

19th Euro Congress on Cancer Science and Therapy & 25th Cancer Nursing & Nurse Practitioners Conference

July 17-19, 2017 Lisbon, Portugal

The network biology of microtubule-targeting agents

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Cancer causes millions of deaths annually, and the most commonly used anti-cancer drugs are microtubule-targeting agents (MTAs). However, the high MTA's toxicity is cause for concern. We performed an analysis of the MTA interaction network in a non-cancerous human cell. Subnetworks of fourteen MTAs were reconstructed using STITCH 4.0 and Cytoscape 3.4.0. The merged network was compared against a randomized network and the functional richness level was determined using the MCODE, BINGO and KEGG database. A comparison between the paclitaxel and the doxorubicin networks was made to determine common topological properties and synergistic effects of MTAs. It was determined that 71.4% of the MTA interactome is common between drugs and consists of 363 nodes and 2327 connections. MTAs affect cellular processes such as apoptosis, cell differentiation, cell cycle control, stress response and regulation of energy metabolism. Additionally, possible secondary targets were identified as client proteins of interphase microtubules. MTAs affect apoptosis signaling pathways by interacting with client proteins of interphase microtubules, suggesting that their primary targets are not tumor cells. The paclitaxel and doxorubicin networks share essential topological axes that suggest a synergistic effects that explain the exacerbate toxicity observed when they are used together against cancer disease.

Biography

Andrés Julián Gutiérrez-Escobar is a member Biomedical and Applied Human Genetics Research Group at the University of Applied and Environmental Sciences UDCA, Colombia. Currently, he leads the research on computational and evolutionary biology of *Helicobacter pylori* and cancer.

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