DEVELOPMENT OF A DESMOCOLLIN-3 ACTIVE MOUSE MODEL RECAPITULATING HUMAN ATYPICAL PEMPHIGUS

Lotti R.¹, Atene C.G.², Marconi A.¹, Quadri M.¹, Palazzo E.¹, Di Rocco G.², Zanocco-Marani T.², Pincelli C.¹

¹ Laboratory of Cutaneous Biology, ² Department of Life Sciences, University of Modena and Reggio Emilia, Modena (MO), Italy

Introduction

Pemphigus is predominantly characterized by the presence of autoAbs against desmosomal proteins Desmoglein3 (DSG3) and Desmoglein1 (DSG1). On the other hand, non-DSG antigens and autoAbs have been detected in PV and other forms of pemphigus, such as atypical pemphigus^{1,2}. Non-DSG antigens observed in pemphigus include cadherins, cholinergic receptors, mitochondrial proteins, and members of the armadillo family of proteins. In particular, Desmocollins, that are responsible for the structure of the desmosome and play a fundamental role in cell-to cell adhesion, seem to be highly relevant. Indeed, DSC1 and DSC3 autoAbs have been found in several forms of atypical pemphigus, in the absence or - less frequently- in the presence of anti-DSG autoAbs^{3,4}.

Objective

To better understand the pathogenic role of non-DSG autoantibodies, here we report the first DSC3 active pemphigus mouse model. In addition, we present a new active model expressing both anti-DSC3 and anti-DSG3 antibodies.

Results

PRODUCTION OF MOUSE RECOMBINANT DSG3 AND DSC3 AND IMMUNIZATION SCHEME OF MICE

PHENOTYPIC, HISTOPATHOLOGICAL AND IMMUNOLOGICAL EVALUATION OF PEMPHIGUS MODELS

EFFECT OF METHYL-PREDNISOLONE (m-PSL) IN THE THREE PEMPHIGUS MOUSE MODELS

Conclusions

- ✓ DSC3 mouse recapitulates aspects of the human **atypical pemphigus**
- ✓ DSC3/DSG3 mice express a more severe phenotype that fail to respond to systemic steroids.

The animal model presented can open the way to the generation of active pemphigus models based on different antibodies in order to create valuable tools for personalized drug discovery

References

1. Sinha AA, Sajda T. Front Med. (2018)5:218.
2. Amber KT, Valdebran M, Grando SA. Front Immunol. (2018) 9:1190.
3. Mindorf S, Dettmann IM, Krüger S, et al. Exp Dermatol. (2017) 26:1267–70
4. Müller R, Heber B, Hashimoto T, et al. Clin Exp Dermatol. (2009) 34:898–903.

Recently published in Front Immunol 2019