EBioMedicine 7 (2016) 7–8

Contents lists available at ScienceDirect

EBioMedicine

journal homepage: www.ebiomedicine.com

Commentary

Diagnostic Potential of lncRNAs in Cancer

Chi Han Li [a], Yangchao Chen [a,b,c,*]

[a] School of Biomedical Sciences, Faculty of Medicine, The Chinese University of Hong Kong, Shatin, Hong Kong
[b] Shenzhen Research Institute, The Chinese University of Hong Kong, Shenzhen, China
[c] State Key Laboratory of Digestive Disease, Institute of Digestive Disease, The Chinese University of Hong Kong, Shatin, NT, Hong Kong

ARTICLE INFO

Available online 12 May 2016

For decades, diversification of cancers, in terms of origin of organs or cell types, allows precise understanding of genetic and epigenetic aberrations. Indeed, this approach has vastly improved cancer management for numerous cancer types. For instance, patients of breast cancer are benefitted by different management schemes according to distinct breast cancer subtypes (i.e. luminal A, luminal B, HER2 and basal-like). It is widely accepted that the feasibility of personalized medicine battling cancer is laid by exploiting the complete malignant/driver events within a particular cancer subtype. However, the direction of cancer research is tilted recently by a suggestion that cancer management can be improved by bringing out a bigger picture of the cancer population. Here, the idea of pan-cancer analysis is raised by The Cancer Genome Atlas (TCGA) program in which different cancer types are gathered together for analysis, as it is believed that diverging driver events among various cancer types most often generate converging genetic signatures and biological pathways during cancer development. The pan-cancer analysis project builds a joint data set from separate TCGA disease projects of multiple cancer types, which increases the statistical power to detect functional genomic determinants of disease. Subsequently, it allows the identification of both tissue-specific aspects of cancer and intrinsic molecular commonalities across tumor types (Cancer Genome Atlas Research Network et al., 2013). With this approach, several groups have already identified critical oncogenic signatures (Ciriello et al., 2013), mutation landscape (Kandoth et al., 2013) and microRNA-target interactions (Jacobsen et al., 2013) across diverse cancer types. In this issue of EBioMedicine, Ching et al. utilize the pan-cancer analysis to explore the diagnostic and prognostic potentials of long non-coding RNAs (lncRNAs), and subsequently reveal a panel of six lncRNAs as biomarkers for multiple cancer types (Ching et al., 2016).

Previous work showed that lncRNAs show higher tissue specificity compared to mRNAs (Derrien et al., 2012). The work of Ching et al. supported this notion, and extended it by showing a reduction of specificity after malignant transformation, which is consistent with the de-differentiation status of cancers widely observed. They further show that lncRNA profiles in cancer cells are highly specific to distinct cancer types, which pinpoint the predicting values of lncRNA expressions during cancer management. Numerous studies have demonstrated the potential of different lncRNAs for cancer diagnosis and prognosis, but the investigations are mainly focusing on a single cancer subtypes. Ching et al. take a global approach and identify six pan-cancer lncRNAs that robustly and accurately predict a wide range of cancer types. The six pan-cancer lncRNAs are also meritorious in predicting overall survival and relapse free survival in different cancer types. This finding should have laid the foundation for the development of biomarker screening platform for non-invasive testing of cancer incidence and outcome. More importantly, the pan-cancer analysis approach makes the translation of the finding more convenient, and shortens the timeframe of clinical trials because of the availability of a larger pool of patients. This may be an important step towards a more practical health-checking module in the future. On the other hand, the role of the putative pan-cancer lncRNAs identified in this study is potentially pivotal to cancer biology. It is interesting that their analysis suggested that well characterized lncRNAs such as HOTAIR does not meet the stringent selection criteria as a pan-cancer lncRNA, despite its frequently association and overexpression in several cancer types such as breast cancer (Gupta et al., 2010), liver cancer (Yang et al., 2011), and pancreatic cancer (Kim et al., 2013). Given the consistent expression pattern of pan-cancer lncRNAs across cancer types, it is interesting to extrapolate the possible roles of every one of them. Although as biomarkers, the pan-cancer lncRNAs may not necessarily link to any driver event as passenger genetic alterations can still demonstrate good value of prediction. Ching et al. has shown that they may regulate critical pro-cancerous effects such as cell proliferation and cell migration. Future study is warranted to unveil the underlying reason for their consistency across different cancer types. It is also of interest to understand the difference between these pan-cancer lncRNAs with other cancer-associated lncRNAs regarding their roles in cancer.

As pointed out by the pioneers of the pan-cancer project, there are still limitations of analysis across cancer types in terms of inconsistent data acquisition method, incompatible clinical data across cancer

DOI of original article: http://dx.doi.org/10.1016/j.ebiom.2016.03.023.
* Corresponding author at: School of Biomedical Sciences, Faculty of Medicine, Chinese University of Hong Kong, Shatin, Hong Kong.
E-mail address: frankch@cuhk.edu.hk (Y. Chen).

http://dx.doi.org/10.1016/j.ebiom.2016.05.013

types and false-positive discovery due to loosen statistical analysis (Cancer Genome Atlas Research Network et al., 2013). Nonetheless, diversification of cancer is still proven to be the essential strategy in exploiting the uniqueness of every cancer types, as agreed by the Ching et al. As such, it is possible to pick the suitable candidates out of various targets for effective pharmaceutical intervention, as the current technology is limiting the selection of druggable targets.

References

Cancer Genome Atlas Research Network, Weinstein, J.N., Collisson, E.A., Mills, G.B., Shaw, K.R., Ozenberger, B.A., Ellrott, K., Shmulevich, I., Sander, C., Stuart, J.M., 2013. The Cancer Genome Atlas Pan-Cancer analysis project. Nat. Genet. 45 (10), 1113–1120 (Oct).

Ching, T., Peplowska, K., Huang, S., Zhu, X., Shen, Y., Molnar, J., Yu, H., Tiirikainen, M., Fogelgren, B., Fan, R., Garmire, L.X., 2016. Pan-cancer analyses reveal long intergenic non-coding RNAs relevant to tumor diagnosis, subtyping and prognosis. EBioMedicine 7, 62–72.

Ciriello, G1., Miller, M.L., Aksoy, B.A., Senbabaoglu, Y., Schultz, N., Sander, C., 2013. Emerging landscape of oncogenic signatures across human cancers. Nat. Genet. 45 (10), 1127–1133 (Oct).

Derrien, T., Johnson, R., Bussotti, G., Tanzer, A., Djebali, S., Tilgner, H., Guernec, G., Martin, D., Merkel, A., Knowles, D.G., Lagarde, J., Veeravalli, L., Ruan, X., Ruan, Y., Lassmann, T., Carninci, P., Brown, J.B., Lipovich, L., Gonzalez, J.M., Thomas, M., Davis, C.A., Shiekhattar, R., Gingeras, T.R., Hubbard, T.J., Notredame, C., Harrow, J., Guigó, R., 2012. The GENCODE v7 catalog of human long noncoding RNAs: analysis of their gene structure, evolution, and expression. Genome Res. 22 (9), 1775–1789 (Sep).

Gupta, R.A., Shah, N., Wang, K.C., Kim, J., Horlings, H.M., Wong, D.J., Tsai, M.C., Hung, T., Argani, P., Rinn, J.L., Wang, Y., Brzoska, P., Kong, B., Li, R., West, R.B., van de Vijver, M.J., Sukumar, S., Chang, H.Y., 2010. Long non-coding RNA HOTAIR reprograms chromatin state to promote cancer metastasis. Nature 464 (7291), 1071–1076 (Apr 15).

Jacobsen, A., Silber, J., Harinath, G., Huse, J.T., Schultz, N., Sander, C., 2013. Analysis of microRNA-target interactions across diverse cancer types. Nat. Struct. Mol. Biol. 20 (11), 1325–1332. http://dx.doi.org/10.1038/nsmb.2678 (Nov, Epub 2013 Oct 6).

Kandoth, C., McLellan, M.D., Vandin, F., Ye, K., Niu, B., Lu, C., Xie, M., Zhang, Q., McMichael, J.F., Wyczalkowski, M.A., Leiserson, M.D., Miller, C.A., Welch, J.S., Walter, M.J., Wendl, M.C., Ley, T.J., Wilson, R.K., Raphael, B.J., Ding, L., 2013. Mutational landscape and significance across 12 major cancer types. Nature 502 (7471), 333–339. http://dx.doi.org/10.1038/nature12634 (Oct 17).

Kim, K., Jutooru, I., Chadalapaka, G., Johnson, G., Frank, J., Burghardt, R., Kim, S., Safe, S., 2013. HOTAIR is a negative prognostic factor and exhibits pro-oncogenic activity in pancreatic cancer. Oncogene 32 (13), 1616–1625 (Mar 28).

Yang, Z., Zhou, L., Wu, L.M., Lai, M.C., Xie, H.Y., Zhang, F., Zheng, S.S., 2011. Overexpression of long non-coding RNA HOTAIR predicts tumor recurrence in hepatocellular carcinoma patients following liver transplantation. Ann. Surg. Oncol. 18 (5), 1243–1250 (May).