Pemphigus pathogenesis

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About the author

Ena Sokol was born in Banja Luka, Bosnia and Herzegovina, on January 19, 1986. After graduating from gymnasium in Bihać in 2004, she enrolled at the Faculty of Medicine, University of Sarajevo, with a firm decision to become a medical doctor. She successfully graduated from the Faculty of Medicine in 2010 with the thesis “Application of immunotherapy in the treatment of gastrointestinal and urogenital tumors” and did a one-year internship at University Clinical Center of Sarajevo as a medical intern.

In 2011, Ena was awarded a JoinEU-SEE scholarship for academic exchange between EU and Western Balkan countries for the PhD project at the Department of Dermatology and the Department of Cell Biology, the University Medical Center Groningen (UMCG). For the past four years she has been dedicated to her research on pathomechanism of the loss of cell-cell adhesion in autoimmune blistering skin disease pemphigus, spending time in the laboratory and microscopy center.

Besides her laboratory experiments, as a PhD student, Ena guided students and attended a number of medical meetings and congresses and presented her research results in poster sessions, such as at the Annual Meeting of the Dutch Society of Experimental Dermatology, for which in 2013 she received the price for the best poster, Dynamics of desmoglein 1 in pemphigus. She participated in the organization of the Graduate School of Medical Sciences Development Conference 2015 as a program director. In her free time in Groningen, Ena attended Dutch language courses and for many years has been dancing salsa.

Pemphigus is a life-threatening autoimmune blistering disease caused by antibodies against proteins of desmosomes. Desmosomes are adhesion junctions that interconnect intermediate filament networks of neighboring cells. By targeting transmembrane proteins of desmosomes, desmoglein 1 (Dsg1) and desmoglein 3 (Dsg3), pemphigus autoantibodies induce their clustering and loss of cell-cell adhesion (acantholysis) in the epidermis of the skin and epithelium of the mucous membranes, which results in blistering. How pemphigus autoantibodies induce blisters is the main research question of this thesis. Skin and mucosa taken from pemphigus patients were analyzed using large scale electron microscopy, named "nanotomy" and novel findings are described. The datasets are open source available at *www.nanotomy.org*. Pemphigus skin was further investigated using an overlay of light and electron microscopy showing that desmoglein clusters are interdigitations between cells in which the amount of Dsg1 in desmosomes is reduced. Lastly antibodies from pemphigus patients were applied to cultured human skin cells, revealing redistribution of the targeted desmogleins in specific patterns. This thesis suggests that loss of cell-cell adhesion in pemphigus occurs due to the depletion of the targeted desmogleins which then cannot be incorporated into the desmosomes. If other desmoglein isoform is not expressed, desmosomes will 'melt' away resulting in loss of cell-cell adhesion.

On the cover: Typical invaginations between two cells induced by pemphigus auto-antibodies (electron microscopy).