Title: Targeting Epstein-Barr Virus driven Nasopharyngeal Cancer with beer molecule involved with RNA driven mechanism of weight loss

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Abstract:
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Nasopharyngeal cancer (NPC) is a deadly cancer in Singapore, primarily driven by Epstein-Barr virus (EBV) infection. Therefore, we aimed to target virus-specific vulnerabilities for more effective, well-tolerated therapies. In unpublished studies, we found that the EBV episome forms Super EBV Clusters of chromatin interactions to transcriptionally promote a protective increase in lipid storage. Interestingly, this creates a vulnerability to Xanthohumol, a beer-derived compound known for potential weight loss effects, however with unknown mechanism of action. We showed that Xanthohumol alters lipid metabolism to induce ferroptosis in EBV+ NPC. Further, Artificial Intelligence (AI) modeling revealed Xanthohumol specifically interacts with Fat Mass and Obesity-associated (FTO) protein, an mRNA demethylase. Using Nanopore mRNA sequencing, we discovered that Xanthohumol promotes the removal of m6A RNA methylation on lipid metabolism genes. Therefore, Xanthohumol appears to hinder lipid storage by increasing FTO m6A RNA demethylase function, which is specifically cytotoxic in EBV+ NPC cells.