A DNA Copy Number Co-deletion Network Identifies Genetic Interactions

Xianlong Wang[*,1], Dongqing Huang[†,1], Chenwei Lin[1], Brian D. Piening[1], Amanda G. Paulovich[1], Pei Wang[1]

[1]Fred Hutchinson Cancer Research Center, Seattle, WA, USA
[*]Correspondence: contact email, xwan2@fhcrc.org
[†]Correspondence: contact email, dhuang@fhcrc.org

Abstract

The complex interplay among multiple genes in breast cancer etiology remains an important yet largely unexplored phenomenon. Therefore, understanding gene-gene interactions will shed new light on the genetic architecture of breast cancer. Since genome stability, partially reflected by copy number variation, plays a key role in breast cancer initiation and progression, copy number co-deletion events may help us reveal important disease-related genetic interactions. Such co-deletion events may be quantified on a genome-wide level using comparative genome hybridization (CGH) arrays. In this work, a bioinformatics pipeline was implemented to detect and prioritize disease-related genetic interactions using a copy number co-deletion network coupled with association scores between genomics signatures and patient clinical outcome. We applied the pipeline on a collection of genomics arrays of breast cancer and identified a list of candidate disease-related genetic interactions. As a proof of principle, we successfully validated a subset of candidate genetic interactions using yeast as a model organism from the perspectives of DNA repair and growth. Further experiments indicate that the growth defect may result from genome instability.

Keywords: gene-gene interaction; copy number co-deletion network; gene prioritization; integrative genomics analysis; data integration