How Circos Ideograms Complement Networks: A Case Study in Asthma

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Abstract

Although networks provide a powerful approach to analyze complex relationships, they are limited in the number of node attributes that can be visually represented simultaneously. We therefore conducted a case study on how Circos Ideograms (designed to represent multiple node attributes) could help reveal complex relationships between cytokine expressions, asthma patients, and their attributes. The results suggest that while Circos Ideograms are neither designed to identify clusters, nor to exploit distance for representing similarity between nodes, they can play a complementary role to networks by enabling domain experts to discover complex relationships between molecular and phenotype information.

Introduction

Networks have helped to reveal complex relationships in numerous biomedical datasets. For example, in a recent study[1] we used a bipartite network to analyze how cytokine expressions co-occurred across asthma patients. The analysis revealed a complex but understandable relationship between three clusters of cytokines, and three clusters of patients. However, the network was limited in the number of patient attributes that could be *simultaneously* represented. For example, while gender and race for each patient could be represented by node color and shape respectively, it precluded analysis of many more such variables simultaneously. Given this limitation, we posed the question: *Can Circos Ideograms help to identify patterns between cytokines, patients, and their attributes?*

Method

As shown in Figure 1, we generated a Circos Ideogram[2] where: (1) 83 patient and 18 cytokine nodes were on the inner circle, organized in clusters identified through network analysis[1]; (2) links between the nodes represented cytokine expression, and their color and saturation represented cytokine type and expression value respectively; (3) 6 lung functions, with continuous values represented as a heatmap, were in outer concentric circles, and 4 categorical variables were in the outermost circles. Patients in each cluster were sorted based on MaxFEV1pp/MPVLung, a key indicator of lung function.

Results and Conclusion

Three asthma experts inspected the ideogram and identified three new complex patterns: (1) Patient-Cluster-1 and -2 had relatively low values of BASELINE FEV1PP, but had high values of cytokines in Cytokine-Cluster-2 and -3 (as shown by the dark
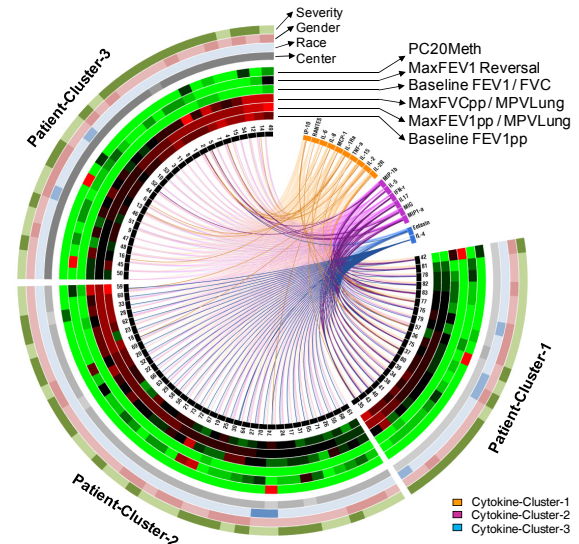

Figure 1. The Circos Ideogram complements network analysis by revealing how the patient and cytokine clusters identified from the network, relate to patient attributes, and how those attributes relate to each other.

blue and purple links). (2) Patient-Cluster-3 had high values of BASELINE FEV1PP, with low values of cytokines in Cytokine-Cluster-2 and -3. (3) There was a high correlation between the BASELINE FEV1PP, MAXFEV1PP / MPVLUNG, and MAXFVCPP / MPVLUNG (as shown by the three dark inner rings). The above patterns appeared independent of gender, race, and severity. The study therefore suggests that an ideogram can play a complementary role to networks by enabling domain experts to quickly formulate hypotheses about complex relationships between clusters identified from network analysis, and several patient attributes simultaneously. Such analysis can therefore lead to deeper insights about the complex interactions between molecular and phenotypical information. Future research should explore methods for interactively sorting patients on different attributes, with associated statistics to verify hypotheses generated from the visual analysis.

References

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2. Krzywinski, M. et al. Circos: an Information Aesthetic for Comparative Genomes. *Genome Res* (2009) 19:1639-1645.