Abstract

Collagen VI is a ubiquitously expressed, microfibril forming protein in the extracellular matrix. Mutations in the genes coding for the α1, α2 and α3 chains cause the muscle diseases *Ullrich congenital muscular dystrophy* (UCMD) and *Bethlem myopathy* (BM), which also show skin phenotypes.

Recently, three new chains α4, α5 and α6 were identified, which have been suggested to replace the α3 chain. Studies of the assembly of the novel chains showed that neither cell lines nor primary cells secrete these in conventional cell culture models. Collagen VI molecules containing the novel chains, could only be found inside the cells. However, a small amount of extracellular collagen VI containing the α6 chain was detected in organotypic 3D-cultures. The expression or secretion of the α5 chain could not be detected under any conditions; even the transfection of SaOS2 cells with cDNA coding for the α5 chain was not successful. The novel chains obviously need highly specific conditions for their expression and secretion. However, oligomers consisting of the classical chains and of the novel α5 and α6 chains could be extracted from heart and testis and analysed.

Col6α1$^{-/-}$ mice, which do not form functional collagen VI, were studied to shed light on the skin phenotypes of UCMD and BM patients. Normal skin and healing wounds in these mice show no macroscopic differences. However, the α3 chain is very widely expressed in skin and wounds and the α5 and α6 chains are associated with basement membranes. Ultrastructural analysis of wounds showed alterations of collagen I fibrils and abnormal basement membranes of vessels and nerves, similar to findings in UCMD and BM patients. In addition, tests of tensile strength of the skin of *Col6α1*$^{-/-}$ mice gave first indications of a decreased mechanical loading capacity. *Col6α1*$^{-/-}$ mice are therefore a relevant model to study the skin phenotypes of UCMD and BM patients. However, keloid formation could not be detected in these mice, in agreement with former results.