World Journal of Pharmacology & Toxicology

Abstract

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

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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.

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.

Recent Publications:

1. Ryong Nam Kim, et al BMC Cancer, 2020.
2. Ryong Nam Kim, et al Micromachines (Basel), 2020.
3. Ryong Nam Kim, et al Cancer Res Treat, 2020.
4. Ryong Nam Kim, et al Genome Biol, 2018.
5. Ryong Nam Kim, et al Int J Mol Sci, 2018.
6. Ryong Nam Kim, et al Oncotarget, 2017.
7. Ryong Nam Kim, et al Oncotarget, 2017.

Webinar on Pharmaceutical Chemistry | May 22, 2020 | Paris, France

Citation: Ryong Nam Kim; Post-zygotic Mosaic Mutations in Normal Tissues of Breast Cancer Patients and Pharmacogenomics; Pharmaceutical Chemistry 2020; May 22, 2020; Paris, France