Basement Membrane Zone

Discovery of Basement Membrane Components

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The dermal–epidemal basement membrane can arguably be said to be the most well studied of all basement membranes, and is a structure that plays an important role in cutaneous biology. While the discovery of genes coding for basement membrane components has provided exciting advances in our understanding of the basement membrane zone, it is easy to forget that initial molecular discovery of the major basement membrane zone proteins took place largely at the protein level. Indeed, in many instances the biochemical characterization of basement membrane zone (BMZ) proteins created the foundation for the subsequent molecular biologic advances.

The entire field of basement membrane biochemistry as we know it today was pioneered during a highly productive period of work by a group at the Max Planck Institute in Germany during the late 1970s and 1980s, which included Drs Rupert Timpl and George Martin. The activity of this group catapulted the field forward, and Dr Timpl continued this work until his untimely death in October 2003. During this period, a great many of the current leading figures in BMZ biology received their training in this group, and Timpl, Martin and others isolated and characterized the major BMZ components from the Engelbreth–Holm–Swarm tumor. The isolation and characterization of laminins, type IV collagen, nidogen (also known as entactin) and a heparan sulfate proteoglycan, ultimately named perlecan, provided a foundation for future studies at both the protein and molecular level (Timpl *et al.*, 1978, 1979; Martin and Timpl, 1987).

Subsequent to the discoveries of the major ubiquitous BMZ components from Engelbreth–Holm–Swarm tumors, a number of important associated and specialized BMZ components were discovered. Type VII collagen was discovered in the early 1980s, which coincided with our appreciation of this molecule's roles in acquired and inherited skin disease (Woodley *et al.*, 1988; Burgeson *et al.*, 1990). At the same time, the BMZ-associated molecule fibrillin, which was proven to show altered expression in Marfan's syndrome (Sakai *et al.*, 1986), was also discovered.

During the late 1980s and early 1990s, it became clear that multiple isoforms of laminins existed (Ehrig *et al.*, 1990). Some of these isoforms had important roles in the skin, most especially laminin-5, which was independently discovered by three separate groups (Verrando *et al.*, 1988; Carter *et al.*, 1991; Rousselle *et al.*, 1991), as well as laminin-6 (Marinkovich *et al.*, 1992) and laminin-10/11 (Miner *et al.*, 1995). Shortly after this report, laminin 5 was found to be the target antigen for patients with a form of mucosal pemphigoid (Domloge-Hultsch *et al.*, 1992). Nomenclature has always been a favorite subject of laminin biologists, and recently a new terminology has been adopted, which lists the numbers of the α-, β- and γ-subunits in succession. Thus laminin-5, 6 and 10 are now known as laminin-332, 311, and 511 (Aumailley *et al.*, 2005).

Finally, the topic of BMZ biochemistry cannot be complete without mentioning the discovery of the hemidesmosome proteins. Discoveries of bullous pemphigold (BP) antigens (Stanley *et al.*, 1981; Diaz *et al.*, 1990), plectin (Wiche *et al.*, 1982) and a6b4 integrin (Sonnenberg *et al.*, 1988) in the 1980s and early 1990s all led to extensive subsequent investigations of the role of these molecules in a variety of human diseases, including cancer, inherited and autoimmune blistering diseases and wound healing. Notably, it has been the study of skin biology and skin cells that has propelled much of this research forward.

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