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Introducing *in silico* based strategies for modeling and predicting protein-protein interactions involved in anticancer mechanisms of actions of metformin against thyroid carcinoma

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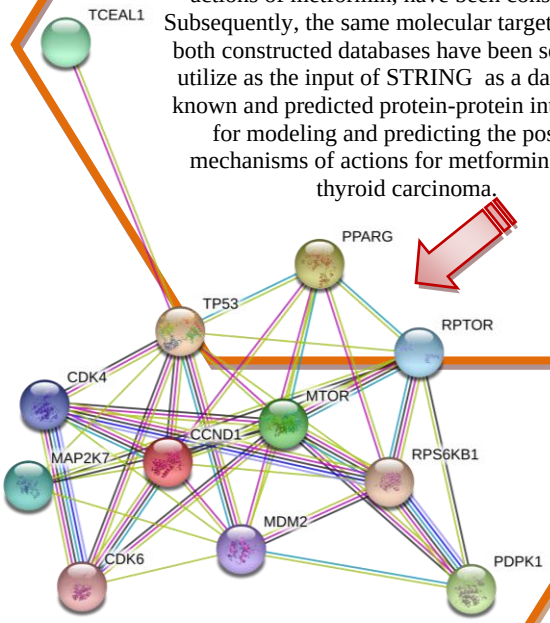
Objective and Background

Thyroid cancer is the utmost common endocrine malignancy with more deaths yearly than all other endocrine cancers combined.
Numerous researches have suggested that metformin can inhibit the growth of thyroid cells by affecting the insulin/IGF1 and mTOR pathways *in vitro* and *in vivo*.
Based on this evidence, metformin appears to be a promising therapeutic tool in patients with thyroid disease.
Despite the mentioned research and relevant results, as yet the mechanisms underlying the antitumor effect of metformin against thyroid carcinoma are complex and still not fully understood.

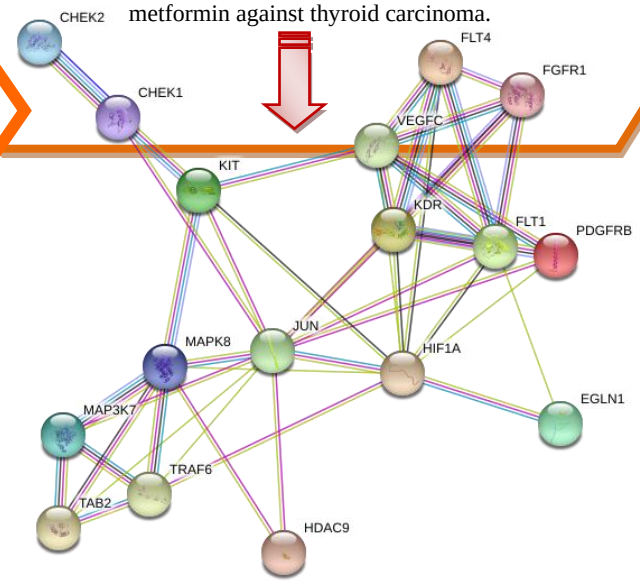
Methods and Results
First Strategy

Based on investigation the reported data in valid scientific sources parallel to studying the relevant online databases, the two databases including I. thyroid carcinoma-related molecular targets and II. relevant molecular targets with mechanisms of actions of metformin, have been constructed. Subsequently, the same molecular targets form the both constructed databases have been selected to utilize as the input of STRING as a database of known and predicted protein-protein interactions for modeling and predicting the possible mechanisms of actions for metformin against thyroid carcinoma.



Methods and Results
Second Strategy

Based on investigation of Genomics of Drug Sensitivity in Cancer (GDSC) database as a resource for therapeutic biomarker discovery in cancer cells, 43 drugs and drug like-compounds with significant toxicity against 17 thyroid cancer cell lines and identified molecular targets has been selected.
The string similarity search between generated SMILES for each selected drugs with metformin has been performed.
Furthermore, the Lipinski rule of 5 parameters were calculated for metformin and 34 selected drugs.
Finally, six drugs and drug like compounds with more than 70% similarity between their SMILES strings and more than 80% similarity in average of calculated Lipinski rule of 5 parameters, have been selected to use their identified molecular targets as the input of STRING to model and predict the possible mechanisms of actions for metformin against thyroid carcinoma.



Conclusions

It would be notable that an *in silico* comprehensive analysis of biological systems can predict the possible cellular responses at the level of proteins, presents opportunities to accelerate the process of drug design/discovery across the entire channel.
The current research by employing two different innoative *in silico* strategies based on protein- protein interaction modeling has introduced possible mechanisms of actions for metformin against thyroid carcinoma towards successful molecular cancer therapy.

References

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