**Editorial: GAPDH should be prohibited as housekeeping gene for internal normalization in human cancer research**

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Running Title: Optimized Housekeeping as Internal Control

GAPHD as a stable expressed house-keeping gene has been widely applied as the internal control for the real-time PCR (RT-PCR) to normalize the gene expression since last centery1. However, in our own experience and previous reports (Reference), different internal control or housing-keeping gene selection sometimes provides obviously different result and corresponding interpretation. Effective internal control could help researcher to avoid common sense errors and misstatement of the study. It also help the independent researcher to compare the result with each other to increase the reproducibility of the human medical research in which inter-variation and intra-variation should be significantly limited between cancer and normal samples as well as among different cancer types. GAPHD is not suitable to be used in colorectal cancer has been mentioned previously2. However, it is not discussed or extended to other cancers. Here, in order to evaluate the reasonability for the best house-keeping genes to be considered as the most effective internal control, we conducted differential gene expression and survival analysis to >2,000 human house-keeping genes which were manually collected recently with TCGA Pan-cancer dataset which have been frequently used in our previous studies (reference). Sparingly, we found more than 22.1% house-keeping showed significantly differential gene expression between cancer and normal samples (meta-analysis to 23 cancer types with xx sample, random effect model, P<2.5x10-5) and 40% showed significantly variation between different cancer types (meta-analysis, random-effect model, I2> ). Furthermore, we found more than 7.2% housing keeping genes showed significant association with overall survival time (mete-analysis, fix-effect model, P<2.5x10-5). Finally, we found xx house-keeping genes showed over-expression in cancer and belong to significant risk factors for overall survival time (for example, xxx, xx, xx, and xx) while xx house-keeping genes showed down-regulation and played as protective factors for overall survival time (for example, xx, xx, xx, and xx).

Actually, GAPDH plays multiple roles in apoptosis3,4, inflammation5 and cell death and carcinogenesis which indicating it might be significantly related with cancer status, progress and prognosis.

Reference

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