Since the pioneering work of Oliver (1980) the hair follicle dermal papilla, the specialized body of dermal cells at the base of the structure, has been recognized as having a governing influence on follicle epithelium. As the key signaling center, the papilla is responsible for maintaining the growth of hair and orchestrating events during the hair cycle, and the cells of the papilla have a developmental gene expression profile that reflects this complex role (Stenn and Paus, 2001). Recently, however, considerable interest has switched to the adjacent dermal sheath, the other main dermal component of the follicle. Anatomically, sheath cells connect with the base of the dermal papilla and then form a sleeve around the epithelium along the length of the follicle. Papilla and sheath cells have the same embryological origin, and sheath cells can replace the dermal papilla in experimentally amputated follicles (Oliver, 1966a); therefore, perhaps unsurprisingly, they possess many common features. However, sheath cells have generally been regarded as a reserve population, not normally recruited into undamaged papillae, and lacking some of the inductive properties of the papilla cells.

In this issue, McElwee et al (2003) have revisited the relationship between follicle dermal papilla and dermal sheath cells. Using GFP labeled mice they show that cells from the dermal sheath population immediately adjacent to papilla bulb termed the dermal sheath cup (DSC), can induce follicle formation when transplanted into the ear or footpad skin. They conclude that cells in this DSC compartment are functionally similar to the DP cells, and different from dermal sheath cells located higher up the follicle. In addition, DSC and DP cells both express alkaline phosphatase in vivo and in vitro, leading the authors to suggest that this might be a marker of inductive follicle dermis. Here, the significance of these findings is examined in the context of the older dogma, other recent studies, and some new thoughts about dermal stem cells in the hair follicle.

DERMAL SHEATH – DERMAL PAPILLA TRANSITION

McElwee et al look beyond their experimental study and suggest that DSC cells may also be a source of cells for the dermal papilla via migration during the normal hair cycle. The idea that there is movement of cells between the dermal sheath and dermal papilla during the normal hair cycle is not new (Oliver, 1991; Jahoda, 1998). Upward follicle regression at catagen and downward extension in early anagen have previously been identified as likely points for cell movements since these are when follicle reorganization is at its most mobile/labile. However, in this regard another recent study (Tobin et al, 2003a) is of crucial significance because, for the first time, the authors provide direct evidence that dynamic interconversion between the dermal sheath and dermal papilla does take place, and that the DP population is not as stable as previously thought. Specifically, the work provides evidence that dermal sheath cell division contributes directly to the recruitment of cells into the dermal papilla in early anagen, and that migration of cells into the dermal sheath (rather than apoptosis) causes the reduction in size of the papilla during catagen. The implications of these findings are discussed further in a related article (Tobin et al, 2003b). By demonstrating experimentally that cultured bulb dermal sheath cells can be incorporated into existing follicle dermal papillae, McElwee et al (2003) add to evidence from regeneration experiments that sheath cells can supplement papilla cell numbers or indeed replace a complete papilla (Oliver, 1966b). Conversely, where new follicles have been induced by the interaction of intact papillae with skin epithelium, it appears that the new dermal sheath is derived from the dermal papilla (Jahoda, 1992).

COMPARTMENTS IN THE HAIR FOLLICLE DERMIS

The cumulative evidence suggests that, within the follicle, DS cells are a reservoir or stem cell source for the papilla. In this regard, there are distinctive parallels with the epithelial outer root sheath of the follicle, an anatomically distinct subpopulation of which (the bulge cells) are believed to contribute to the matrix during the cycle (Cotsarelis et al, 1990). This brings up the question of whether there are also specific DS cell compartments. If McElwee et al are correct, the close phenotypic and functional relationship between the DSC cells and the DP segregates them from the rest of the DS. But what is the evidence that this is a...
HAIR FOLLICLE DERMIS AND SKIN DERMIS

The papers by McElwee et al and Tobin et al both reinforce the stem cell role of dermal sheath cells within the follicle; however, recent findings suggest that this may only be part of the story. McElwee et al point to the fact that DSC cells and DP cells both express alkaline phosphatase expression in vivo and in vitro, as a marker of inductive follicle dermis. However, we now know that follicle dermal papilla and sheath cells can be differentiated into bone and adipose tissue (Jahoda et al, 2003). Therefore, the expression of alkaline phosphatase, a marker of osteocyte differentiation, could reflect the broader stem cell capabilities of these populations, or indeed could just be incidental.

Possibly the most intriguing observation made by Tobin et al (2003a) is the bi-directional flow of follicle dermal cells. Not only are DS cells recruited into the DP, but there is also a loss of DP cells into the DS at catagen. But is this cellular exchange limited to the follicle? It is long established that epithelial cells of the follicle ORS are crucial in the regeneration of wounded interfollicular epidermis. We have hypothesized that in the same way that ORS cells are recruited into wounded follicles, the DS/DP cells play a parallel role as stem cells in dermal wound repair (Jahoda and Reynolds, 2001), and have shown that DS cells can incorporate into healing wounds (Gharzi et al, 2003). Therefore, there is some evidence that follicle dermal stem cell activity extends to the interfollicular dermis in the context of trauma. The perception of the relationship between follicle epithelium and skin epidermis underwent a major revision when labeling experiments showed that follicle stem cells in the epithelial bulge region contribute to normal undamaged skin (Taylor et al, 2000). If the parallels between the DS and ORS were to be extended further, then one could envisage that, in a similar way, dermal sheath cells could contribute to the interfollicular skin fibroblast population. An exciting observation described in the work of Tobin and colleagues, but whose significance is not considered, further is the "release" of dermal sheath cells from the follicle during catagen. From my perspective this could well be the first evidence of the follicular dermis contributing to the interfollicular dermis in undamaged skin. Some of these ideas are summarized in Fig 1.

Figure 1. Speculative diagram illustrating movements of dermal cells between the dermal papilla and dermal sheath within the follicle, and also into the skin dermis.

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