A New Anti-aging Strategy: A Yeast Extract to Reinforce the DEJ

Maud Jouandeaud, Christa Chauprade, Catherine Soulie, Sylvie Bordes, Brigitte Closs, SILAB, France

The dermal-epidermal junction (DEJ) is a complex region that is the interface between the dermis and the epidermis. This structure is involved in a number of biological processes such as tissue repair, migration, proliferation and differentiation of epidermal cells.

The DEJ is a physical and chemical barrier responsible for the cohesion between dermis and epidermis and resistance to external traction forces on the skin. Thanks to a complex network of interconnecting proteins, the DEJ presents an important mechanical stability (Burgeson *et al,* 1997).

The DEJ favors exchanges from the dermis to the epidermis ensuring the nutrition and renewal of the epidermis via the passage of dermal growth factors. The DEJ also participates in epidermal communication by releasing cellular messages toward the dermis that cause inflammatory phenomena.

The dermal-epidermal junction is divided in several zones, which could be distinguished by electronic microscopy:

- The hemidesmosomes distributed on keratinocyte membranes.
- The basal membrane is composed of two areas: a clear area called the lamina lucida and an underlying dense area, the lamina densa.
- The anchoring molecules, which form an anchoring plaque between the lamina densa and other molecules of the superficial dermis.

Each of these zones also contains ubiquitous basement membranes components, which are able to form a complex architecture of anchoring fibrils: including laminin and nidogen, type IV and type VII collagen, heparan sulfate proteoglycan, laminin and integrins.

Collagen IV is a fibrous, non-specific protein of the DEJ, synthesized by fibroblasts and keratinocytes. It is the "structural frame" of the basal membrane to which other proteins are linked (nidogen, 5- and 6-laminins or perlecan) to form a stable molecular network (Timpl *et al,* 1996).

Collagen VII is another important component of the basement membrane and represents the major structural component of anchoring fibrils responsible for attaching the lamina densa of the basal membrane to the superficial dermis and ensuring good cohesion between the dermis and epidermis (Burgeson *et al,* 1990). Collagen VII can bind to the N-terminal extremities of collagen IV and laminin 5. (Burgeson *et al,* 1997). Recent work (Craven *et al,* 1997) on the appearance of wrinkles in photo-aged skin, i.e.; chronically exposed to the sun, has suggested the participation of collagen VII in the mechanism of wrinkles formation. The authors showed that decreased levels of collagen VII in photo-damaged skin was correlated with the formation of wrinkles and would thus correspond to a loss of anchoring fibrils composed primarily of collagen VII, responsible for the integrity of the DEJ (Craven *et al,* 1997).

Integrins are the major receptors involved in cell-cell and cell-matrix adhesion and the transduction of signals that regulate such processes as cell growth, cell differentiation, cell migration, healing and tissue remodeling. Integrins are surface glycoproteins composed of two subunits, α and β. Their specificity is largely determined by their heterodimeric composition, even though some integrins can have different specificities depending on the cell type that expressed them. The principal species expressed in cultured cells are integrins $\alpha2\beta1$, $\alpha3\beta1$ and $\alpha5\beta1$ (Eberhard Klein *et al,* 1991). Integrins $\alpha2\beta1$ expressed by keratinocytes and fibroblasts are cellular receptors for type I and IV collagens, laminin and fibronectin. They participate in cell-matrix interactions by maintaining the spatial organization of the DEJ and the integrity between dermis and epidermis.

Laminins are heterodimeric glycoproteins composed by three distinct polypeptidic chains (alpha, beta, gamma). Laminins could be considered as key components of the anchoring network, which are essential to epidermal cell attachment (Nishiyama *et al,* 2000 ; Burgeson *et al,* 1997) and are essential to the basement membrane integrity (Bernard *et al,* 1997). Laminin 1 and laminin 5 may serve as nucleation sites for further polymerization of proteic compounds by a self-assembly process (Fleischmaier *et al,* 1998). Laminin 5 directly binds the amino-terminal end (NC-1) domain of type VII collagen (Rousselle *et al,* 1997).

The dermal-epidermal junction zone is involved in the surface state of the skin. Thus, if the DEJ is folded, the surface of the