptosis inducing gene DFFA in MCF-7 but not in MDA-MB-231 cells. As these two cell lines are known to have distinct characteristics in terms of morphology, invasiveness and physiological responses, it is feasible that RNA editing could contribute to the phenotypic differences observed between the two cell lines and help explain why an increased incidence of ADAR activity is detected in a number of malignancies. Broadly, these results suggest that the creation of miR targets may be an underappreciated function of ADAR and may help further elucidate the role of RNA editing in tumor pathogenicity.

Biography

Glen M Borchert has completed his PhD in Genetics from University of Iowa in the year 2006. He did his first Postdoctorate in Structural Biology from University of California in the year 2008 and the second one in Immunology from Illinois State University in the year 2012. After which he joined as Assistant Professor in University of South Alabama and currently working as Assistant Professor, Pharmacology in USA College of Medicine. He has been honored by NIH with a Research award to study hypoxia induced mutation. Also, National Science Foundation (NSF) gave him the CAREER award of $533,000 to research miRNA targeting.

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