

## Research Assessment Exercise 2020

### Impact Case Study

**University:** The Hong Kong University of Science and Technology

**Unit of Assessment (UoA):** 1 - Biological Sciences

**Title of case study:** Sustaining the Bird's Nest Industry and Development of Skincare and Skin Repair Products through Biotechnology

#### **(1) Summary of the impact**

Over the past two decades, the HKUST biotechnology cluster has looked east and west to spearhead the development of new uses for compounds discovered and derived from nature, such as edible bird's nest, Chinese herbs, and various bacteria, and devised technologies to make them usable in a wide range of applications in skin and healthcare. Breakthroughs led by Chair Professor Karl WK Tsim involve the identification and authentication of active ingredients in edible bird's nest, and technology to extract them from nest fragments previously discarded in the preparation of the product for human consumption, leading to the development of a highly successful range of skincare products. They have also been pivotal for the revival and sustainability of the edible bird's nest industry in Southeast and East Asia, with important economic benefits for the thousands of people involved in the supply chain, from breeders and nest collectors through to the companies mass producing and selling the new products across Greater China. Meanwhile, Professor Raymond WK Wong's research on recombinant proteins that act as skin growth factors has resulted in skin healing and rejuvenation products, with health and well-being benefits for consumers, and economic benefits for the companies.

#### **(2) Underpinning research**

Research led by Tsim (joined HKUST, 1992; Director of the Center for Chinese Medicine Research and Development, 2007 onward), together with PhD graduate Dr Gallant KL Chan, has scientifically explored the contents of edible bird's nest (EBN) and how to extract active ingredients. This has been particularly timely, given that concerns about excessive nitrite and other toxins found in EBN led to a ban on its import into China in 2011 and an industry crisis. The HKUST researchers discovered the natural origin of nitrite contamination and invented a detoxification approach to cleanse out contaminants for safe consumption of EBN [R1]. At the same time, they discovered that EBN has extensive quantities of sialic acid (~10% by weight of EBN), which in turn could be effectively detected to allow quick and scientific product authentication [R2]. They also discovered that sialic acid inhibited tyrosinase activity, which suppresses the synthesis of the skin pigment, melanin, thus producing a skin lightening effect [R3]. China patents (ZL 2010 1 0162516.8) and (ZL 2013 1 0391376.5) for these discoveries were granted in September 2012 and October 2015 respectively.

Tsim and Chan went on to collaborate with skincare product manufacturer Shenzhen Mannay to invent a means to extract sialic acid through novel enzymatic degradation technology [R4] for commercial use. This method also meant that for the first time the active ingredients of EBN could be extracted from previously discarded bird's nest residue fragments. A China patent was granted in March 2015 (ZL 2013 1 0331828.0). Together, these breakthroughs paved the way for mass production of new ranges of skincare products containing the active ingredients from EBN and other Chinese medicine [R5], with 12 more patents filed from 2014 onward. In 2016, the team's work was nominated for China's Ministry of Education Higher Education Outstanding Scientific Research Output Award (Science and Technology): Technological Innovation.

In a separate line of research within the cluster, Wong (joined HKUST 1990) has explored over the past 20 years how to produce two skin growth factors – for the epidermis (human epidermal growth factor, or hEGF) and dermis (basic fibroblast growth factor, or bFGF). These skin growth factors when combined as E:FGF have high efficacy in skin restoration and rejuvenation, with applications such as wound-healing and as an active ingredient in anti-aging cosmetics. The hEGF, produced from novel engineering of gene expression systems in *Escherichia coli* (*E.coli*) to create the recombinant proteins, was first trialed in Hong Kong in 2000, for patients with diabetic foot ulcers.

The successful outcomes were identified as an emerging treatment for wound healing [R6], and further developed and patented in different countries over the subsequent 14 years. However, they were prohibitively expensive for widespread commercial use. In 2013, one of Wong's PhD students successfully produced an authentic form of bFGF through sophisticated purification systems, allowing for more cost-effective production of E:FGF, found to promote production of collagen and elastin in the dermis and to have a synergistic effect with hEGF for enhancing skin restoration and wound recovery [R7]. Between 2009-14, patents were granted for the US, China, Taiwan, Europe, and Hong Kong for the products developed from this research.

### (3) References to the research

[R1] Chan GK, Zhu Y... **Tsim, KW** (2013). Surveillance of nitrite level in cubilose: Evaluation of removal method and proposed origin of contamination. *Food Control* 34:637-644.

[R2] Chan GK, YZ Zheng... **Tsim KW** (2013). Determination of free N-acetylneuraminic acid in edible bird nest: A development of chemical marker for quality control. *J. Ethnobiol Trad. Med.* 120: 620-628

[R3] Chan GK, Wong, ZCF... **Tsim KW** (2015). Edible bird's nest, an Asian health food supplement, possesses skin lightening activities: identification of N-acetylneuraminic acid as an active ingredient. *JCDSA* 5: 262-274.

[R4] Chan GK, **Tsim KW**, Wan DC, Cheung FY and Wen C (2015). A preparation method of edible bird's nest extract with strong antioxidant capacity. **China Patent ZL 2013 1 0331828.0**, filed on 2 August 2013 and issued on 25 March 2015.

[R5] Wong CF, Chan GK... **Tsim KW** (2018). Complete digestion of edible bird's nest releases free N-acetylneuraminic acid and small peptides: an efficient method to improve functional properties. *Food Function* 9:5139-5149.

[R6] Tsang, MW, **Wong WKR**, et al. (2003). Human epidermal growth factor enhances healing of diabetic foot ulcers. *Diabetes Care* 26: 1856-61.

[R7] Kwong K W Y, Sivakumar T, **Wong WKR**. (2016). Intein mediated hyper-production of authentic human basic fibroblast growth factor in *Escherichia coli*. *Scientific Reports*. 6:33948.

### **Funding**

**Tsim:** 1) Optimization of the extraction method 1) for cubilose: an industrial application in skin care products. University-Industry Collaboration Program, Innovation and Technology Fund (UICP, ITF) (UIM/254), Jul 2014-Jun 2016: HK\$2,656,865; 2) A new generation of preservatives from herbal sources: development and application in cosmetic products. UICP, ITF (UIM/302), Jan 2017-Dec 2018; HK\$2,650,672. By 2019, related patents totaled 21.

**Wong:** 1) Development of an intein-mediated expression platform for the production of heterologous proteins. RGC-GRF (16101515), Aug 2015-Feb 2018: HK\$600,000; 2) Development of bacterial systems for recombinant production of potentially valuable proteins. Private company contract research through RDC HKUST (13142580), Jul 2014-Jul 2016: HK\$960,000.

### (4) Details of the impact

Research led by Tsim and Wong has had significant and wide-reaching impact for the *economy, environment, society, and culture*, with benefits for the sustainable development of the edible bird's nest industry in East and Southeast Asia; for companies and their staff involved in the production and sale of new health and skincare products; for the well-being and health of consumers through the availability of safer, highly popular and effective products; and cultural benefits from new appreciation of Chinese natural products as alternatives to major western skincare brands.

**Economic and environmental impact on recovery of the bird's nest industry:** Tsim's research on free sialic acid and extraction technologies has had a highly significant impact on the bird's nest industry in Southeast and East Asia. In 2011, the industry was in steep decline, following China's ban on bird's nest imports, with the global market value slumping from HK\$3 billion in 2004 to less than

HK\$0.3 billion in 2014, according to the Federation of Malaysia Bird's Nest Merchants Association [S1]. Since 2015, there has been a dramatic recovery, made possible by the HKUST research that: a) showed that high nitrite content was only found in crude EBN extracts, not processed products; b) developed novel and cost-effective extraction processes enabling EBN fragments that would previously have been discarded as a waste by-product of processing EBN for consumption to gain new market value as a raw material for mass-produced EBN skincare products using sialic acid as the active ingredient [S1, S2]. These breakthroughs provided an important new source of revenue for the bird's nest industry. Yiu Hing Choi, Chairman, Bird's Nest Group, Hong Kong Chinese Medicine Merchants Association Ltd, explained that Tsim's patented extraction technology for sialic acid had *"resulted in a major change in business opportunities"* for EBN merchants. Broken fragments produced in the primary production stages *"became a newly valuable material in the market"*. This had increased sales and made *"industry members less dependent on a single line of business. As an indication of the change, between 2013 and 2019, the market price of edible bird's nest residue rose from HK\$2,000 per kg to HK\$7,000-8,000 per kg. It also added to consumer confidence in the safety and efficacy of bird's nest products."* [S2] Yiu also highlighted the environmental impact. The innovation had *"greatly reduced bird's nest residue detritus, providing a great example of 'turning waste into energy' and sustainable development"*.

Allen Tan Swee Meng, President, Federation of Malaysia Bird's Nest Merchants Association, also affirmed the research *"proved very useful for ... restoring trust in the sector"*. [S1] It *"helped re-start the market and create a new market in such fine pieces, really assisting the EBN industry's revival in every connected enterprise in East and Southeast Asian EBN industry (breeding, collection, processing, wholesale, logistics, retail, import and export business)."*

**Bird's nest skincare line:** A key use for the active ingredients extracted from bird nest fragments has been in the cosmetic industry, in particular face-whitening products. Highly successful knowledge transfer leveraging the HKUST research has ensured there are now strong domestically developed products produced for Watson's, a global health and beauty chain store, and other retailers, to balance the current dominance of multinational companies in the China skincare market – forecast by Euromonitor to become the largest in the world by 2021. In 2013, Shenzhen Mannay Cosmetic Co Ltd, a Hong Kong-owned manufacturer of skincare products and cosmetics for the domestic and Asian markets, began a collaboration with Tsim's team to mass produce a new series of skin-whitening products based on EBN, using extraction technology developed and refined with the HKUST team and with funding support from Hong Kong's Innovation and Technology Commission. It also put in place quality control processes based on the Tsim team's patented sialic acid biomarker technology (TTC.PA0451).

The first EBN skincare products using this technology were launched in China in 2013 and the business relationship continues to grow today. Cheung Yim Fong, General Manager, attested: *"This brand-new technology... facilitated not only more cost-effective production through use of the less expensive bird's nest residue but... enabled the upgrading of the quality and value of our product through superior extraction and scientifically based quality testing procedures."* [S3] The process was used to develop a bird's nest whitening facial mask, night cream, and eye gel for Watson's for sale in its retail outlets, including mainland China where it now has 3,000 stores [S4]. The series has been extremely popular with retail customers, indicated by it securing Watson's Health Wellness and Beauty annual best-selling product awards for Greater China from 2013-19 [S5]. As stated by Cheung [S3], the EBN skincare line, which had resonance with Chinese customers due to bird's nest's long history as a health-boosting substance in Chinese culture *"fitted in perfectly with the trend for natural cosmetics. These cultural factors combined with the advanced biotechnology-based extraction and quality assurance technologies provided by the HKUST research team created a winning formula with Mainland skincare buyers."* This success led to the development of other product lines, retailed in Watson's, based on HKUST extraction methods from non-medicinal elements of traditional Chinese herbs. For example, a *Cordyceps* series and a separate line derived from a Tibetan flower were launched in 2015 [S6]. This knowledge transfer has had significant economic impact for

Shenzhen Mannay, reflected in annual revenue increasing by 20% since 2013, and the workforce engaged in R&D and production growing by 30%, from 750 to 1,000. The Mannay-HKUST Cosmetic Innovation R&D Center at the HKUST Shenzhen Research Institute was launched in 2015 to support further science-based development of new products. Manufacturing facilities have also been upgraded and Good Manufacturing Practice certification obtained in 2015. A new 120,000-square-meter plant in Huizhou, Guangdong, is now under construction.

Since 2017 the HKUST team has worked with a second distributor, Infinity SGC in Hong Kong, on the sale of luxury EBN masks – produced by Mannay – for Infinity’s high-end beauty salons in Hong Kong, mainland China and the US, and for online customers [S7]. Managing director Venice Tsoi affirmed customers regarded the products as “*excellent quality and remarkably effective*”. The impact on business is reflected in its sale of 30,000 boxes of masks in 2019, and 10,000 boxes produced under OEM contracts for two other companies. This has been transformational for Infinity. “*We are able to develop our business model from a service provider into a wholesaler, from a beauty salon into the field of E-commerce. We are expanding on a very solid base due to the invention.*” This includes setting up subsidiary Cosmotech for further product development, with Chan a director.

**Skin repair and rejuvenation:** Wong’s breakthroughs in creating authentic hEGF and bFGF-related skin repair and care products are benefiting patients, such as those with diabetic ulcers, pressure sores, and burns, and consumers of skin rejuvenation products, while generating economic benefits for companies involved in their development and sale. The spin-off company, Gene-vinate Ltd (GVN), established in 2006 and which Wong chairs, produces and sells 15 items – three related to wound healing and 12 to healthcare and beauty treatment [S8]. Between 2013-18, 12,200 items were sold in Hong Kong, mainland China, Malaysia, Canada, and the US, with a total revenue of HK\$5.62M, according to the company. Recently, a joint venture, Master Key Biotech Limited, has been formed between Wong’s team and Merika Medicine Factory Ltd in Hong Kong, to commercialize a cosmetic product range developed from the research [S9]. Meanwhile, Lilian Li, Chief Executive, Direction Association for the Handicapped, Hong Kong, attested to three of its members successfully using products for healing serious pressure sores [S10]. In addition, Dr Tsang Man Wo, the United Christian Hospital doctor involved in the original trials and a diabetologist in private practice since 2014, continues to use recombinant EGF products for his foot ulcer and bed sore patients. He does so when their conditions do not respond readily to conventional treatment, with positive outcomes [S11], providing an alternative that was not available previously for these hard-to-heal skin conditions.

#### **(5) Sources to corroborate the impact**

[S1] Letter. Allen Tan Swee Meng, Chairman, Persekutuan Persatuan Pedagang Sarang Burung Malaysia (Federation of Malaysia Bird’s Nest Merchants Association). [On file]

[S2] Letter. Yiu Hing Choi, Chairman, Bird’s Nest Group, Hong Kong Chinese Medicine Merchants Association Ltd. [On file]

[S3] Letter. Cheung Yim Fong, General Manager, Shenzhen Mannay Cosmetic Co Ltd. [On file]

[S4] Bird’s Nest by Watson’s [https://www.watsons.com.hk/product-bird-nest-by-watsons/silk-snail-2-step-mask-kit-5pcs/p/BP\\_233496](https://www.watsons.com.hk/product-bird-nest-by-watsons/silk-snail-2-step-mask-kit-5pcs/p/BP_233496)

[S5] Watson’s Awards [www.mannay.com/en/honor.aspx?AboutCateId=121&CateId=121&parid=110](http://www.mannay.com/en/honor.aspx?AboutCateId=121&CateId=121&parid=110)

[S6] Mannay: Raw materials <http://www.mannay.com/en/features.aspx?parid=113&page=1>

[S7] Letter: Venice Tsoi, Managing Director of Infinity SGC (HK) Ltd. [On file]

[S8] Gene-vinate Ltd website <https://www.gene-vinate.com>

[S9] Letter: Robin Law Lok Bun, Managing Director, Merika Medicine Factory Ltd. [On file]

[S10] Lilian Li, Chief Executive, Direction Association for the Handicapped, Hong Kong [On file]

[S11] Letter: Dr Tsang Man Wo, diabetologist. [On file]