**Institution:** University of Manchester

**Unit of Assessment:** UoA5

**Title of case study:** The Manchester Patch Test Assay: providing a scientific test for the efficacy of anti-ageing products

## 1. Summary of the impact

Extensible fibrillin-rich microfibrils support elastic fibres that endow tissues with elastic recoil. We showed that microfibrils are degraded in photodamaged skin, causing loss of elasticity and wrinkling. 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, showcased on BBC *Horizon* in 2007. Impacts include: dramatically increased sales for Boots, investment and changes to product development strategies of international personal care companies, who now use 'The Manchester Patch Test Assay' to support product claims.

## 2. Underpinning research

The impact case is based on research that took place in Manchester from 1994 to date. The key researchers are:

**Professor Cay Kielty** (Professor of Medical Biochemistry, 1999 to date; MRC Senior Research Fellow, 2003-1993; Wellcome Trust Postdoctoral Research Fellow, 1993-1990)
**Dr Adrian Shuttleworth** (Reader in Biochemistry, 1968 – 2012)
**Professor Chris Griffiths** (Foundation Professor of Dermatology, 1994 to date)
**Dr Rachel Watson** (Senior Lecturer, 2009 to date; Clinical Scientist and Honorary Senior Lecturer, 2008-2009; Clinical Scientist and Honorary Lecturer, 2001-2008; Post-Doctoral Research Associate, 1997-2000; Research Assistant, 1994-1997)
**Dr Michael Sherratt** (Lecturer, 2012 to date; Fellow, 2005-2007; Post-Doctoral Research Associate, 1996-2004; PhD student, 1993-1996)

The aim of the research was to understand the effects of chronic solar irradiation on the structure and function of human skin. Fibrillin-rich microfibrils act as a template for elastin deposition, which provides skin tissue with elasticity and recoil. Kielty's research group conducted the underpinning research that led to the characterisation of fibrillin-rich microfibrils in terms of assembly, structure and function [1,2]. Furthermore, Kielty's research group demonstrated that fibrillin-rich microfibrils are prone to degradation by photodamage [3,4].

From a clinical perspective, Griffiths went on to demonstrate that clinical improvement of photoaged skin by use of topical all-*trans* retinoic acid (RA) is accompanied by restoration of the fibrillin-rich 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 enabled efficacy-testing for over-the-counter, topical anti-ageing products [5].

The key steps were as follows:

1. UoM has a long history of fundamental research into the elastic fibre network (dating back to the 1970's). Kielty's research group are leading the international programme to define aspects of the assembly, structure and function of fibrillin-rich microfibrils [1,2].
2. UoM researchers demonstrated that in photoaged skin, the fibrillin-rich microfibril network was incomplete and in severe cases lost [3]. The researchers also showed that fibrillin-rich microfibrils are highly susceptible to proteolysis by matrix metalloproteinases and elastases that are produced as part of the inflammatory process associated with sun exposure [3, 4].
3. UoM researchers demonstrated that the gold-standard clinical treatment for photoageing, RA, resulted in the deposition of new fibrillin-rich microfibrils in the papillary dermis of photoaged skin [5].
4. Furthermore, the ability of topical RA to deposit fibrillin-rich microfibrils *in vivo* was recapitulated by application under occlusion to photoaged extensor forearm for 12 days. Three millimetre diameter skin microbiopsies were used to provide histological confirmation of responses [5].

UoM researchers showed that this novel assay system, 'The Manchester Patch Test Assay', could be used by the anti-ageing skin industry to screen putative ingredients or finished formulations for anti-ageing properties [6].

The research is on-going and many commercial products are being assessed using 'The Manchester Patch Test Assay'. Novel bioinformatic approaches have been used in combination with biochemistry to investigate the molecular mechanisms of irradiation-induced fibrillin-rich microfibril remodelling and/or degradation [6]. 'The Manchester Patch Test Assay' has also been used to test novel protection strategies, including novel small molecule inhibitors of key proteolytic enzymes [4] that degrade fibrillin-rich microfibrils.

## 3. References to the research

The research has been published in leading Dermatology and Pathology journals (*Journal of Investigative Dermatology* and *British Journal of Dermatology*, as well as biochemical and cell biology journals (*Biochemical Journal* and *Journal of Cell Biology*).

Kielty has authored >80 publications on fibrillin from 1 Jan 1993 to date. A selection of these are listed below:


1. Wess, T.J., Purslow, P.P., **Sherratt, M.J.**, Ashworth, J., **Shuttleworth, C.A., Kielty, C.M**. (1998). Calcium determines the supramolecular organization of fibrillin-rich microfibrils. *J Cell Biol*. 141(3):829-37. DOI: 10.1083/jcb.141.3.829
2. Baldock, C., Koster, A.J., Ziese, U., Rock, M.J., **Sherratt, M.J.**, Kadler, K.E., **Shuttleworth, C.A., Kielty, C.M**. (2001). The supramolecular organization of fibrillin-rich microfibrils. *J Cell Biol.* 152(5):1045-56. DOI: 10.1083/jcb.152.5.1045
3. **Watson, R.E.B., Griffiths, C.E.M**., Craven, N.M., **Shuttleworth, C.A., Kielty, C.M.** (1999). Fibrillin-rich microfibrils are reduced in photoaged skin: Distribution at the dermal-epidermal junction. *J Invest Dermatol.* 112:782-787. DOI: 10.1046/j.1523-1747.1999.00562.x.
4. Ashworth, J.L., Murphy, G., Rock, M.J., Sherratt, M.J., Shapiro, S.D., **Shuttleworth, C.A., Kielty, C.M.** (1999). Fibrillin degradation by matrix metalloproteinases: implications for connective tissue remodelling. *Biochem J.* 340:171-81. DOI: 10.1042/0264-6021:3400171
5. **Watson, R.E.B.,** Craven, N.M., Kang, S., Jones, C.J.P., **Kielty, C.M., Griffiths, C.E.M.** (2001). A short-term screening protocol, using fibrillin-1 as a reporter molecule, for photoaging repair agents. *J Invest Dermatol.* **116**:672-678. DOI: 10.1046/j.1523-1747.2001.01322.x
6. **Watson, R.E.B.,** Ogden, S., Cotterell, L.F., Bowden, J.J., Bastrilles, J.Y., Long, S.P., **Griffiths, C.E.M.** (2009). A cosmetic 'anti-ageing' product improves photoaged skin: a double-blind, randomized controlled trial. *Br J Dermatol.* 161:419-426.DOI: 10.1111/j.1365-2133.2009.09216.x


## 4. Details of the impact

### 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 into 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 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, 'No. 7 Protect & Perfect Beauty Serum', restored the microfibril network, implying potential to rejuvenate aged skin. There was significant public interest, resulting in a sell-out of the 'Protect & Perfect' product. The Boots manufacturing plant was retooled to cope with demand. [Text removed for publication].

**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].
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% [D]. 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 [D].

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. The No7 'Protect & Perfect' brand was reported as a 'star beauty product from Boots at its US partner' [C].

***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].

1.

**5. Sources to corroborate the impact**

A. Ranking of UK anti-ageing serums from IRI data and NPD data, 52-week period 2012-2013. *[Confidential]*

B. Sales data 2007-2008 provided by Alliance Boots. *[Confidential] Development of products based on UoM research.*

C. *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

D. Alliance Boots Ltd Annual Report, 2012/13: http://media.allianceboots.com/App_Media/AllianceBoots/financial%20information/Alliance_Boots_Annual_Report_2012-13.pdf

E. UoM research grant awards data, 2008-2013.