Parent-child signals identify candidate cancer driver genes

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Abstract (300 word limit)

Background: The DREAM Challenge evaluated methods to identify molecular pathways facilitating the detection of multiple genes affecting critical interactions and processes. Dysregulation of pathways by well-known driver genes is often found in the development and progression of cancer. We used the gene interaction networks provided and the scoring rounds to test disease module identification methods to nominate candidate driver genes in these modules.

Method: Our algorithm calculated the proportion of the whole network accessible in two steps from each node in a combined network, which was defined as a 2-reach gene value. Genes with high 2-reach values were used to form the center of star cover clusters. These clusters were assessed for significant modules. Within these modules we identified novel candidate driver genes, by considering the parent-child relationship of well-known driver genes. Disturbance to such driver genes or their upstream parents, can lead to disruption of highly regulated signals affecting the normal functions of cells. We explored these parents as a potential source for candidate driver genes.

Results: An initial list of 57 candidate driver genes was identified from 13 significant modules. Analysis of the parent-child relationships of well-known driver genes in these modules prioritized PRKDC, YWHAB, GSK3B, and PPP1CB.

Conclusion: Our method incorporated the simple m-reach topology metric in disease module identification and its relationship with known driver genes to identify candidate genes. The four genes shortlisted have been highlighted in recent publications in the literature, which supports the need for further wet lab experimental investigation.

Image

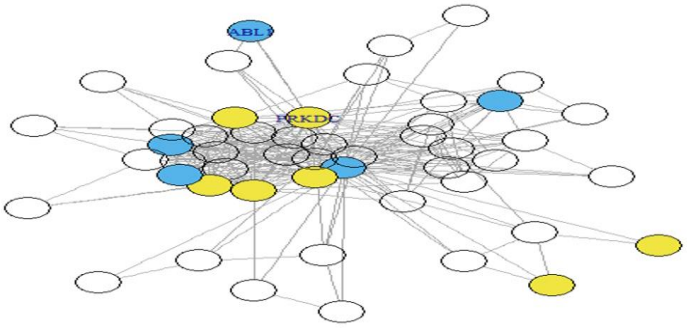


Figure 1 Subgraph of Module 15 in the signalling network, including all parents of the driver genes. Five blue nodes are the known drivers. Only driver gene ABL1 is seen to have a parent which forms part of module 15.

Recent Publications (minimum 5)

1. Ramsahai, E. A., Tripathi, V., & John, M. (2021). Parent-child signals identify candidate cancer driver genes. F1000Research, 10(67), 67.
2. Khan, K., & Ramsahai, E. (2020). Categorizing 2019-N-CoV Twitter Hashtag Data by Clustering. Available at SSRN 3680616..
3. Ramsahai, E., Tripathi, V., & John, M. (2019). Cancer driver genes: a guilty by resemblance doctrine. PeerJ, 7, e6979.LiX, SchwachaMG, ChaudryIH, ChoudhryMA (2008)Acutealcohol intoxication potentiates neutrophil-mediated intestinal tissue damage after burn injury. Shock 29:377.
4. Choobdar, S., Ahsen, M. E., Crawford, J., Tomasoni, M., Fang, T., Lamparter, D., ... & Marbach, D. (2019). Assessment of network module identification across complex diseases. Nature methods, 16(9), 843-852.5.
5. Ramsahai, E., Walkins, K., Tripathi, V., & John, M. (2017). The use of gene interaction networks to improve the identification of cancer driver genes. PeerJ, 5, e2568.

Photograph



Biography (150 word limit)

Dr Ramsahai is a consulting Data Scientist, with more than 20 years industry experience. She has lectured in Statistics, Computer Science and Life Sciences at the University of the West Indies. Her research work qualified her for the prestigious research fellowship at the International Centre for Genetic Engineering and Biotechnology (ICGEB) in New Delhi, India where she worked on Breast Cancer and molecular docking simulations. She is also instrumental in developing and delivering Bioinformatic courses at both the undergraduate and postgraduate level. She is proficient as a Bioinformatician and works well in this interdisciplinary field. Performing in silico analyses and developing methods and tools that combines biology, computer science, mathematics and statistics.

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Notes/Comments: