Institution: The University of Manchester

Unit of Assessment: 1

Title of case study:
Fibrillin-rich microfibrils and efficacy of anti-ageing cosmetics

1. Summary of the impact

Extensible fibrillin-rich microfibrils are the template for elastic fibres that endow dynamic tissues with elastic recoil. Researchers at the University of Manchester (UoM) showed that microfibrils are degraded in photoaged skin. We developed a rapid *in vivo* assay, 'The Manchester Patch Test Assay', which predicts the potential of anti-ageing products to restore microfibrils in photoaged skin. The assay was used to demonstrate the efficacy of a Boots Healthcare anti-ageing product and was showcased on the BBC's *Horizon* in 2007. Impacts include: dramatically increased sales for Boots, investment and changes to the product development strategies of more than 10 international personal care companies, which have used our assay to support product claims.

2. Underpinning research

See section 3 for references 1-6. UoM researchers are given in bold.

The impact case is based on research that took place at UoM from 1994-date, with the first major publication in 1999 (1). The key researchers were:

- **Chris Griffiths** (Foundation Professor of Dermatology, 1993-date)
- **Rachel Watson** (RA, 1994-1997; PDRA, 1997- 2000; Clinical Scientist and Honorary Lecturer, 2001-2008; Clinical Scientist and Honorary Senior Lecturer, 2008-2009; Senior Lecturer, 2009-date)
- **Cay Kielty** (Wellcome Trust Postdoctoral Research Fellow, 1993-1999; MRC Senior Research Fellow, 1993-2003; Professor of Medical Biochemistry, 1999-date)
- **Adrian Shuttleworth** (Reader in Biochemistry, 1968-2012)

The aim of the research was to understand the effects of chronic solar irradiation on the structure and function of human skin. It was known that wrinkling associated with chronically sun-exposed skin (photoageing) was linked to loss of collagen and that this could be restored in part by the use of the prescription drug topical all-*trans* retinoic acid (RA). We investigated the role of a key component of the skin's elastic fibre network, fibrillin-rich microfibrils, in the pathogenesis and clinical appearance of photoaged skin. We showed that microfibrils are central to skin elasticity and their loss contributes to the clinical manifestations of photoaged skin. We demonstrated that loss of microfibrils occurs early in chronically sun-exposed, photoaged skin. We showed that clinical improvement of photoaged skin by use of topical RA is accompanied by restoration of the microfibril network in the papillary dermis. These observations led to the development of a controlled, short-term *in vivo* assay – 'The Manchester Patch Test Assay' – which allowed assessment of efficacy of over-the-counter topical anti-ageing products.

The key steps were as follows:

1. In photoaged skin, the microfibril network – historically known as cutaneous oxytalan fibres – was incomplete and in severe cases lost (1);
2. The gold-standard clinical treatment for photoageing, RA, resulted in the deposition of new microfibrils in the papillary dermis of photoaged skin (2);
3. We were able to recapitulate the ability of topical RA to deposit microfibrils *in vivo* by application under occlusion to photoaged extensor forearm for 12 days. Three mm diameter skin microbiopsies were used to provide histological confirmation of responses (2);
4. We showed that this novel assay system, 'The Manchester Patch Test Assay', could be used by the personal skincare industry to screen putative ingredients or finished formulations for anti-ageing properties (3-6).

The work is ongoing and many commercial products have been and are being assessed using the assay system. For example, we are using novel bioinformatic approaches in combination with biochemistry to test hypotheses on the molecular mechanisms of irradiation-induced microfibril remodelling and/or degradation (See Sherratt MJ et al. *Journal of Pathology*. 2010; 222(1):32-40).

3. References to the research

The research has been published in leading Dermatology and Pathology journals (*Journal of Investigative Dermatology, British Journal of Dermatology* and *Journal of Pathology*). Additionally, reference 4 was the most downloaded *British Journal of Dermatology* manuscript in both 2009 and 2010.

Key Publications

1. **Watson REB, Griffiths CEM**, Craven NM, **Shuttleworth CA, Kielty CM**. Fibrillin-rich microfibrils are reduced in photoaged skin. Distribution at the dermal-epidermal junction. *Journal of Investigative Dermatology.*1999; 112(5):782-7. DOI: 10.1046/j.1523-1747.1999.00562.x
2. **Watson REB**, Craven NM, Kang S, Jones CJP, **Kielty CM, Griffiths CEM**. A short-term screening protocol, using fibrillin-1 as a reporter molecule, for photoaging repair agents. *Journal of Investigative Dermatology*. 2001; 116(5):672-8. DOI: 10.1046/j.1523-1747.2001.01322.x
3. **Watson REB**, Long SP, Bowden JJ, Bastrilles JY, Barton SP, **Griffiths CEM**. Repair of photoaged dermal matrix by topical application of a cosmetic 'antiageing' product. *British Journal of Dermatology*. 2008; 158(3):472-7. DOI: 10.1111/j.1365-2133.2007.08364.x
4. **Watson REB**, Ogden S, Cotterell LF, Bowden JJ, Bastrilles JY, Long SP, **Griffiths CEM**. Effects of a cosmetic 'anti-ageing' product on photoaged skin. *British Journal of Dermatology.* 2009; 161(2):419-26. DOI: 10.1111/j.1365-2133.2009.09216.x

Other Relevant Publications

5. Farwick M, **Watson REB,** Rawlings AV, Wollenweber U, Lersch P, Bowden JJ, Bastrilles JY, **Griffiths CEM**. Salicyloyl-phytosphingosine: a novel agent for the repair of photoaged skin. *International Journal of Cosmetic Science.* 2007; 29(4):319-29. DOI: 10.1111/j.1467-2494.2007.00394.
6. Tran C, Michelet JF, Simonetti L, Fiat F, Garrigues A, Potter A, Segot E, **Watson REB, Griffiths CEM**, de Lacharrière O. *In vitro* and *in vivo* studies with tetra-hydro-jasmonic acid (LR2412) reveal its potential to correct signs of skin ageing. *Journal of the European Academy of Dermatology and Venereology.* 2013 (in press). DOI: 10.1111/jdv.12113

4. Details of the impact

See section 5 for corroborating sources S1-S5.

Context

Prior to the research at UoM, it was known that wrinkling associated with chronically sun-exposed skin (photoageing) was linked to loss of collagen and that collagen could be restored in part by the use of the prescription drug RA. UoM researchers generated new insights about the role of fibrillin-rich microfibrils in the pathogenesis and clinical appearance of photoaged skin and the effects of RA on the skin's microfibril network. These insights led to the development of the 'Manchester Patch Test Assay', which is now widely used by the personal care industry. Before the UoM research, many product claims for over-the-counter anti-ageing products were not verified by an external, scientific source.

Pathways to impact

The research was presented at leading conferences (British Society for Investigative Dermatology, European Society for Dermatological Research, International Investigative Dermatology, American Aging Association, Gordon Conferences) and published in leading scientific journals (see above). This exposure has led to significant interest from the biogerontological and personal care communities, both academic and commercial.

In 2007, the underpinning research was showcased by the BBC2 science documentary series *Horizon*. The programme highlighted the assay and described how it had been used to demonstrate that a Boots Healthcare over-the-counter anti-ageing product, No7 'Protect & Perfect Beauty Serum', restored the microfibril network, implying potential to rejuvenate aged skin. There was very significant public interest. This interest resulted in a sell-out of the 'Protect & Perfect' product and the retooling of the Boots manufacturing plant to meet demand. [Text removed for publication.] Following the showcasing of our *in vivo* system by the BBC on *Horizon* there was a sea-change in the public's perception of the science underpinning product claims. This has resulted in a consumer-driven requirement by personal care companies to support product claims with rigorous scientific data and controlled trials of efficacy.

Reach and significance of the impact

Commercial impact on Boots

Following the broadcast of the BBC *Horizon* programme at the end of March 2007, sales of Boots No7 'Protect & Perfect Beauty Serum' rose dramatically. [Text removed for publication.]

[Text removed for publication.]

In 2012-2013, Alliance Boots Ltd Health and Beauty operation (including the No7 range) posted the highest profit growth of all Boots divisions, with the trading profits at the arm growing 6.8% (S4). Trading profits of the Health & Beauty operation have shown an annual increase from £667m in 2008/09 to £865m in 2012/13, amounting to a 30% increase (S4).

In 2012, the American pharmaceutical company Walgreens invested £4.4bn in an agreement with Alliance Boots Ltd to create the largest global pharmaceutical wholesale and distribution network (S3). The No7 'Protect & Perfect' brand was reported as a 'star beauty product from Boots at its US partner' (S3).

Impact on the personal care industry

The impact of the UoM research extends beyond Boots, influencing the product development strategies of other key players in the personal care industry. Several major national and international personal care companies (as listed below) have made use of the 'Manchester Patch Test Assay' to provide confidence in product efficacy prior to product launch. This facilitates more cohesive development strategies, leading to significant savings for R&D departments.

The importance of the research to the industry is evidenced by significant and sustained investment in research on both basic science and translational studies using the 'Manchester Patch Test Assay'. The following research contracts awarded to UoM indicate the scale of this investment.

[Text removed for publication.]

5. Sources to corroborate the impact

S1. Ranking of UK anti-ageing serums from IRI data and NPD data, 52-week period 2012-2013. *(Confidential)*

S2. Sales data 2007-2008 provided by Alliance Boots. *(Confidential)*

S3. *The Telegraph*, 15 May 2013. 'US greets Boots with anti-ageing serums'. Online version: http://www.telegraph.co.uk/finance/newsbysector/retailandconsumer/10060043/US-greets-Boots-anti-ageing-serums.html

S4. Alliance Boots Ltd Annual Report, 2012/13: http://annualreport2012-13.allianceboots.com/Assets/PDFs/overview.pdf

S5. UoM awards data, 2008-2013.