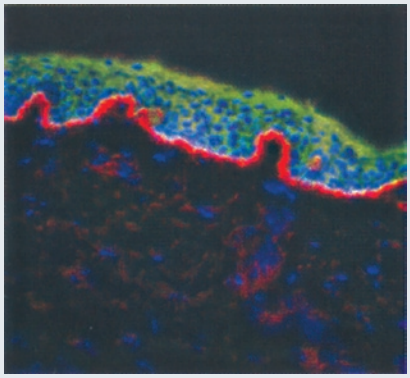
For the article: http://www.nature.com/jid/journal/vaop/ncurrent/full/5700878a.html
For discussion and answers: http://network.nature.com/group/jidclub

Recessive Dystrophic Epidermolysis Bullosa and Squamous-Cell Carcinoma: the Role of Type VII Collagen

Robert S. Kirsner[1] and Shasa Hu[1]

Journal of Investigative Dermatology (2007), **127**, 2292. doi:10.1038/sj.jid.5701086



Recessive dystrophic epidermolysis bullosa (RDEB) is a severe mechanobullous disease characterized on the molecular level by mutations in the COL7A1 gene, which encodes the keratinocyte-secreted protein type VII collagen, and clinically by an increased risk of developing squamous-cell carcinoma (SCC). The consequences of SCC development can be significant—55% of patients with the Hallopeau–Siemens subtype of RDEB die from metastatic SCC by age 40 (Fine *et al*., 1999). Thus, patients with RDEB require close monitoring for development and treatment of potential life-threatening cancers. A recent paper by Ortiz-Urda *et al*. (2005) reported, as part of a broader work describing the role of Ras and type VII collagen in epidermal tumorigenesis, that in an analysis of 10 patients with RDEB who developed SCC, all 10 displayed type VII collagen within their tumors. The results suggested that only a subset of patients who express type VII collagen develop SCC. These findings led Pourreyron and colleagues (2007, this issue) to attempt to confirm the results. They studied a discrete subset of 11 patients with RDEB (8 with the Hallopeau-Siemens subtype) who developed 17 SCCs. Of 10 patients (16 tumors), 8 demonstrated type VII collagen expression. In 2 patients (3 tumors) no type VII collagen was detected. The 2 patients and their tumors without type VII collagen detection exhibited compound heterozygous nonsense mutations within the region encoding the NC1 domain of the COL7A1 gene. Through the following questions we delve into this paper in greater detail. For brief answers please refer to http://network.nature.com/group/jidclub.

REFERENCES

Fine JD, Johnson LB, Suchindran C, Bauer EA, Carter M, McGuire J *et al.* (1999) Cancer and inherited epidermolysis bullosa: lifetable analyses of the National Epidermolysis Bullosa Registry population. In: *Epidermolysis Bullosa: Clinical, Epidemiologic and Laboratory Advances and the Findings of the National Epidermolysis Bullosa Registry* (Fine JD, Bauer EA, McGuire J, Moshell A, eds), Johns Hopkins University Press: Baltimore, 175–92

Ortiz-Urda S, Garcia J, Green CL, Chen L, Lin Q, Veitch DP *et al.* (2005) Type VII collagen is required for Ras-driven human epidermal tumorigenesis. *Science* 307:1773–6

Pourreyron C, Cox G, Mao X, Volz A, Baksh N, Wong T *et al.* (2007) Patients with recessive dystrophic epidermolysis bullosa develop squamous-cell carcinoma regardless of type VII collagen expression. *J Invest Dermatol* 127:2438–44

QUESTIONS

1. Why is the NCI domain crucial to SCC development according to Ortiz-Urda *et al*.?

2. Is the hypothesis being tested that patients with dystrophic EB require the presence of type VII collagen for development of SCC?

3. Why were immunofluorescence and immunoblotting used in this study?

4. What controls were used?

5. Do the findings of this study contradict the findings of Ortiz-Urda *et al*.?

6. What clinical implications does the article suggest?

[1]*Department of Dermatology and Cutaneous Surgery, University of Miami Miller School of Medicine, Miami, Florida, USA*