

GENETICS OF STRUCTURAL SKIN DISORDERS

Milestones in Genetics of Structural Skin Disorders

Jouni Uitto¹

¹Department of Dermatology and Cutaneous Biology, Jefferson Medical College, and Jefferson Institute of Molecular Medicine, Thomas Jefferson University, Philadelphia, Pennsylvania, USA

Correspondence: Jouni Uitto, E-mail: Jouni.Uitto@jefferson.edu

doi:10.1038/skinbio.2012.1

Heritable skin diseases consist of a group of conditions in which the cutaneous findings can be relatively minor at one end of the spectrum, whereas at the other end the cutaneous manifestations—often part of multisystem pathology—can cause significant morbidity and untimely demise of the affected individuals (Uitto *et al.*, 2012). Tremendous progress has been made in the past two decades in molecular genetics of heritable skin diseases, and candidate genes and pathogenic mutations have been identified in as many as 500 different genes in a manner that the genetic lesions explain the cutaneous manifestations (Feramisco *et al.*, 2009). Examination of the mutation databases in different diseases has revealed both obvious candidate genes and a number of surprises, but nevertheless the identification of the mutant genes has been very helpful in providing increased understanding of the pathogenetic mechanisms of these conditions. Many of these diseases could be characterized as metabolic disorders with cellular perturbations, or characterized as multisystem diseases

with structural defects. Identification of the mutated genes and specific underlying mutations has been instructive not only in providing information of the molecular basis of the disease but also providing critical understanding of the pathophysiologic role of structural components and specific proteins in normal skin. Particularly instructive have been those diseases affecting the structural components of the skin.

This series of milestones articles deals with genetic disorders with cutaneous manifestations affecting primarily the structural components of the skin. These include identification of defects in the cutaneous basement membrane zone in epidermolysis bullosa (Milestone 1), and the role of collagen and elastic fibers in providing physiologic properties to the dermis, as exemplified by the Ehlers-Danlos syndrome, cutis laxa, and pseudoxanthoma elasticum (Milestones 2–4). Heritable filaggrin disorders, with atopic dermatitis as the paradigm, have provided critical information on the role of epidermal barrier function under physiologic conditions

(Milestone 5), and dissecting the genetics of structural hair disorders has been highly instructive in understanding the growth and maintenance of normal hair (Milestone 6). In a broader sense, development of the next-generation diagnostics (Milestone 7) and molecular therapeutics (Milestone 8) for these disorders is the next step to build improved diagnosis and treatment of these, currently often intractable, disorders.

CONFLICT OF INTEREST

The author states no conflict of interest.

TO CITE THIS ARTICLE

Uitto J (2012) Milestones in genetics of structural skin disorders. *J Invest Dermatol* 132: E1

REFERENCES

- Feramisco JD, Sadreyev RI, Murray ML *et al.* (2009) Phenotypic and genotypic analyses of genetic skin disease through the Online Mendelian Inheritance in Man (OMIM) database. *J Invest Dermatol* 129:2628–36.
- Uitto J, Christiano AM, McLean WH *et al.* (2012) Novel molecular therapies for heritable skin disorders. *J Invest Dermatol* 132:820–8.

ARTICLES

- Milestone 1 Molecular Heterogeneity of Blistering Disorders: The Paradigm of Epidermolysis Bullosa—Leena Bruckner-Tuderman and Cristina Has
Milestone 2 Heritable Collagen Disorders: The Paradigm of the Ehlers-Danlos Syndrome—Peter H. Byers and Mitzi L. Murray
Milestone 3 The Complexity of Elastic Fiber Biogenesis: The Paradigm of Cutis Laxa—Zsolt Urban
Milestone 4 Heritable Ectopic Mineralization Disorders: The Paradigm of Pseudoxanthoma Elasticum—Qiaoli Li and Jouni Uitto
Milestone 5 Heritable Filaggrin Disorders: The Paradigm of Atopic Dermatitis—W.H. Irwin McLean and Alan D. Irvine
Milestone 6 Genetics of Structural Hair Disorders—Sivan Harel and Angela M. Christiano
Milestone 7 Next Generation Diagnostics for Genodermatoses—Raymond J. Cho, Michael A. Simpson, John A. McGrath
Milestone 8 Molecular Therapeutics for Heritable Skin Diseases—Jouni Uitto