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Kefalides N A, Alper R & Clark C C. Biochemistry and metabolism of basement membranes. *Internal. Rev. Cytol.* **61**:167-228, 1979. [Depts. Medicine, and Biochemistry and Biophysics. University of Pennsylvania. Philadelphia. PA]

This paper summarizes our knowledge of the **structure and cell biology of basement membrane (BM) macromolecules published during the period from 1972 to 1978. The data represent up-to-date information on the biosynthesis, secretion, and extracellular packaging of BM components, on the permeability properties of BMs, and on their biochemical changes in disease. [The *SCI*® indicates that this paper has been cited in more than 380 publications.]**

Type IV Collagen: From the Basement to the Penthouse

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Interest in this article was generated as a result of a series of studies dealing with aspects of the synthesis of basement membrane (BM) macromolecules and their extracellular deposition during embryologic development.[1,3]

In the middle and late 1970s important questions on the nature of the biosynthetic products of cells and tissues which synthesize BM components were being answered in our laboratory and others, and it's for this reason that I was asked by the editors of the *International Review ofCytologyto* write this article. At the time I solicited the aid of Charles C. Clark and Robert Alper, who worked with me. Although peer pressure dictated that our data, dealing with BM (type IV) collagen, had to conform to those obtained for type I collagen (the "gold standard"), studies by Clark, M.E. Grant, and R.R. Minor in our laboratory clearly pointed to aspects of type IV collagen biosynthesis and structure that were different from those of type I. The field of BM research was aided when the matrix produced by the Engeibreth-Holm-Swarm (EHS) mouse tumor became a source of soluble BM components: collagen, laminin, entactin, and proteoglycans. This attracted new investigators into the BM arena, and information on the gene structure of the α1 and α2 chains of type IV collagen soon emerged, to be followed by the cloning of the α3, α4, and α5 chains.[4-6]

The wealth of new structural information was not limited to the BM collagen but was relevant to other macromolecular components as well. Studies by M. Ohno,[7] in our laboratory, for example, showed that normal tissues contain more than one isoform of laminin. In the meantime, Wisdom et al. (in Billy Hudson's laboratory at the University of Kansas) demonstrated that the α3(I V), α4(I V), and α5(IV) collagen chains were absent in the EHS type IV collagen, while studies by Lance Liotta and his group at the National Cancer Institute emphasized the role of type IV collagenase in tumor cell metastasis.

This explosion of new information has permitted recent work to focus on the involvement of BM collagen chains in the pathogenesis of diseases such as Alport syndrome [α5(IV)] and Goodpasture syndrome [α3(IV)] and the role of the α3(IV) chain in the regulation of the inflammatory response. The picture of BMs that has evolved over the years emphasizes their complexity and the realization that structural diversity among them is critical to their ability to perform diverse functions.

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