GELCC Phenotype Database: Familial Lung Cancer Data Across Families

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Introduction: Lung cancer is the leading cause of cancer mortality in the USA while having the second highest incidence rate. Often presenting with aggressive development and rapid lethality, lung cancer is influenced by several environmental factors, including tobacco and arsenic. Furthermore, prior studies illustrate the genetic influences in lung cancer linked to specific genes, such as TP53, RB1, and PARK2 (1, 2). The Genetic Epidemiology of Lung Cancer Consortium (GELCC) is a collective study of data and bio-samples from individuals with strong family history of lung cancer. The data was compiled into a phenotype database.

Results: GELCC features 10 different participating sites with [n = 10,624] database entries: the University of Toledo accounts for [n = 1,951] entries. Prior comparison between sequenced data and pedigrees from the GELCC database (e.g., multipoint linkage analysis) found significant linkages on 6q , which uncovered susceptible genes, such as RGS17, through targeted sequencing analysis (3). Subsequently, it is probable that other genes impacting the incidence of familial lung cancer have yet to be discovered, which the GELCC aims to achieve. To facilitate this aim with the latest and accurate information, numerous records and data were validated and updated in the GELCC database. Five UToledo families, including [n = 729] individuals and 3 new lung cancer cases, were updated or added into the database. Furthermore, family pedigrees were generated for each of these families, and multisite linkage analysis will be completed at the Baylor College of Medicine.

Conclusion: Overall, these pertinent updates alongside performing further linkage analysis can help elucidate and characterize the underlying causes, pathways, and mechanisms influencing familial lung cancer incidence. The characterization can potentially aid in screening at-risk individuals with the goal of increasing early diagnoses that corresponds with better clinical outcomes.

References

1. George, J., Lim, J.S., Jang, S.J., Cun, Y., Ozretić, L., Kong, G, Leenders, F., Lu, X., Fernández-Cuesta, L., Bosco, G., Müller, C., Dahmen, I., Jahchan, N.S., Park, K.S., Yang, D., Karnezis, A.N., Vaka, D., Torres, A., Wang, M.S., Korbel, J.O., Menon, R., Chun, S.M., Kim, D., Wilkerson, M.,

Hayes, N., Engelmann, D., Pützer, B., Bos, M., Michels, S., Vlasic, I., Seidel, D., Pinther, B., Schaub, P., Becker, C., Altmüller, J., Yokota, J., Kohno, T., Iwakawa, R., Tsuta, K., Noguchi, M., Muley, T., Hoffmann, H., Schnabel P.A., Petersen, I., Chen, Y., Soltermann, A., Tischler, V., Choi, C.M., Kim, Y.H., Massion, P.P., Zou, Y., Jovanovic, D., Kontic, M., Wright, G.M., Russell, P.A., Solomon, B., Koch, I., Lindner, M., Muscarella, L.A., la Torre, A., Field, J.K., Jakopovic, M., Knezevic, J., Castaños-Vélez, E., Roz, L., Pastorino, U., Brustugun, O.T., Lund-Iversen, M., Thunnissen, E., Köhler, J., Schuler, M., Botling, J., Sandelin, M., Sanchez-Cespedes, M., Salvesen, H.B., Achter, V., Lang, U., Bogus, M., Schneider, P.M., Zander, T., Ansén, S., Hallek, M., Wolf, J., Vingron, M., Yatabe, Y., Travis, W.D., Nürnberg, P., Reinhardt, C., Perner, S., Heukamp, L., Büttner, R., Haas, S.A., Brambilla, E., Peifer, M., Sage, J., Thomas, R.K. *Comprehensive genomic profiles of small cell lung cancer*. Nature, 2015. **524**(7563): pp. 47-53.

2. Xiong, D., Wang, Y., Kupert, E., Simpson, C., Pinney, S.M., Gaba, C.R., Mandal, D., Schwartz, A.G., Yang, P., de Andrade, M., Pikielny, C., Byun, J., Li, Y., Stambolian, D., Spitz, M.R., Liu, Y., Amos, C.I., Bailey-Wilson, J.E., Anderson, M., You, M. *A recurrent mutation in PARK2 is associated with familial lung cancer*. The American Journal of Human Genetics, 2015. **96**(2): pp. 301-308.

3. You, M., Wang, D., Liu, P., Vikis, H., James, M., Lu, Y., Wang, Y., Wang, M., Chen, Q., Jia, D., Liu, Y., Wen, W., Yang, P., Sun, Z., Pinney, S.M., Zheng, W., Shu, X.O., Long, J., Gao, Y.T., Xiang, Y.B., Chow, W.H., Rothman, N., Petersen, G.M., de Andrade, M., Wu, Y., Cunningham, J.M., Wiest, J.S., Fain, P.R., Schwartz, A.G., Girard, L., Gazdar, A., Gaba, C., Rothschild, H., Mandal, D., Coons, T., Lee, J., Kupert, E., Seminara, D., Minna, J., Bailey-Wilson, J.E., Amos, C.I., Anderson, M.W. *Fine mapping of chromosome 6q23-25 region in familial lung cancer families reveals RGS17 as a likely candidate gene*. Clinical cancer research, 2009. **15**(8): pp. 2666-2674.

