

Mechanisms by which fruit polyphenols act as cancer chemopreventive agents

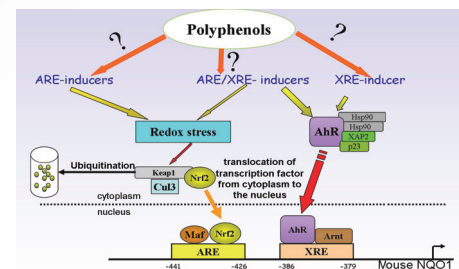
Han Xiao^{1,2}, Michael McMahon², John Hayes² and Derek Stewart¹

¹Plant Products and Food Quality Programme, Scottish Crop Research Institute, Dundee, DD2 5DA;

²Biomedical Research Centre, University of Dundee, Ninewells Hospital and Medical School, Dundee, DD1 9SY.

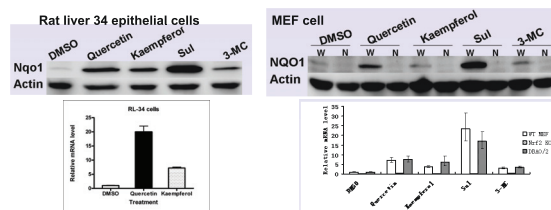
Hypothesis

At what point in the body's antioxidant and detoxification systems do plant polyphenols exert their action, if at all?

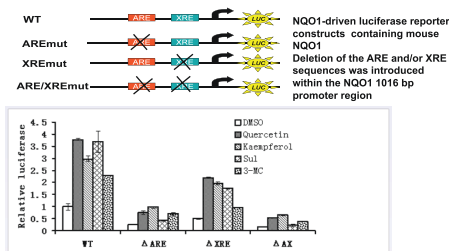


Experimental Approach and Results

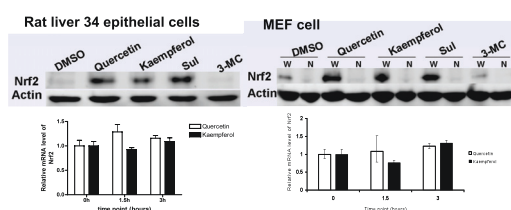
1. Quercetin and Kaempferol Can Increase the Expression of NQO1



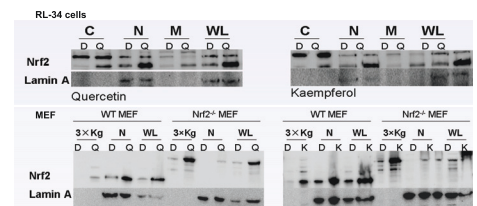
2. The Involvement of ARE and XRE in the Induction of NQO1 by Quercetin and Kaempferol.



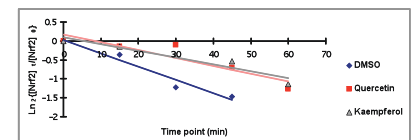
3. Quercetin and Kaempferol can increase the expression of Nrf2 at the protein level but have no effect on the mRNA level.



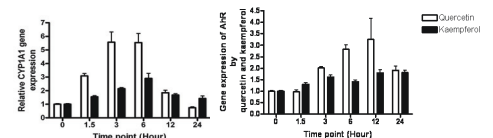
4. Quercetin and Kaempferol alter the intracellular localisation and localization of Nrf2.



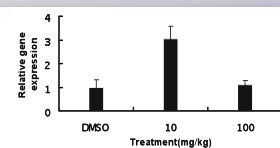
5. CHX chase experiment was carried out in the presence and absence of either Quercetin or Kaempferol to showing both chemicals can increase the half life of Nrf2 protein in RL34 cells



6. Quercetin and Kaempferol increase mRNAs of CYP1A1 and AhR



7. Quercetin can increase the gene expression of CYP1A1 in mouse small intestine



Conclusion

Quercetin and Kaempferol can increase the expression of antioxidant and detoxification enzymes NQO1 and CYP1A1.

The induction of NQO1 is dependent on ARE and partially on XRE.

Induction is regulated by Nrf2 which can be stabilized by Quercetin and Kaempferol.

Furthermore, intervention studies with mice using Quercetin at 10mg/kg for 4 days saw an associated increase in CYP1A1 mRNA level in the mouse's small intestine perhaps suggesting positive benefits with regard to risk of digestive tract cancers.