Abstract Template

Title: Post-zygotic Mosaic Mutations in Normal Tissues of Breast Cancer Patients and Pharmacogenomics

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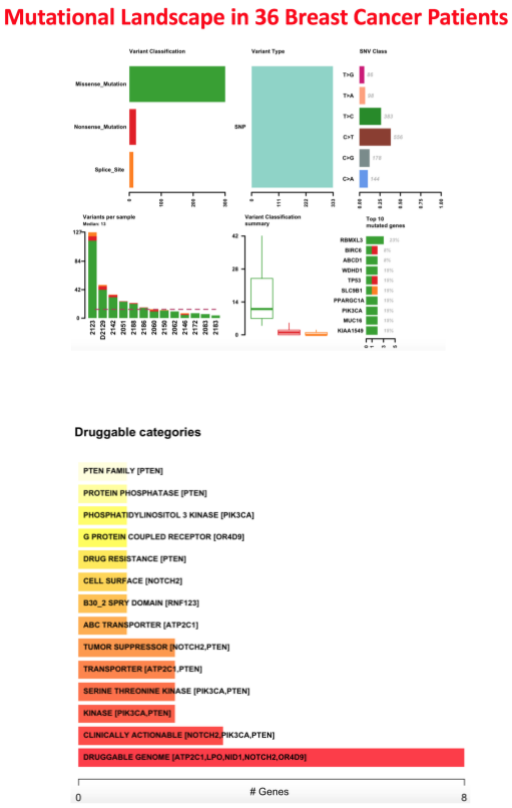
Keywords: post-zygotic mosaic mutation, breast cancer

1. Abstract

Even though numerous previous investigations had shed fresh light on somatic mutations in cancer tissues, the mutation-driven transformation mechanism from normal to cancerous tissues remains still mysterious. In this study, we performed whole exome sequencing analysis of paired normal and cancer samples from 36 breast cancer patients in order to elucidate the post-zygotic mosaic mutations that might affect the predisposition to breast cancer. We found 10 post-zygotic mosaic mutations from 5 breast cancer patients (PIK3CA p.F1002C, PTEN p.D265Y, NOTCH2 p.A1721G, RNF123 p.V951A, TMEM191C p.L165P, LPO p.I611M, OR4D9 p.H131Q, NID1 p.S1139T, HSPA6 p.V473I, ATP2C1 c.422+2T>C) with less than 5% of variant allele fraction in normal tissues, whose respective VAFs in their matched breast cancer tissues had increased by more than 20%. Such expansion of variant allele fractions from normal to cancer tissue may implicate those mosaic mutations in association with the causation underlying the breast carcinogenesis. Most of the post-zygotic mosaic mutations are estimated to be deleterious mutations by relatively well-established mutation annotation software programs, SIFT_pred, Polyphen2_HDIV_pred, Polyphen2_HVAR_pred, LRT_pred, MutationTaster_pred, FATHMM_pred, PROVEAN_pred, fathmm.MKL_coding_pred, MetaSVM_pred, and MetaLR_pred. By performing analysis of 18 well-known drug-gene interaction databases as a pharmacogenomics approach, we identified possible candidate drugs targeting those genes harboring the mosaic mutations. Taken together, these results imply that post-zygotic mosaic mutations may be targets for diagnosing and treating breast cancer patients in the upcoming future.



2. Image:



3. Recent publications

1: Ryong Nam Kim. Mutational Mosaicism in Breast Cancer. J Pharm Sci Emerg Drugs 2019, 7:2

2: Kim S, Lee AC, Lee HB, Kim J, Jung Y, Ryu HS, Lee Y, Bae S, Lee M, Lee K, Kim RN, Park WY, Han W, Kwon S. PHLI-seq: constructing and visualizing cancer genomic maps in 3D by phenotype-based high-throughput laser-aided isolation and sequencing. Genome Biol. 2018 Oct 8;19(1):158.

3: Kim RN, Moon HG, Han W, Noh DY. Perspective Insight into Future Potential Fusion Gene Transcript Biomarker Candidates in Breast Cancer. Int J Mol Sci. 2018 Feb 7;19(2). pii: E502.

4: Kwon MJ, Kim RN, Song K, Jeon S, Jeong HM, Kim JS, Han J, Hong S, Oh E, Choi JS, An J, Pollack JR, Choi YL, Park CK, Shin YK. Genes co-amplified with ERBB2 or MET as novel potential cancer-promoting genes in gastric cancer. Oncotarget. 2017 Sep 21;8(54):92209-92226.

5: Jeong HM, Kim RN, Kwon MJ, Oh E, Han J, Lee SK, Choi JS, Park S, Nam SJ, Gong GY, Nam JW, Choi DH, Lee H, Nam BH, Choi YL, Shin YK. Targeted exome sequencing of Korean triple-negative breast cancer reveals homozygous deletions associated with poor prognosis of adjuvant chemotherapy-treated patients. Oncotarget. 2017 Jun 27;8(37):61538-61550.

6: Lee MS, Kim RN, I H, Oh DY, Song JY, Noh KW, Kim YJ, Yang JW, Lira ME, Lee CH, Lee MK, Kim YD, Mao M, Han J, Kim J, Choi YL. Identification of a novel partner gene, KIAA1217, fused to RET: Functional characterization and inhibitor sensitivity of two isoforms in lung adenocarcinoma. Oncotarget. 2016 Jun 14;7(24):36101-36114.

4. Biography

Dr. Ryong Nam Kim had completed his PhD in a major of Functional Genomics and has his expertise in discovering biomarker and pharmaceutic drug candidates by applying genomics and pharmacogenomics approaches to diverse cancer types, including breast, lung and stomach cancers.

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