



Identification of core genes and outcomes related to the effect of Crizotinib on gastric cancer using bioinformatics analysis



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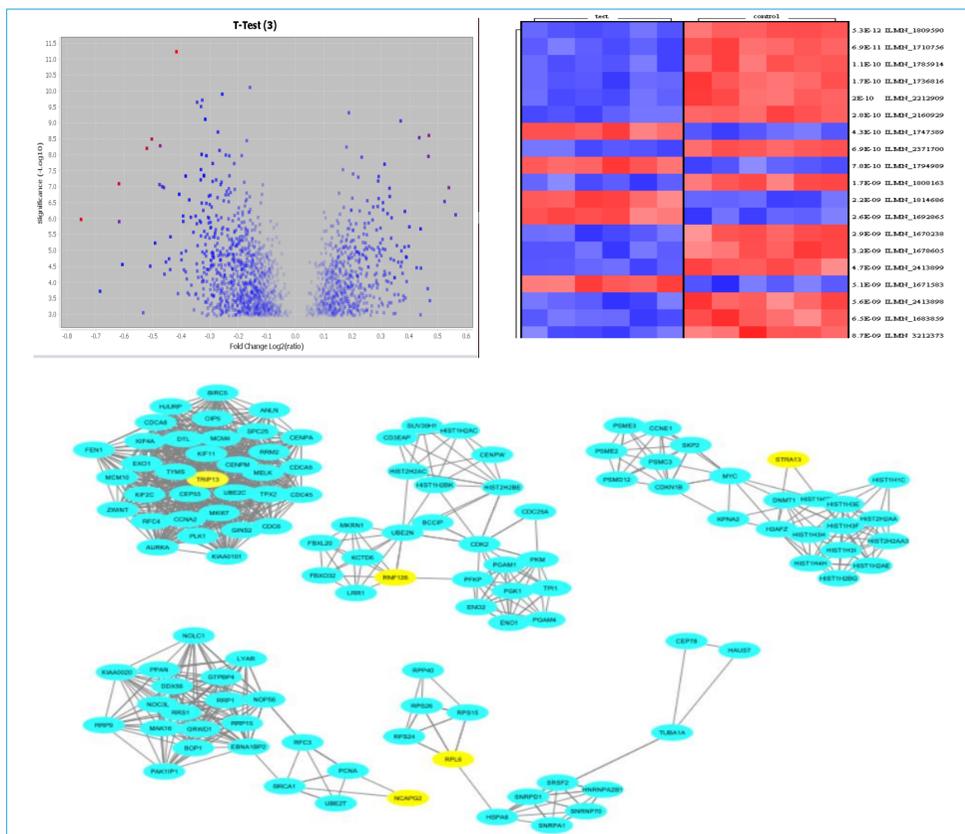
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Abstract

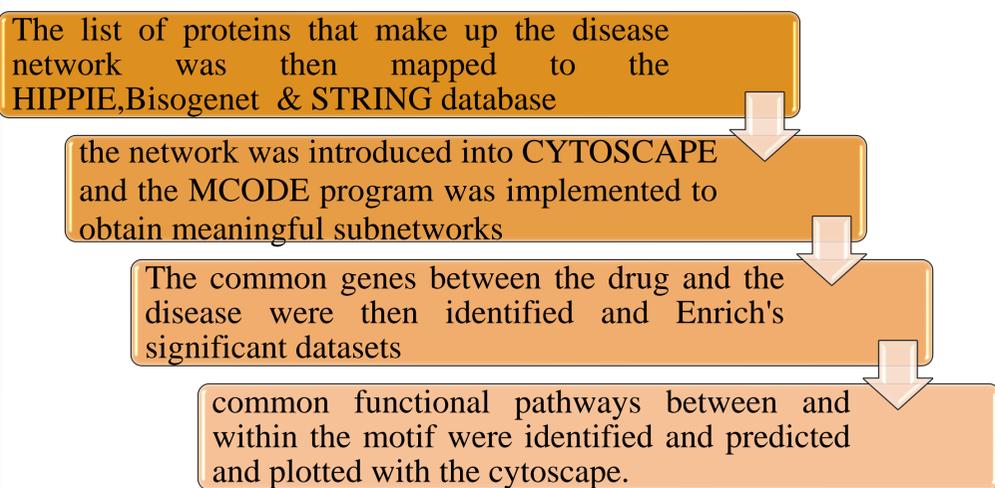
Gastric cancer (GC) is a common malignant neoplasm of gastrointestinal tract. Currently, gastric cancer therapies mainly include surgery, adjuvant and palliative chemotherapy, biologic therapy, targeted therapy, and radiation therapy. However, most gastric cancer patients have missed the chance of surgery at the time of diagnosis. Traditional radiotherapy and chemotherapy are less effective and molecular targeted drugs for gastric cancer are also limited. Therefore there is a great need for screening new targets and developing and approving targeted drugs. Recent studies have shown that preoperative chemotherapy with FLOT regimens (5-FU, leucovorin, oxaliplatin, and docetaxel without radiotherapy) are the standard treatment in the West. Two-drug chemotherapy is the best primary treatment for the metastatic disease. It is better than S-1 monotherapy (4), but studies on the safest drug with the least side effects and longer patient survival are still ongoing.

Results



FIGURES: Clusters network & Protein-protein interaction of significant genes that determined the sub-network of seed genes connected to first connected nodes

Methods



References

1. Ramly B, Afiah-Aleng N, Mohamed-Hussein ZA. Protein-Protein Interaction Network Analysis Reveals Several Diseases Highly Associated with Polycystic Ovarian Syndrome. International journal of molecular sciences. 2019;20(12).
2. Marano L, Chiari R, Fabozzi A, De Vita F, Boccardi V, Roviello G, et al. c-Met targeting in advanced gastric cancer: An open challenge. Cancer letters. 2015;365(1):30-6.
3. Ou SH, Kwak EL, Siwak-Tapp C, Dy J, Bergethon K, Clark JW, et al. Activity of crizotinib (PF02341066), a dual mesenchymal-epithelial transition (MET) and anaplastic lymphoma kinase (ALK) inhibitor, in a non-small cell lung cancer patient with de novo MET amplification. Journal of thoracic oncology : official publication of the International Association for the Study of Lung Cancer. 2011;6(5):942-6.
4. Okamoto W, Okamoto I, Arai T, Kuwata K, Hatashita E, Yamaguchi H, et al. Antitumor action of the MET tyrosine kinase inhibitor crizotinib (PF-02341066) in gastric cancer positive for MET amplification. Molecular cancer therapeutics. 2012;11(7):1557-64.
5. Schroeder RD, Choi W, Hong DS, McConkey DJ. Autophagy is required for crizotinib-induced apoptosis in MET-amplified gastric cancer cells. Oncotarget. 2017;8(31):51675-87.
6. Sun C, Yuan Q, Wu D, Meng X, Wang B. Identification of core genes and outcome in gastric cancer using bioinformatics analysis. Oncotarget. 2017;8(41):70271-80.
7. Yong WP, Rha SY, Tan IB, Choo SP, Syn NL, Koh V, et al. Real-Time Tumor Gene Expression Profiling to Direct Gastric Cancer Chemotherapy: Proof-of-Concept "3G" Trial. Clinical cancer research

Discussion, Conclusion and Suggestions

The majority of the top genes and biological processes which scored in the two types of analysis, were all verified in other published experimental studies about GC. Those studies were used to verify the PPI network and based on this ground we recommended the other genes available in the models for further investigation of their probable role in the effect of Crizotinib on gastric cancer.

Pathway enrichment analysis was performed to find pathways that are statistically involved in Gastric cancer and crizotinib. The identification of significant pathways, such as cell cycle, Oocyte meiosis, progesterone-mediate Oocyte maturation and viral carcinogenesis between gastric cancer and crizotinib.

Sublist	Category	Term	RT	Genes	Count	%	P-Value	Benjamini
	KEGG_PATHWAY	Cell cycle	RT		8	38.1	1.6E-9	8.4E-8
	KEGG_PATHWAY	Progesterone-mediated oocyte maturation	RT		4	19.0	6.4E-4	1.7E-2
	KEGG_PATHWAY	Hepatitis B	RT		4	19.0	2.8E-3	4.9E-2
	KEGG_PATHWAY	Oocyte meiosis	RT		3	14.3	2.1E-2	2.6E-1
	KEGG_PATHWAY	Epstein-Barr virus infection	RT		3	14.3	2.5E-2	2.6E-1
	KEGG_PATHWAY	PI3K-Akt signaling pathway	RT		4	19.0	3.0E-2	2.6E-1
	KEGG_PATHWAY	DNA replication	RT		2	9.5	7.1E-2	5.3E-1