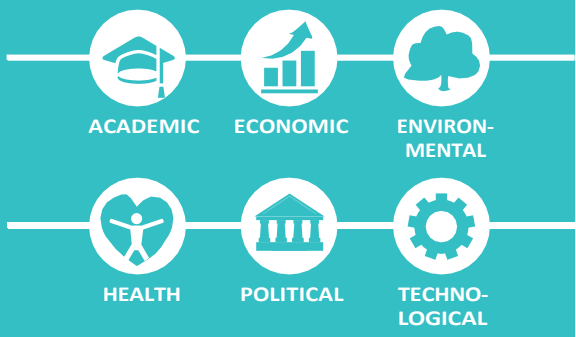
UCD Impact Case Study

Selenium named after Selene, the Greek goddess of the moon, lights up a link to cancer prevention.

Dr David Hughes
UCD School of Biomolecular and Biomedical Science
UCD Conway Institute of Biomolecular and Biomedical Research



SUMMARY

The findings inform knowledge of optimal levels of both selenium and its transport protein Selenoprotein-P for regulatory bodies, health professionals, and the agricultural industry for nutritional advice and the production of fortified-foods.

Selenoprotein-P is the best biological indicator of functional selenium levels. Thus, it is a promising diagnostic marker for people who could benefit from increased dietary selenium. Development of a new biochemical Selenoprotein-P 'finger-prick' blood test informed by this work can improve clinical assessment of selenium sufficiency and is feasible for primary health-care settings.

The research should also improve the context and conduct of future randomized control trials examining whether selenium can help prevent certain cancers.

"Liver cancers are often diagnosed at late stages and have limited treatment options. Further research is needed into the modifiable determinants of these cancers and effective prevention strategies"

(Dr Mazda Jenab, WHO-IARC, on the importance of the research findings)

RESEARCH

Selenium is a chemical element essential for human health present in certain foods. We need a small amount of this micronutrient to make proteins, called selenoproteins, some of which help remove free radicals that cause DNA damage.

Low levels of selenium have been linked to the development of cancer and other chronic diseases[1]. Due to differing soil selenium levels and resultant food content, many Europeans receive a relatively low amount of dietary selenium compared with North Americans for example (image 2).

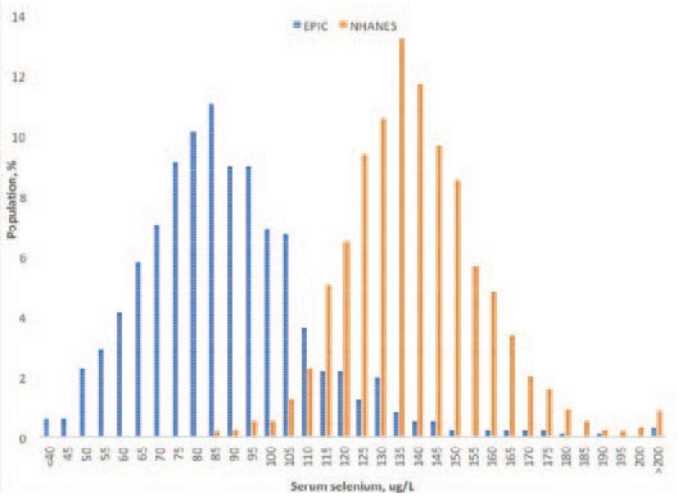
In this research, higher blood levels of both selenium and Selenoprotein-P (which distributes selenium around the body) were linked in both men and women to a significantly lower risk of developing colorectal cancer (especially in women for this cancer) and liver cancer, even when considering other major risk factors for these cancers[2-4].

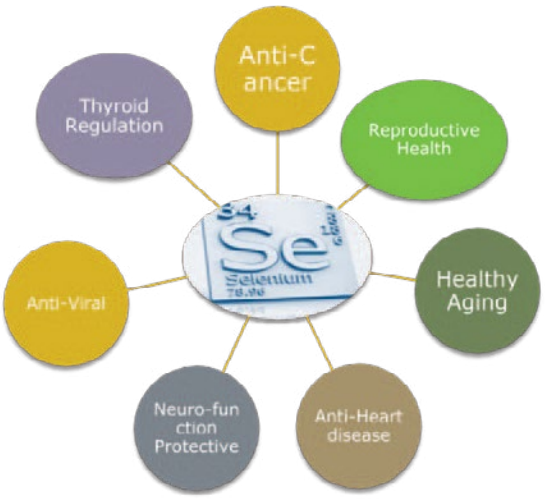
The research was based on the large, long-term European Prospective Investigation of Cancer and Nutrition Cohort (EPIC), where in the 1990s around 500,000 people across 10 European countries donated blood samples and provided detailed information on their diets and lifestyles.

The investigators measured selenium and Selenoprotein-P in blood from over 1,200 people who eventually developed colorectal or liver cancer compared to an equal number in the study who remained cancer-free.

The latest findings from this work provide the most comprehensive existing evidence that inherited genetic changes impacting selenium metabolism are also linked to colorectal cancer development in areas of marginally low Se status, such as Europe[5].

The research involves colleagues at the International Agency for Research on Cancer (IARC), Lyon, France; Charité-Medical School Berlin, Germany; Newcastle University, UK, and EPIC collaborators.





RESEARCH IMPACT

A World Health Organization (WHO)-IARC press release highlighted the importance of the research findings for cancer prevention, where Dr Jenab, a senior WHO-IARC scientist and co-author, noted that "Liver cancers are often diagnosed at late stages and have limited treatment options. Further research is needed into the modifiable determinants of these cancers and effective prevention strategies"[6].

As highlighted in an interview with Dr Hughes by News-Medical[7] and the 2017 HRB health-research-in-action report[8], the findings are informing current debate about Dietary Reference Intakes (DRIs) to the resultant beneficiaries such as governmental health boards and nutritional bodies.

In general, although dependent on sex and life-stage such as pregnancy, our research suggests a blood selenium concentration of approximately 120 ng/ul is required, corresponding to an adult DRI of about 80 µg/day. This is higher than current recommendations by the WHO (16-40 µg/day), the USA Food and Nutrition Board (55 µg/day), but comparable with the latest 2014 European Food Safety Authority (EFSA) RDI of 70 µg/day[9].

Selenoprotein-P level as a functional (biologically working) measure of selenium in the body offers a more accurate approach to identify and monitor people who could benefit from increased dietary selenium (or as a supplement).

To this end, Prof Lutz Schomburg, a senior collaborator, developed a company (selenomed.com) to improve selenium-related clinical diagnostics.

Within UCD, Dr Clare Corish leads a study to improve prescribing of oral nutritional supplements by Irish doctors. The detailed results of Dr Hughes' work on the optimal range of selenium levels will enable evidence-based clinical advice and maximize public health benefit. The use of selenium diagnostic devices such as Selenoprotein-P-*selenomed*, requiring only a pinprick of blood, would be ideal for use in primary health clinics.

Thus, will individuals with low selenium levels or certain gene variants benefit from increased selenium intake? Although the results of this work contribute to accumulating evidence indicating an important role of selenium and selenoproteins for cancer prevention, further examination of these findings in other populations is required before more definite public health recommendations.

The evidence for a medical benefit of selenium supplementation is not as robust as the evidence linking low selenium to disease risks. A recent expert review by Dr Hughes and Prof Schomburg highlighted another significant impact of the findings – in recommending future randomized control trials (RCTs) to include individuals with the risk range of selenium intake (best ascertained by measuring Selenoprotein-P that can reliably reflect nutrient status), applicable use of different forms of selenium, and how previous costly RCTs that showed no benefit were probably due to most study participants already having selenium levels sufficient for adequate selenoprotein activity and whom should not have been given extra nutrients[4].

A national program of adding selenium to fertilizers in Finland indicated that selenium levels can be safely increased on a population-wide basis in low selenium areas[10.] Advisory-governmental bodies of Ireland and other European countries should consider whether to implement a similar policy. Knowledge of optimal levels of selenium in our diet and for improved animal health is prevalent in the livestock and agricultural industry such as Alltech (alltech.com/sel-plex).

Dr Hughes has provided scientific advice to Selena (selena.ie), a family-farm from Dublin harvesting potatoes in selenium-enriched soils (image 1), and nutritious foods are preferable to taking supplements.

RESEARCH REFERENCES

1. Méplan C. Selenium and chronic diseases: a nutritional genomics perspective. Nutrients. 2015 May 15;7(5):362151. doi: 10.3390/nu7053621.

2. Hughes DJ, Fedirko V, et al, and Hesketh JE. Selenium Status is Associated with Colorectal Cancer risk in the European Prospective Investigation of Cancer and Nutrition Cohort. Int J Cancer 2015 Mar 1; 136(5): 1149-61. doi: 10.1002/ijc.29071.

3. Hughes DJ, Duarte-Salles T, et al, and Jenab M. Pre-diagnostic selenium status and hepatobiliary cancer risk in the European Prospective Investigation into Cancer and Nutrition Cohort. Am J Clin Nutr 2016; 104: 1–9. doi: 10.3945/ajcn.116.131672.

4. Schomburg L, Hughes DJ. The missing link? The potential role of selenium in the development of liver cancer and significance for the general population. Expert Rev Gastroenterol Hepatol 2017; 11(8):707-709. doi: 10.1080/17474124.2017.1320219.

5. Fedirko V, Jenab M, et al, and Hughes DJ. Association of selenoprotein and selenium pathway genotypes with risk of colorectal cancer and interaction with selenium status. Nutrients (in press, May 2019).

6. IARC press release no. Low selenium levels linked to liver cancer development. https://www.iarc.fr/en/media-centre/pr/2016/pdfs/pr245_E.pdf

7. http://www.news-medical.net/news/20160822/Low-selenium-levels-linked-to-liver-cancer-risk-An-interview-with-Dr-David-Hughes.aspx (A Thought Leaders Series)

8. HRB health research in action report; http://www.hrb.ie/fileadmin/publications_files/Health_Research_in_Action_2017_web.pdf

9. European Food Safety Authority: https://www.efsa.europa.eu/sites/default/files/2017_09_DRVs_summary_report.pdf

10. Alfthan G, Eurola M, et al. Selenium Working Group. Effects of nationwide addition of selenium to fertilizers on foods, and animal and human health in Finland: from deficiency to optimal selenium status of the population. J Trace Elem Med Biol 2015;31:142–7. doi: 10.1016/j.jtemb.2014.04.009.