

DISPROPORTIONALITY ANALYSIS AND MULTIMODAL GENETIC ASSESSMENT OF PAPILLEDEMA ASSOCIATED WITH PROTEASOME INHIBITORS

Ritesh Giri¹, Tania V. Abraham², Priya Anand¹, Likitha YV¹, Prizvan L. D Souza², GR Saraswathy¹

¹Department of Pharmacy Practice, Faculty of Pharmacy, M.S. Ramaiah University Of Applied Sciences

²Department of Clinical Pharmacy, M.S. Ramaiah Memorial Hospital

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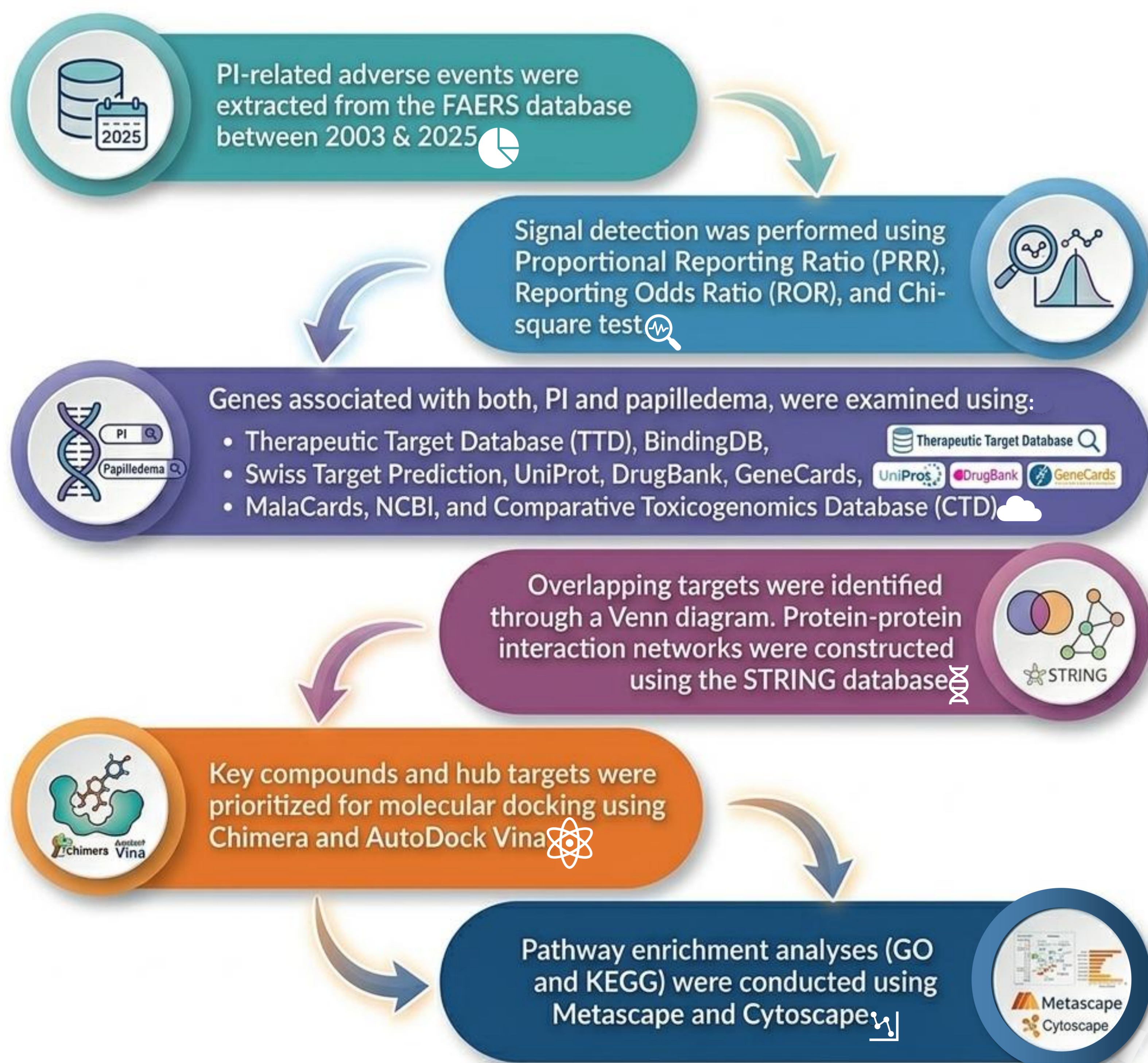
INTRODUCTION

Proteasome Inhibitors (PI) are widely used in treating multiple myeloma and certain lymphomas. However, potential ophthalmic adverse events may be underreported.

OBJECTIVE

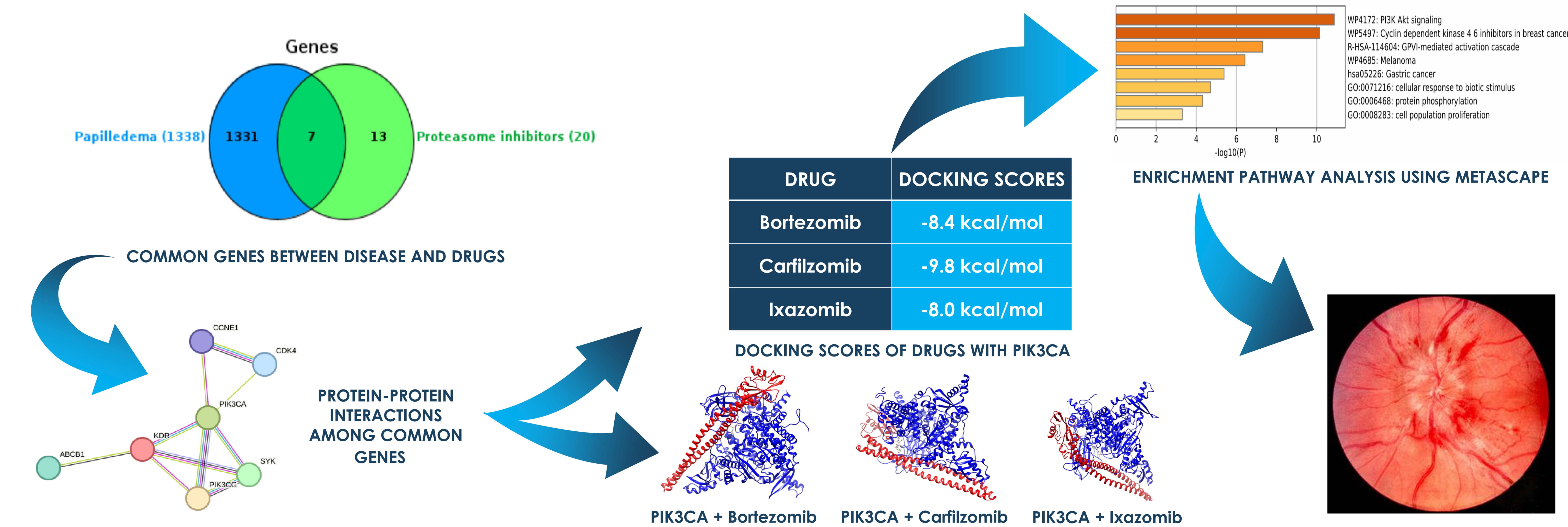
This study aimed at evaluating an association between papilledema and PI by detecting pharmacovigilance safety signals using disproportionality analysis and exploring plausible mechanisms through bioinformatics and computational modelling.

METHODOLOGY



RESULTS

A total of 1,962 signals were identified, of which 58 papilledema cases were associated with Bortezomib (n=35), Carfilzomib (n=10), and Ixazomib (n=13). Disproportionality analysis showed PRRs of 3.52, 3.38, and 3.21, respectively. Additionally, identical ROR values were obtained, indicating a positive safety signal. Systematic target identification revealed 20 common genes across the three drugs, of which seven overlapped with papilledema-related targets. Among these, PIK3CA exhibited significant docking for Bortezomib (-8.4 kcal/mol), Carfilzomib (-9.8 kcal/mol), and Ixazomib (-8.0 kcal/mol). Further, network analysis and pathway enrichment implied that proteasome inhibition may sustain PI3K-Akt signaling, contributing to stress-related autophagy, astrocyte swelling, axonal transport dysfunction, and VEGF-associated vascular permeability at the optic nerve head, eventually promoting optic disc edema.



CONCLUSION

This study identified a potential association between PI and papilledema through disproportionality analysis and comprehensive genetic assessment. Although further clinical research is crucial to verify this corroboration, healthcare providers are opined to be vigilant.

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