2019;27(1):8-10

SHORT SCIENTIFIC COMMUNICATION

# Detection of IgG Autoantibodies against Desmocollin-3 in Greek Patients with Pemphigus

# Parthena Meltzanidou<sup>1, 2, 3</sup>, Aikaterini Patsatsi<sup>1</sup>, Aikaterini Kyriakou<sup>1</sup>, Katerina Vareli<sup>2</sup>, Alexandros Lambropoulos<sup>3</sup>

<sup>1</sup> 2<sup>nd</sup> Dermatology Department, Aristotle University School of Medicine, Papageorgiou General Hospital, Thessaloniki, Greece; <sup>2</sup> Department of Biological Applications and Technologies, University of Ioannina, Ioannina, Greece & Interscience Molecular Oncology Laboratory (iMol), University of Ioannina Cancer Biobank Center (UICBC), Ioannina, Greece; <sup>3</sup> Molecular Biology Laboratory, 1<sup>st</sup> Department of Obstetrics and Gynecology, Aristotle University School of Medicine, Papageorgiou General Hospital, Thessaloniki, Greece

#### **Corresponding author**

Parthena Meltzanidou, MSc, PhD candidate Molecular Biology Laboratory Aristotle University School of Medicine Papageorgiou General Hospital 57500 Thessaloniki Greece meltzanidou.parthena@gmail.com

Received: January 12, 2018 Accepted: February 11, 2019 **ABSTRACT** Pemphigus is an autoimmune bullous disorder caused by autoantibodies against desmosomal cadherins. The most common clinical forms are pemphigus vulgaris (PV) and pemphigus foliaceus (PF). Among the numerous proteins that are considered responsible for the cohesion of keratinocytes in epidermis, desmocollin-3 (Dsc-3) has been initially reported to participate in epidermal blistering in mice. There have been reports in which autoantibodies against Dsc-3 have been detected. In PV, a limited number of studies found no presence of IgG or IgA autoantibodies against Dsc-3. In this study we examined sera from Greek patients with PV and PF for the presence of IgG autoantibodies against Dsc-3. Immunoblotting for the detection of autoantibodies against Dsc-3 was performed in sera from all cases. Dsc-3 autoantibodies were not detected in either group (PV and PF). Our results confirm the hypothesis that the pathogenic role of Dsc-3 in epidermal blistering in PV and PF remains controversial.

KEY WORDS: pemphigus, desmocollin

### INTRODUCTION

Pemphigus represents a spectrum of autoimmune bullous disorders caused by autoantibodies against desmosomal cadherins with subsequent acantholysis. The main target antigens in pemphigus vulgaris (PV) are desmoglein-1 (DSG-1) and desmoglein-3 (DSG-3), while in pemphigus foliaceus (PF) it is DSG-1 (1). Desmocollins (Dsc) are another group of transmembrane proteins of the Ca<sup>2+</sup>-dependent cadherin family, including three different isoforms of Dsc (Dsc1-3) (2). Dsc3 is a major molecule of the adhesion complex of epidermal keratinocytes (3). The aim of this study was to examine sera from Greek patients with PV and PF for the presence of IgG autoantibodies against Dsc-3.

# PATIENTS AND METHODS

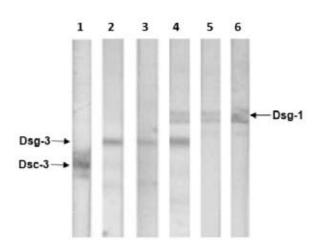
Sera were obtained from patients with PV, PF, and healthy subjects, in order to identify any reactivity to Dsc-3. Diagnosis of PV or PF was established with histology, immunofluorescence techniques, and commercial ELISAs (anti DSG-1, anti DSG-3). Analysis of the epidermal protein extracts was performed with electrophoresis in polyacrylamide 7.5% gel using the Laemmli method. The epidermal extract proteins separated were by SDS-page and transferred to nitrocellulose membrane. Immunoblotting for the detection of autoantibodies against Dsc-3 was performed in all sera.

# RESULTS

Presence of autoantibodies against Dsc-3 was not detected in any of the 45 patients with PV and of 8 patients with PF (Figure 1).

## DISCUSSION

Dsc-3 is among the numerous proteins considered to be responsible for the cohesion of keratinocytes in epidermis and has been reported to participate in epidermal blistering in mice. There are reports showing autoantibodies against Dsc-3 (4-6) in case series of patients with pemphigus herpetiformis or paraneoplastic pemphigus and pemphigus cases with atypical immunological profile (4-6). Additionally, there is published data supporting the hypothesis that Dsc-3 participates in PV pathogenesis, whereas other data indicate that Dsc-3 does not constitute an immunological target. Chen *et al.* reported that loss of function of Dsc-3 in the epidermis of mice causes disorders similar to those observed in patients with PV (3). Spindler *et al.* demonstrated the important role of



**Figure 1.** Detection of IgG antibodies against the desmocollin-3 antigen by immunoblotting using human epidermal extract. Lane 1: anti-desmocollin-3 IgG (PROGEN, GER-MANY); lanes 2, 3, 4: sera of patients with pemphigus vulgaris diluted 1:50; lane 5: sera of patients with pemphigus foliaceus diluted 1:50; and lane 6: anti-desmoglein-1 IgG (PROGEN, GERMANY). Dsc-3 in the integrity of the epidermis and concluded that desmocollin-3 is probably involved in PV pathogenesis (2). It has been suggested that anti-Dsc3 may be pathogenic in cases of dual reactivity against Dsg-3 and Dsc-3 (6).

However, there have been studies demonstrating opposing results. Hisamatsu *et al.* did not find autoantibodies against Dsc-3 in the serum of patients with PV and PF (7). Muller *et al.* also reported that existing evidence on the pathogenic role of anti-desmocollin IgA or IgG autoantibodies are probably circumstantial and need to be verified by future research (8).

In the present study we did not detect anti-Dsc-3 antibodies in Greek patients with PV or PF using immunoblotting. Our results support the hypothesis that there is no pathogenic role of Dsc-3 in epidermal blistering in classic PV and PF. Very recently, Mindorf *et al.* concluded that, based on state-of-the-art assay systems, detection of serum IgG and IgA against Dsc has no significant role in the routine diagnosis of PV, pemphigus foliaceus, or paraneoplastic pemphigus and is only useful in patients with atypical pemphigus (9).

As reported by Duker *et al.*, the pathophysiology of pemphigus is much more complicated than what it was believed in the past and its complexity should be further evaluated. IgA antibodies against Dsc-1, 2, and 3 could be produced separately and are not necessarily involved in the pemphigus cascade of immunological events (10).

#### **CONCLUSION**

Studies in separate ethnic groups could also contribute to thoroughly clarifying whether a possible causative role of Dsc in pemphigus may be attributed to environmental or genetic factors.

### **References:**

- 1. Richard W Groves. Pemphigus: a brief review. Clin Med. 2009;9:371-5.
- Spindler V, Heupel WM, Efthymiadis A, Schmidt E, Eming R, Rankl C, *et al.* Desmocollin 3-mediated binding is crucial for keratinocyte cohesion and is impaired in pemphigus. J Biol Chem. 2009 30;284:30556-64.
- Chen J, Den Z, Koch PJ. Loss of desmocollin 3 in mice leads to epidermal blistering. J Cell Sci. 2008;121:2844-9.
- Nakamura Y, Takahata H, Teye K, Ishii N, Hashimoto T, Muto M. A case of pemphigus herpetiformislike atypical pemphigus with IgG anti-desmocollin 3 antibodies. Br J Dermatol. 2014;171:1588-90.

- Ishii N, Teye K, Fukuda S, Uehara R, Hachiya T, Koga H, *et al.* Anti-desmocollin autoantibodies in nonclassical pemphigus. Br J Dermatol. 2015;173:59-68.
- Kamiya K, Aoyama Y, Wakashima C, Kudo T, Nakajima K, Sano S, *et al*. Atypical pemphigus with immunoglobulin G autoantibodies against desmoglein 3 and desmocollin 3. J Dermatol. 2016;43:429-31.
- Hisamatsu Y, Amagai M, Garrod DR, Kanzaki T, Hashimoto T. The detection of IgG and IgA autoantibodies to desmocollins 1-3 by enzyme-linked immunosorbent assays using baculovirus-expressed proteins, in atypical pemphigus but not in ty-

pical pemphigus. Br J Dermatol. 2004;151:73-83.

- 8. Müller R, Heber B, Hashimoto T, Messer G, Müllegger R, Niedermeier A, *et al*. Autoantibodies against desmocollins in European patients with pemphigus. Clin Exp Dermatol. 2009;34:898-903.
- 9. Mindorf S, Dettmann IM, Krüger S, Fuhrmann T, Rentzsch K, Karl I, *et al.* Routine detection of serum antidesmocollin autoantibodies is only useful in patients with atypical pemphigus. Exp Dermatol. 2017;26:1267-70.
- 10. Düker I, Schaller J, Rose C, Zillikens D, Hashimoto T, Kunze J. Subcorneal pustular dermatosis-type IgA pemphigus with autoantibodies to desmocollins 1, 2, and 3. Arch Dermatol. 2009;145:1159-62.