The story behind ‘super broccoli’

A case study in the successful commercialisation of UK bioscience.

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When Beneforté 'super broccoli' was launched onto selected UK supermarket shelves in October 2011, it represented a special achievement for UK bioscience - a consumer-focused, nutritionally-enhanced product developed over more than two decades through collaboration between two BBSRC-supported research world-class institutes and a specialist technology transfer company, part-owned by BBSRC.

Beneforté broccoli is two to three times higher in a compound called glucoraphanin from which sulforaphane is derived upon ingestion. Studies in animal model systems have shown that sulforaphane can lead to lower rates of heart disease, act against some forms of cancer, and boost the body's levels of antioxidant enzymes which can protect DNA from damage and is thought to be a useful component of healthy ageing (ref 1, 2, 3, 4, 5).

Beneforté broccoli was launched in the UK 4 October. Image: IFR

Beneforté broccoli, developed by conventional breeding techniques, is born from research on the fundamental biology of plants and the link between human nutrition and health at the John Innes Centre (JIC) and the Institute of Food Research (IFR), respectively. Both institutes receive strategic funding from BBSRC, in 2010 £28M for JIC and £13M for IFR, which provides for long-term research programmes and supporting infrastructure. This allows the institutes to pursue mission-led, far-reaching research programmes that translate their science into new products, services or advice.

But the journey from wild broccoli variety to supermarket product has taken decades (see 'Timeline') and is not just about science. Translating work from laboratory bench to supermarket shelf also requires specialist commercial and legal expertise, which was achieved in collaboration with Plant Bioscience Limited (PBL), a company formed in 1994 to develop innovative research into patented and licensable technologies. PBL is jointly and equally owned by JIC, BBSRC, and the Sainsbury Laboratory and also located on the Norwich Research Park with JIC and IFR, forming a unique nucleus of cutting-edge science in the UK. BBSRC has representation of the board of the company. "The broccoli is selling well at M&S," says PBL Managing Director Jan Chojecki. "If this is sustained, there will certainly be a flow back to British science."

The Italian connection

The story begins in the Mediterranean in the early 1980s when Professor Richard Mithen, currently at IFR, was on a field trip to collect rare plants as part of his PhD at the University of East Anglia. "We collected wild brassicas in southern Italy and Sicily, and that material was sent into various seed banks in Italy, Sweden and Spain," says Mithen. "I was able to go on this expedition due to Professor Harold Woolhouse, the then Director of the John Innes Institute, who provided me with a small grant to cover some of my travel costs."

His PhD involved analysing chemicals in the wild brassicas called glucosinolates which were thought to protect the plants from pathogen and insect attack. Mithen, in collaboration with Professor Roger Fenwick and his team at IFR, was the first person to analyse these plants for glucosinolates, which at this time were considered toxins. Later, their role as a 'phytonutrient' became apparent. Research at IFR and elsewhere in the UK and US suggested that a particular compound, sulforaphane, derived from the glucosinolate, glucoraphanin, had certain anti-cancer and health-promoting properties. After a stint in Africa working on germplasm conservation of wild cowpeas, Mithen returned to JIC to look at brassicas afresh.

"I knew that a certain wild brassica could be the source of novel alleles that may boost the level of glucoraphanin, although, at that time we did not understand the genetics underlying the accumulation of these compounds," says Mithen. "So we started a programme to explore the genetics of glucosinolates as well as to develop broccoli breeding lines with high levels of these compounds." Some of the work was funded through a 1996 BBSRC Case studentship award to Kathy Faulkner at JIC.

‘Super broccoli’ is derived from natural wild brassicas. Image: Richard Mithen

Beyond the lab

But a great deal more investment would be needed to bring a product downstream from plant breeding all the way to a finished product on supermarket shelves. To attract and justify such investment, PBL secured the intellectual property (IP) and applied for relevant patents in the mid-90s. "Developing a product with a health-related consumer benefit, based on a nutrient that the consumer has never heard of - a novel approach at the time - is still unprecedented in a fresh vegetable," says Chojecki.

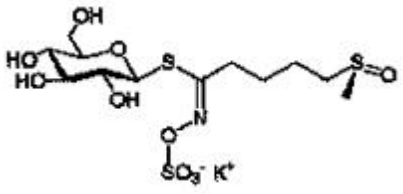
In 2000 PBL teamed up with Seminis, one of the major vegetable seed companies, which at the time accounted for almost half of the global broccoli seed market. Chojecki explains that PBL's reasoning for partnering with Seminis was to achieve broad public benefit. "It was necessary to work with a major company that could deliver high quality varieties, and that had the long-term commitment and market presence to work with the supply chain to communicate the benefits of such an innovative concept all the way to the consumer."

Refining the wild broccoli to a supermarket product took years. Image: Seminis Vegetable Seeds

Working into the new millennium, the high glucosinolate broccoli underwent an intensive breeding programme. In a process that would have gone unseen by the average shopper, traits such as uniform shape and growing at the right time of year, with no yield loss, were selected - a process that took another ten years. "It's not trivial. It's a slow, laborious and you need to be completely competitive with or better than current varieties, plus you need two or three varieties to supply produce in every month of the year and in different growing areas," says Chojecki.

Brassica health benefits

While the plant was being fine-tuned right down to the final florets, by 2003 Mithen was now at IFR building up a portfolio of evidence that the broccoli did indeed have health benefits. There is worldwide interest in understanding why people with a higher proportion of brassicas (others being cabbage, Brussels sprouts) in their diet have lower risks of some diseases, as revealed by epidemiological studies (ref 6), and other analyses (ref 7).



Glucosinolates such as glucoraphanin are converted to health benefitting compounds such as sulforaphane in the body.

Mithen and colleagues first showed that the high level of sulforaphane delivered by the new broccoli to the gut was indeed absorbed into the systemic circulation (ref 3). This established that the body takes it up rather than just excreting it.

Collaborating with the Norfolk and Norwich University Hospital, Mithen then showed that men with early signs of prostate cancer who ate the enriched broccoli showed changes in gene expression metabolites consistent with reductions in the risk of cancer developing later (ref 4).

A more recent trial (unpublished as of Nov 2011) measured biomarkers for cardiovascular disease and compared a group eating 400g super broccoli a week in people with an intermediate risk compared to a two control groups.

Bigger, better studies

Moving forward, based upon data from the current study, funding has been secured from the Technology Strategy Board (TSB), as part of its Nutrition for Life programme, to complete a larger study with two recruitment centres. One will be in Norwich and one at the University of Reading (ref 8). This study will continue to validate heart health benefits of the high glucoraphanin broccoli variety.

"There is a huge worldwide effort on sulforaphane which has many different types of activity," says Mithen. "Data from animal and cell models show that it induces anti-oxidant enzymes, suppressed cell proliferation and chronic inflammation. Our ongoing goal is to pin down the mechanisms of action in people with normal diets as opposed to giving large amounts to mice or rats."

Chojecki is impressed in the way that Mithen has applied himself to each field necessary to continue to develop the science behind the product - from plant biochemistry to genetics, and then plant breeding through to human health and nutrition. "He is an all too rare example of a scientist who has started in one field but, taking a risk with his scientific career, has moved his research into completely new areas and continued to publish in top journals. And all the while continuing to support the knowledge exchange process."

He is also looking forward to future publications. "We can be extremely positive. There is a lot of strong science around glucoraphanin the diet and there is a 2006 EU legal frame work to protect consumers," says Chojecki. "Some headline writers make leaps we don't endorse, but to be fair most of the media content pretty faithfully reflected the press statements that were released by IFR and M&S."

Professor Richard Mithen plans more human studies on super broccoli health benefits. Image: IFR

Timeline

1984: PhD student Richard Mithen participates in an international mission to conserve wild *Brassica* species, coordinated by the International Board for Plant Genetic Resources, to Southern Italy and Sicily, and seeds are deposited in Italian and Spanish seed banks.

1990: Mithen appointed as research leader at the John Innes Centre (JIC) and begins work on genetics of glucosinolates in *Brassica* and *Arabidopsis*. Seeds of wild Brassicas are obtained from seed collections.

1994: Plant Bioscience Limited (PBL) formed in Norwich to commercialise innovative science. Founded originally by JIC and the Gatsby Foundation.

1996: Kathy Faulkner begins four-year BBSRC Case Studentship at John Innes Centre.

1998: PBL files patent on high glucosinolate broccoli.

2000: Mithen becomes Professor of Crop Science at University of Nottingham.

2000: PBL licenses HG-broccoli (IP and germplasm) to Seminis to transfer high glucosinolate trait into proprietary germplasm.

2000-2009: Seminis develops elite 'super' broccoli varieties suitable for commercial production in different broccoli growing regions (EU and USA).

2002: First patents granted - Europe and USA.

2003: European patent opposed by Syngenta and Limagrain.

2003: Mithen moves from Nottingham to Institute of Food Research (IFR).

2004: BBSRC becomes shareholder in PBL.

2005: Monsanto purchase Seminis for $1.5Bn.

2000 to present: Supported by IFR, BBSRC, PBL and Seminis Mithen leads studies on health benefits of high glucosinolate broccoli, focussing on people with enhanced risk of cardiovascular disease and prostate cancer.

2007: European Patent Office Technical Board of Appeal rules on patent Opposition. Case referred to Enlarged Board of Appeal.

2008 to present: Production and supply chain established by Seminis-Monsanto, partnering with production, distribution and retail players globally, using a downstream value sharing model.

2010: Enlarged Board of Appeal of EPO issues ruling - case returns to Technical Board.

2011 (April): Limited initial launch in selected retail chains in the US (California and Texas).

2011: Beneforté broccoli launched in Marks & Spencer stores in UK on 4 October.

2011: PBL patent claims to high glucosinolate broccoli confirmed.

2012: Beneforté to become available nationwide in UK and US.

References

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4. Broccoli consumption interacts with GSTM1 to perturb oncogenic signalling pathways in the prostate (cancer changes)
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7. Dietary glucosinolates as blocking agents against carcinogenesis: glucosinolate breakdown products assessed by induction of quinone reductase activity in murine hepa1c1c7 cells
8. New research will help make foods healthier, safer and more nutritious

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