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To the Editor,
Thank you for the invitation to write a short commentary on the Letter…
Joo, K.M., et al., *Metabolomic analysis of amino acids and lipids in human hair altered by dyeing, perming and bleaching.* Exp Dermatol, 2016 recently published in Experimental Dermatology.

In search of hair damage using metabolomics?

Gillian E Westgate. Centre for Skin Sciences, University of Bradford,
g.westgate@bradford.ac.uk

Hair fibres are extraordinary materials, not least because they are exquisitely formed by each of the 5 million or so hair follicles on our bodies and have functions that cross from physiology to psychology, but also because they have well known resistance to degradation as seen in hair surviving from archaeological and historical samples [1]. Hair fibres on the head grow at around 1cm each month, together totalling approximately 12km of growth per person per year. Each fibre is incredibly strong for its small diameter; with one fibre typically holding 100g and together a well-formed ponytail [allegedly] has the collective strength to support the weight of a small elephant! Hair – and from here I mean scalp hair – is under constant scrutiny by each of us; whether it be style, split ends, the first few grey hairs or the collection of hairs in the shower that should be firmly attached - leading to the fear that is hair loss. Such is this emotional attachment we have to our hair, that we understand that alterations from the norm, especially those involving major changes such as patchy hair loss in Alopecia Areata, can have strong psychological consequences, indicating just how important hair is to wellbeing [2].

Hair is composed of proteins, lipids and much smaller amounts of carbohydrate. Proteins comprise the largest mass in hair and the unique protein arrangements in fibre cuticle and cortex confer much of the fibre strength and resilience. The different classes proteins in the hair fibre have been well studied with many different gene products now described suggesting both complexity and redundancy of function. Hair fibres contain the cells originally formed in the hair follicle bulb matrix. The arrangement of these cells confers both fibre structure such as cortex cuticle and medulla, as well as determining attributes such as shape and curl [3]. These ‘cells’ are bound by unique membrane complexes containing lipids unique to hair, including the unusual lipid 18-methyl ecosinoic acid, that confers considerable sensory properties to the fibre that translate into key consumer relevant attributes such as shine [4].

Hair – the material/array, is subject to many and diverse cosmetic treatments and by in large, stands up pretty well to the varied and continual stream of innovations in products and devices from the manufacturers in this highly active product category. Similarly, there are many technical methods designed to examine human hairs to detect differences by ethnicity, age, cosmetic, UV, heat and chemical treatment to help discriminate between treatments and differentiate newer ones with added benefits. However, the improvement of the appearance and tactile feel of hair by such treatment is always the subject of a trade off that some new benefit that the consumer seeks outweighs the negative effects of the associated treatment on another (arguably less important) attribute. Such negatives are referred to as 'hair damage' and recently hair damage estimation has entered the 'omics' era. While many non-invasive spectral methods have been used to estimate the effects of chemical, UV and heat treatments on hair (such as FTIR and confocal Raman spectroscopy), it wasn't until the first publications on 'proteomic' analysis of hair samples that the large diversity of hair proteins and post translational alterations, came to be understood [5] and subsequently used as a methods for differentiation in hair by factors such as ethnicity and chemical treatment [6] [7]. Such analysis reveals considerably more information about component proteins in hair, including cuticle vs cortex and they make use of the publicly available human protein databases such as Uniprot to identify natural and modified amino acids in extracts and biomarkers of damage due to oxidation of hair proteins.

Hair fibres are dead. However they can and do reflect the life lived - as the fibre becomes a repository for various chemical moieties that result from cellular metabolism, pollution and metabolites of drugs as they pass from blood to cells in the follicle and remain sequestered in the hair fibre. Fibre morphology can also tell a story of hair damage and more rarely, genetics, as recently described by van Steensel et al who discovered polymorphisms in two hair keratin genes *KRT83* and *KRT86* in monilethrix [8]. However, in cosmetic science, the relationship of fibre morphology to function/behaviour is often a very subtle one, requiring ever more sophisticated methods for differentiating products and their benefits for the consumer.

Metabolomics is most commonly applied to body/tissue fluids, however, recently the concept of metabolomic analysis of hair was successfully introduced by Sulek et al [9] to predict foetal growth restriction (FGR) by examination of maternal hair samples, and they found a distinct metabolite profile that distinguished FGR from normal pregnancy upon statistical comparison. Both proteomic analysis and metabolomics generate complex data sets and all studies require considerable understanding and rigour in the statistical analysis applied. While metabolomics might well be expected, as in the case described, to reflect a metabolic 'root cause' for changes in hair, a recent study by Joo et al [10] published in this Journal, has 'borrowed' the metabolomics approach in a study of chemical damage to hair fibres.

So what makes a study of hair damage metabolomic? Joo et al performed standardised chemical treatment of hair samples (bleaching, dyeing, perming) and used commonly available sensitive analysis methods involving amino acid analysis, chromatographic separation and mass spectroscopy to study hair fibres with and without treatment. However, they also applied the type of statistical analysis more commonly used in metabolomic studies to identify novel biomarkers, including principle components analysis

(PCA), orthogonal projection to latent structures dataset analysis (OPLS-DA) and variable importance for projection (VIP). Their results on the amino acid changes were not surprising with cysteine to cysteic acid conversion and alterations in tryptophan and methionine found after all the chemical treatments. However, the production of a comprehensive hair lipid dataset and subsequent 'metabolomic' statistical treatment of the data identified specific lipid changes in proportion to the severity of hair damage. However, it remains to be seen whether such a 'metabolomic' approach can be used to direct the development of strategies to measure the effect of anti-damage treatments to prevent effects on hair by what are still considered harsh chemical procedures.

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