Taguchi et al reported that Keap1-Nrf2 system can server as molecular target of the cancer treatment (<https://pubmed.ncbi.nlm.nih.gov/33375248/>), it gets me extremely interested.

The SNP (rs6721961) reported as T>A/T>C/T>G with different MAF (<https://www.ncbi.nlm.nih.gov/snp/rs6721961>) is 2kb upstream variant in NFE2L2, there are 39 citations on this SNP

Reszka, E et al (2014) reported this SNP in urinary bladder cancer patient (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4160566/>), which leads to a paper by Marzec (2007)

“The functional significance of NRF2 −617C/A (rs6721961) genetic polymorphism in promoter region is still unraveled. Marzec et al. have found that NRF2 −617A allele presents significantly lower luciferase activity of promoter construct containing single nucleotide polymorphism relative to the wild type at this locus (NRF2 −617CC) (Marzec et al. [2007](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4160566/#CR28)). Recently, Hua et al. ([2010](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4160566/#CR15)) have presented opposite results showing higher luciferase activity of NRF2 −617A than NRF2 −617C construct and suggested interaction with triplet repeat polymorphism of NRF2 (CCG)4or5.”

Marzec reported the function of such variant is the ARE elements for the transcription binding efficiency change of NRF2 expression (<https://pubmed.ncbi.nlm.nih.gov/17384144/> ) .

June 25th, 2021

Discussed with Luke Chen

He did not like the SNP as the association does not directly point to causality, lacks clinical value, etc.

My points are:

1. The SNP (rs6721961) are parts of the ARE element that could have function affecting the enzyme binding. I hope to see:
2. Cancer cell lines from public domain harbor this SNP with “higher MAF” than its population MAF reported in dbSNP

Association of MAF with gene expression changes

Luke suggested ESCC from CCLE, 21 cell lines, some with high Nrf2 and some with low Nrf2