Molecular and Cellular Endocrinology 243 (2005) 1–11

www.elsevier.com/locate/mce

At the Cutting Edge

Hair melanocytes as neuro-endocrine sensors—Pigments for our imagination

D.J. Tobin*, S. Kauser

Cutaneous Biology Research Group, Medical Biosciences, School of Life Sciences, University of Bradford, Bradford, West Yorkshire BD7 1DP, UK

Received 2 August 2005; accepted 2 September 2005

Abstract

We are currently experiencing a spectacular surge in our knowledge of skin function both at the organ and organismal levels, much of this due to a flurry of cutaneous neuroendocrinologic data, that positions the skin as a major sensor of the periphery. As our body's largest organ, the skin incorporates all major support systems including blood, muscle and innervation as well as its role in immuno-competence, psycho-emotion, ultraviolet radiation sensing, endocrine function, etc. It is integral for maintenance of mammalian homeostasis and utilizes locally-produced melanocortins to neutralize noxious stimuli. In particular, the cutaneous pigmentary system is an important stress response element of the skin's sensing apparatus; where stimuli involving corticotrophin-releasing hormone (CRH) and proopiomelanocortin (POMC) peptides help regulate pigmentation in the hair follicle and the epidermis. These pigmentary units are organized into symmetrical functional pigmentary units composed of corticotropin-releasing hormone, and the melanocortin POMC peptides melanocyte stimulating hormone, adrenocorticotropic hormone and also the opiate β-endorphin. These new findings have led to the concept of "self-similarity" of melanocortin systems based on their expression both at the local (skin) and systemic (CNS) levels, where the only major apparent difference appears to be one of scale. This review explores this concept and describes how the components of the CRH/POMC systems may help regulate the human hair follicle pigmentary unit.
© 2005 Elsevier Ireland Ltd. All rights reserved.

Keywords: Hair follicle; Proopiomelanocortin; Skin; Cutaneous neuroendocrinology; Self-similarity; Homeostasis

Contents

1. Background and context

Hair follicles (with mammary glands) signify our sole anatomic distinguishing feature as mammals among all other living things, and so it is reasonable to assume that these skin appendages must have or have had particularly important functions. This view is supported by the fact that the hair follicle

Abbreviations: ACTH, adrenocorticotropin hormone; END, endorphin; MC1R, melanocortin receptor 1; MSH, melanocyte simulating hormone; PC, prohormone convertase; POMC, proopiomelanocortin; TRP, tyrosinase-related protein; UVR, ultraviolet radiation

* Corresponding author. Tel.: +44 1274 233585; fax: +44 1274 309742.
E-mail address: dtobin@bradford.ac.uk (D.J. Tobin).

0303-7207/$ – see front matter © 2005 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.mce.2005.09.001

is our adult body's only permanently regenerating organ (Stenn and Paus, 2001), characterized by life-long transitions through phases of frenetic growth (anagen), apoptosis-driven regression (catagen) and relative quiescence (telogen). Indeed, after the bone marrow, hair follicle epithelium is the human body's most rapidly proliferating tissue. Over 5 million hair follicles perforate our skin surface, though only a paltry 2% reside in the scalp. The most 'alabaster' skinned sports as many of these mini-organs as the 'hairiest'—where fiber's size matters more than number. While hair serves a clear and critical role (e.g., thermoregulation) in furry mammals, for humans this trait is a potent 'signal' (Hadshiew et al., 2004), one that is associated with psychological trauma if deemed either too much, too little or the 'wrong' type.

The hair follicle 'mini-organ' is formed from a bewilderingly complex set of interactions involving ectodermal, mesodermal and neuroectodermal components, which go to elaborate five or six concentric cylinders of at least 15 distinct interacting cell sub-populations (Langbein and Schweizer, 2005). In this way, many if not all of the body's important physiologic processes can be found in the hair follicle including controlled cell growth/cell death, heterotypic cell interactions, cell differentiation and migration, hormone responsitivity, etc. (Paus and Peker, 2003). Moreover, the mode of formation of the hair follicle's fiber product is unique, as this occurs in a highly time-resolved manner to '*lock in*' a snap-shot of an individual's physiology and (bio)chemistry at the time of that section of the hair fiber's formation. Thereafter, the hair fiber does not undergo further biogenic change, and so is an increasingly favored bio-resource of forensic scientists, archeologists and toxicologists (cf. Tobin, 2005a,b).

The ability of the hair follicle to interconnect with systemic regulatory networks is truly remarkable (Slominski and Wortsman, 2000; Slominski et al., 2000a; Ito et al., 2005). Not only can the hair follicle respond to most hormones known to biomedicine but also has the capacity to produce a wide range of these same hormones for itself, via local direct synthesis or transformations, conversions, etc. Important examples include the sex hormones, proopiomelanocortin (POMC) peptides, corticotropin-releasing hormone (CRH), prolactin, cortisol, etc. (Randall et al., 2000; Slominski and Wortsman, 2000; Slominski et al., 2000a; Alonso and Rosenfield, 2003; Ito et al., 2005). The age-old observation that men castrated before puberty did not go bald or grow beards, and the subsequent confirmatory finding that these individuals did so upon treatment with so-called male hormone testosterone, highlights the dominant role of androgens in hair growth. Hair follicles in different regions of the body respond differently to androgens and the inhibition of type II 5α-reductase activity, by the drug finasteride, can induce hair re-growth in some balding men (Kaufman et al., 1998). Moreover, several neuro-peptides/-transmitters/-hormones, previously thought the domain of the central nervous system (CNS), are increasingly implicated in mediating hair follicle events (Botchkarev, 2003), including those related to psycho-emotional stress (Arck et al., 2003).

Another surprise to biomedical scientists was the unique immunological status of the hair follicle (Westgate et al., 1991; Christoph et al., 2000; Paus et al., 2005). The immunology of this mini-organ differs dramatically from that of the skin's epidermis and dermis in that the epithelium of the proximal anagen hair follicle appears to be 'immuno-silent'. This is due to its lack of tissue histo-compatibility antigen expression, found in all other nucleated cells except for recognized 'immune privilege' sites like the testes, eye, parts of the brain and feto-trophoblast (Streilein et al., 1997). The hair follicle appears to enjoy similar immune privilege, and this appears to be designed to prevent inappropriate recognition of proteins that may jeopardize the maintenance of this crucial survival trait for furry animals.

Another striking function of skin and hair follicle is its ability to produce copious amounts of pigment (Slominski et al., 2004a). Skin and hair color provide one of the most striking markers of our overall visual appearance and serves to highlight striking variations between human sub-groups (Tobin and Paus, 2001; Tobin, 2005b), the nefarious exploitation of which has had destructive sociologic ramifications. Skin and hair follicle melanins are formed in cytoplasmic organelles called *melanosomes* produced by neural crest-derived pigment cells called *melano-cytes* and is the product of a complex, phylogenetically ancient, biochemical pathway called *melano-genesis* (Slominski et al., 2004a).

Why humans should have developed such a luxurious growth of pigmented scalp hair is perplexing. One attractive possibility (advanced by Hardy and reviewed in Morgan, 1985) derives from Homo sapiens' littoral evolution by seacoasts and riverbanks. These early humans consumed considerable amounts of fish, many of which concentrated heavy metals. Thus, the ability to rapidly rid the body of these toxic metals, by selectively binding to melanin, would have a selective advantage. Given the very high proliferation rate of hair matrix keratinocytes, heavy metals would be excreted very quickly in the very high turnover of the melanized cortical keratinocytes that go to make up the pigmented hair shaft (Bertazzo et al., 1996). Furthermore, long melanized scalp hair can trap/bind chemicals and toxins, heavy metals, and so prevent access to the living tissue of the highly vascularized scalp. The reactive quinone intermediates generated during melanin biosynthesis have been shown to have potent antibiotic properties, providing further selective advantage given that hair follicles provide numerous ports of entry into the body for micro-organisms (Paus, 1997).

In this review, we focus on the involvement of the CRH and POMC systems in the regulation of follicular pigmentation, as an example of melanogenesis not directly affected by the main regulator of human pigmentation, i.e., ultraviolet radiation (UVR) (Slominski et al., 2004a).

2. The skin and the neuro-endocrine system

There continues to be much excitement about the discovery in the skin's huge capacity to act as a peripheral neuro-endocrine organ (reviewed in Slominski, 2005). Like all significant discoveries, this seems obvious to us now, not least because the skin clearly occupies a very strategic location between the epidermal and internal environments and so would be expected to play a major role in maintaining a constant internal body environment or homeostasis (Slominski and Wortsman, 2000;

Download English Version:

https://daneshyari.com/en/article/9914886

Download Persian Version:

https://daneshyari.com/article/9914886

Daneshyari.com