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Investigating the shared and distinct mode of action of NSAIDs related to gastrointestinal side effects

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Nonsteroidal anti-inflammatory drugs (NSAIDs) are a class of drugs approved by the FDA for use as antipyretic, anti-inflammatory, and analgesic agents. Behind the wide usage of NSAIDs, long-time usage of NSAIDs is often associated with mild to severe gastrointestinal (GI) side effects. To investigate the mode-of-actions (MOAs) in GI side effects of the 16 NSAIDs, we expanded the effects of target genes of each NSAID toward the stomach-specific gene-gene interaction network (GGI-net). The reference GGI-net was retrieved from HumanBase, and the interaction weights of less than 0.3 were discarded. The target gene information in DrugBank was used to designate the initial seed node for the 16 NSAIDs. The initial weights were then propagated across the GGI-net via random walk with restart (RWR) algorithm. Genes with the top 10% of propagated scores were regarded as highly impacted genes and then subsequently passed to the functional enrichment analysis to specify the causal mechanisms in GI side effects. Herein, we applied an interactome-wide approach to identify the causal mechanisms of GI side effects for NSAIDs. We believe that this work may contribute to designing sophisticated approaches to reduce the side effects of NSAIDs.