Mini-Review

Nomenclature of the Desmosomal Cadherins

R. S. Buxton,* P. Cowin,‡ W. W. Franke,§ D. R. Garrod,‖ K. J. Green,¶ I. A. King,* P. J. Koch,§ A. I. Magee,* D. A. Rees,* J. R. Stanley,‡‡ and M. S. Steinberg§§

*Laboratory of Eukaryotic Molecular Genetics, National Institute for Medical Research, Mill Hill, London NW7 1AA, United Kingdom; ‡New York University Medical Center, School of Medicine, New York University, New York 10016; §Institut für Zell- und Tumorbiologie, Deutsches Krebsforschungszentrum, Im Neuenheimer Feld 280, Postfach 10 19 49, D-6900 Heidelberg 1, Germany; ‖Department of Biological Sciences, Stopford Building, University of Manchester, Manchester M13 9PT, United Kingdom; ¶Department of Pathology, Northwestern University Medical School, Chicago, Illinois 60611-3008; ‡‡Dermatology Branch, National Cancer Institute, National Institutes of Health, Bethesda, Maryland 20892; and §§Department of Molecular Biology, Princeton University, Princeton, New Jersey 08544-1014

THE results of recent cDNA cloning and sequencing have established that the major glycoproteins of the desmosome type of cell–cell junctions are members of the cadherin family of cell adhesion molecules (Goodwin et al., 1990; Holton et al., 1990; Koch et al., 1990, 1991*b*; Collins et al., 1991; Mechanic et al., 1991; Nilles et al., 1991; Parker et al., 1991; Wheeler et al., 1991; and for reviews see Schwarz et al., 1990; Magee and Buxton, 1991; Legan et al., 1992). The fundamental structure of the "classical" cadherins, such as E-cadherin (uvomorulin), P-cadherin, and N-cadherin, consists of an extracellular domain, which contains four major repeats and includes sequences involved in Ca^{2+}-binding, a transmembrane domain and a cytoplasmic domain. Two types of desmosomal cadherin have been described, the desmocollins and the desmogleins.

The name 'desmoglein' was originally coined to refer to all desmosomal glycoproteins (Gorbsky and Steinberg, 1981). However, Cowin et al. (1984) introduced the term 'desmocollin' to distinguish two types of desmosomal glycoproteins that seemed to have different properties. In fact, the homology between them is no greater than the homology between the desmosomal and classical cadherins. The desmocollins display a higher degree of homology with the classical cadherins, whereas the desmogleins are distinguished in having an extra carboxy-terminal domain containing a number of repeats of a 29 ± 1 residue sequence not present in the other cadherins nor as yet found in other proteins.

There are experimental observations indicative of an involvement in cell–cell adhesion in the case of a desmocollin and two desmogleins. In the former, this is because Fab' fragments of polyclonal anti-desmocollin antibodies inhibited the formation of antibody-stainable desmosomal plaques in MDBK cells (Cowin et al., 1984). In the case of a desmoglein, the autoantigen in the blistering skin disease pemphigus vulgaris (PV), PV IgG alone, without complement or inflammatory cells, can cause loss of cell–cell adhesion in skin organ culture, with the same histology as seen in PV blisters (Schiltz and Michel, 1976; Hashimoto et al., 1983). Similarly, Fab' fragments from endemic pemphigus foliaceus autoantibodies (desmoglein DGI) cause loss of cell adhesion in neonatal mice (Rock et al., 1990). The desmosomal cadherins appear to be confined to the desmosome type of cell junction, although in the case of one desmoglein, the PV antigen, published results are inconclusive, with some indicating distribution also on the extra-desmosomal cell membrane (Wolff and Schreiner, 1971; Jones et al., 1986). More recent studies show a predominately desmosomal localization (Karpati, S., M. Amagai, K. Cehrs, V. Klaus-Kovtun, and J. R. Stanley. 1992. *J. Invest. Dermatol.* 98: 580a; and for review see Stanley, 1992).

For some time it has been known that certain anti-desmocollin (Parrish et al., 1986) and anti-desmoglein (Jones et al., 1987) antibodies only recognize desmosomes in epidermal suprabasal cells, suggesting variations in the composition of these junctions. While it was possible that these results were due to differential masking of epitopes, it did suggest that there could be variation in the composition of these junctions. In the case of the desmocollins, amino acid sequencing of proteolytic products suggested that there were different isoforms of the desmocollins which were expressed in different locations in human epidermis (King et al., 1991). Moreover, the first published sequences of desmocollins from bovine snout epithelium (Collins et al., 1991; Koch et al., 1991*b*; Mechanic et al., 1991) and from human keratinocytes (Parker et al., 1991) showed only 50% identity of their deduced amino acid sequences. Species homologues of other cadherin subtypes show substantially greater identity than this, so the possibility existed that these desmocollins were not species homologues but represented different subfamilies. This has now been confirmed for two bovine desmocollins, termed desmocollin type 1 and type 2 (Koch et al., 1992). In the case of the desmogleins, determinations of amino acid sequences derived from human cDNA clones encoding desmoglein from different kinds of cells (Koch et al., 1991*a*) or selected using autoantibodies from the blistering skin disease pemphigis vulgaris (Amagai et al., 1991) have also revealed the existence of cell type-specific isoforms for these proteins distinct from the originally described human desmoglein (Wheeler et al., 1991; Nilles et al., 1991; for review see Buxton and Magee, 1992).

The nomenclature of the desmosomal glycoproteins was discussed at a Ciba Foundation symposium held in 1986

Table I. Gene and Protein Names of the Desmosomal Cadherins

Gene name (abbreviation)	Proteins	Human synonyms	Bovine equivalent	Human chromosomal assignment (and reference)
Desmocollins				
DSC1‡‡‡	Dsc1a	DGIV*	band 4a‡] Type 1 desmocollin,§	18§§
	Dsc1b	DGV*	band 4b‡] desmoglein II‖	
DSC2	Dsc2a	§§§	] Type 2 desmocollin§	
	Dsc2b			
DSC3‡‡‡	Dsc3a	DGII	] Type 3 desmocollin‖‖‖	9p‖‖
	Dsc3b	DGIII		
Desmogleins (defined by the presence of the 29 ± 1 residue cytoplasmic repeat)				
DSG1	Dsg1	DGI	band 3,‡ desmoglein I‖ 150–165K¶	18‖‖
DSG2	Dsg2	HDGC**		18¶¶
DSG3	Dsg3	PVA‡‡		18***

* Buxton and Magee, 1991; King, I. A., unpublished data; Theis et al., 1993.
‡ Skerrow and Matoltsy, 1974; Kapprell et al., 1985.
§ Koch et al., 1992.
‖ Giudice et al., 1984.
¶ Cowin and Garrod, 1983.
** Koch et al., 1991a.
‡‡ Amagai et al., 1991.
§§ J. Arnemann, unpublished data.
‖‖ Arnemann et al., 1991.
¶¶ Arnemann et al., 1992b.
*** Arnemann et al., 1992a.
‡‡‡ The genes to which DSC1 and DSC3 refer are changed from DSC2 and DSC1, respectively, described in Buxton and Magee (1991), so as to fit in with the nomenclature proposed in the present paper.
§§§ No human equivalent to the bovine type 2 desmocollin has yet been described.
‖‖‖ Legan, P. R., K. K. M. Yue, and D. R. Garrod, unpublished data; Garrod, 1993; Troyanovsky et al., 1993.

(Bock and Clark, 1987), but unfortunately none of the schemes suggested then is able to embrace the diversity of the different desmosomal cadherin isoforms, the number of which will probably increase. We therefore propose a new nomenclature for the desmocollins and desmogleins (Table I). This is based on the accepted gene symbols which have been approved by the Human Gene Nomenclature Committee. For the desmocollin genes this is DSC and for the desmoglein genes it is DSG.

To date reports have been published of the human chromosomal assignments of three desmoglein genes, viz. DSG1, DSG2, and DSG3 (Arnemann et al., 1991, 1992*a*,*b*). It is proposed therefore that their protein products be named desmoglein 1, 2, and 3 and abbreviated Dsg1, Dsg2, Dsg3, respectively. Dsg3, the pemphigus vulgaris antigen, is included in the desmogleins by virtue of its longer cytoplasmic domain, including the presence of two repeats of the 29 ± 1 residue motif, although the fifth extracellular domain is more like the classic cadherins and the desmocollins than the desmogleins.

In the case of the desmocollins, the assignment of one human gene DSC has been reported (Arnemann et al., 1991). It has been proposed that this gene be termed DSC3, since it codes for the human orthologue of the bovine desmocollin type 3 (Dsc3) (Legan, P. R., K. K. M. Yue, and D. R. Garrod, unpublished data; Garrod, 1993; see also Troyanovsky et al., 1993) and that the type 1 desmocollin gene and protein be DSC1 and Dsc1, respectively. No human equivalent of bovine type 2 desmocollin (Koch et al., 1992) has yet been described. The desmocollin genes each code for two products differing by ~6 kD, derived from alternatively spliced transcripts from single genes. This results in the inclusion of a 46-bp exon containing an in-frame stop codon in the mRNA encoding the smaller form (Collins et al., 1991; Parker et al., 1991). It is proposed that the larger alternatively spliced protein product of each gene should be designated the 'a' form and the smaller the 'b' form. The six desmocollin proteins recognized so far are therefore referred to as 1a, 1b, 2a, 2b, 3a, and 3b. The probable relationships of the bovine and human desmosomal cadherin proteins are indicated in Table I.

This simple type of nomenclature, which is independent of tissue distribution of the proteins, can easily be extended as new genes are discovered and could also encompass other desmosomal proteins such as the desmoplakins, or indeed other junctional or cytoskeletal proteins where a plethora of isoforms renders it difficult to distinguish between types. It will also enable easy comparison between different organisms.

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