

Mutations with pathogenic potential in proteins located in or at the composite junctions of the intercalated disk connecting mammalian cardiomyocytes: a reference thesaurus for arrhythmogenic cardiomyopathies and for Naxos and Carvajal diseases

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Received: 31 January 2012 / Accepted: 3 February 2012 / Published online: 27 March 2012
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Abstract In the past decade, an avalanche of findings and reports has correlated arrhythmogenic ventricular cardiomyopathies (ARVC) and Naxos and Carvajal diseases with certain mutations in protein constituents of the special junctions connecting the polar regions (intercalated disks) of mature mammalian cardiomyocytes. These molecules, apparently together with some specific cytoskeletal proteins, are components of (or interact with) composite junctions. Composite junctions contain the amalgamated fusion products of the molecules that, in

other cell types and tissues, occur in distinct separate junctions, i.e. desmosomes and adherens junctions. As the pertinent literature is still in an expanding phase and is obviously becoming important for various groups of researchers in basic cell and molecular biology, developmental biology, histology, physiology, cardiology, pathology and genetics, the relevant references so far recognized have been collected and are presented here in the following order: desmocollin-2 (Dsc2, DSC2), desmoglein-2 (Dsg2, DSG2), desmoplakin (DP, DSP), plakoglobin (PG, JUP), plakophilin-2 (Pkp2, PKP2) and some non-desmosomal proteins such as transmembrane protein 43 (TMEM43), ryanodine receptor 2 (RYR2), desmin, lamins A and C, striatin, titin and transforming growth factor- β 3 (TGF β 3), followed by a collection of animal models and of reviews, commentaries, collections and comparative studies.

This work was supported in part by the German Cancer Foundation (Deutsche Krebshilfe, grants 10-2049-Fr1 and 106976 to W.W.F.) and the Federal Ministry for Research and Technology (START-MSC; grant 01GN0942). S.P. thanks, in particular, the German Science Foundation (DFG) for funding of a postdoctoral fellowship (Pi 869/1-1) and the British Heart Foundation (BHF) for subsequent funding within the BHF Centres of Research Excellence (BHF CoRE).

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Keywords Arrhythmogenic ventricular cardiomyopathy · Carvajal disease · Composite junction · Desmosomes · Intercalated disk · Naxos disease

Table 1 Desmosomal proteins

Protein	References presented in alphabetical and year order	
Desmocollin-2	Heuser et al. 2006	Christensen et al. 2010a
	Syris et al. 2006b	Cox et al. 2010
	Beffagna et al. 2007	de Bortoli et al. 2010
	Xu et al. 2010	
	Bhuiyan et al. 2009	Gehmlich et al. 2011a
	Simpson et al. 2009	

Protein	References presented in alphabetical and year order		Protein	References presented in alphabetical and year order		
Desmoglein-2	Awad et al. 2006a	Christensen et al. 2010a	Tandri et al. 2008	Nakajima et al. 2011	Ostrowska Dahlgren et al. 2011	
	Pilichou et al. 2006	Cox et al. 2010		Bhuiyan et al. 2009		Pamuru et al. 2011
	Syrris et al. 2007	Gehmlich et al. 2010		den Haan et al. 2009		Paul et al. 2011
	Posch et al. 2008	Xu et al. 2010		Fidler et al. 2009		van der Zwaag et al. 2011a
	Yu et al. 2008	Fressart et al. 2010		Hall et al. 2009		Zhang et al. 2012
	Bhuiyan et al. 2009	Gehmlich et al. 2011b		Qiu et al. 2009		
	den Haan et al. 2009	Kapplinger et al. 2011		Watkins et al. 2009		
		Lahtinen et al. 2011		Wu et al. 2009		
		Nakajima et al. 2011				
		Sato et al. 2011				
Desmoplakin	Norgett et al. 2000	den Haan et al. 2009	Christensen et al. 2010a		Christensen et al. 2010b	
	Rampazzo et al. 2002	Bolling et al. 2010		Cox et al. 2010		
	Alcalai et al. 2003	Christensen et al. 2010a		Xu et al. 2010		
	Bauce et al. 2005	Cox et al. 2010				
	Norman et al. 2005	Mahoney et al. 2010				
	Sen-Chowdhry et al. 2005	Sen-Chowdhry et al. 2010b				
		Xu et al. 2010				
		Fressart et al. 2010				
Plakoglobin	McKoy et al. 2000	Asimaki et al. 2009	Transmembrane protein 43 (TMEM43)	Merner et al. 2008	Christensen et al. 2010b	
	Protonotarios et al. 2001	den Haan et al. 2009		Christensen et al. 2011		
	Protonotarios et al. 2002	Christensen et al. 2010a		Klauke et al. 2011		
	Kaplan et al. 2004	Xu et al. 2010		Larsen et al. 2011		
	Antoniades et al. 2006	Asimaki et al. 2011		Pamuru et al. 2011		
	Garcia-Gras et al. 2006	Gehmlich et al. 2011a				
		D. Li et al. 2011				
		Munkholm et al. 2012				
Plakophilin-2	Gerull et al. 2004	Syrris et al. 2006a	Ryanodine receptor 2 (RYR2)	Rampazzo et al. 1995	Tiso et al. 2001	
	Antoniades et al. 2006	van Tintelen et al. 2006		Milting et al. 2006		
	Awad et al. 2006b	Otterspoor et al. 2007		Koop et al. 2008		
	Calkins 2006					
	Dalal et al. 2006	Joshi-Mukherjee et al. 2008				
	Kannankeril et al. 2006	Lahtinen et al. 2008				
	Nagaoka et al. 2006	Ram and Van Wagoner 2008				
Desmin			Desmin	Klauke et al. 2010	Otten et al. 2010	
				van Spaendonck-Zwarts et al. 2010		
				McLendon and Robbins 2011		
Lamin A/C			Lamin A/C	Quarta et al. 2011		
Striatin			Striatin	Meurs et al. 2010		
Titin			Titin	Taylor et al. 2011		
TGFβ3			TGFβ3	Beffagna et al. 2005		

Table 2 Non-desmosomal proteins

Table 3 Animal models

References presented in alphabetical and year order	
Bierkamp et al. 1996	Martin et al. 2009
Ruiz et al. 1996	McCauley and Wehrens 2009
	Pilichou et al. 2009
Gallicano et al. 2001	
	Meurs et al. 2010
Grossmann et al. 2004	
	Fabritz et al. 2011
Kirchhof et al. 2006	Krusche et al. 2011
Meurs et al. 2006	J. Li et al. 2011
Pilichou et al. 2006	Lombardi et al. 2011
	Pilichou et al. 2011
Meurs et al. 2007	
Oxford et al. 2007	Gomes et al. 2012
	Swope et al. 2012
	Kant et al. 2012
Oyama et al. 2008	

Table 4 Reviews, commentaries, collections and comparative studies published since 2000 reporting that certain mutations in human genes encoding desmosomal proteins and glycoproteins contribute to arrhythmogenic ventricular cardiomyopathies (ARVC) or Naxos and Carvajal diseases

References presented in alphabetical and year order	
Corrado et al. 2000	Navarcikova et al. 2005
Marcus 2000	Schultheiss et al. 2005
	Sen-Chowdhry et al. 2005
Corrado et al. 2001	Thiene et al. 2005
Franz et al. 2001	Wichter et al. 2005
Gemayel et al. 2001	
McRae et al. 2001	Basso et al. 2006
	Calabrese et al. 2006
Kimura et al. 2002	MacRae et al. 2006
Lee et al. 2002	Rampazzo 2006
Wichter et al. 2002	Sen-Chowdhry and McKenna 2006
	Tsatsopoulou et al. 2006
Ahmad 2003	
Bluemke et al. 2003	Bazzi and Christiano 2007
di Cesare 2003	Marcus et al. 2007
Paul et al. 2003	Pereira et al. 2007
	Sen-Chowdhry et al. 2007a
Casolo et al. 2004	Sen-Chowdhry et al. 2007b
Protonotarios and Tsatsopoulou 2004	Thiene et al. 2007
Tomé Esteban et al. 2004	van Tintelen et al. 2007
Basso and Thiene 2005	Awad et al. 2008
Dokuparti et al. 2005	Inama et al. 2008
Haverkamp et al. 2005	Whyte et al. 2008

Table 4 (continued)

References presented in alphabetical and year order	
	Maass 2010
Asimaki et al. 2009	Marcus et al. 2010
Bolling and Jonkman 2009	Migliore et al. 2010
Corrado et al. 2009	Murphy et al. 2010
El Demellawy et al. 2009	Neuber et al. 2010
Gandjbakhch et al. 2009	Pieperhoff et al. 2010
Hamilton 2009	Remme and Bezzina 2010
Herren et al. 2009	Roberts et al. 2010
Mackey-Bojack et al. 2009	Sen-Chowdhry et al. 2010a
Marcus and Zareba 2009	Xu et al. 2010
McCauley and Wehrens 2009 ^a	
Saffitz 2009	
Saffitz et al. 2009	Asimaki and Saffitz 2011
Sheikh et al. 2009	Asimaki et al. 2011
van der Zwaag et al. 2009 ^b	Avramides et al. 2011
	Azaouagh et al. 2011
Andrews et al. 2010	Basso et al. 2011
Barahona-Dussault et al. 2010	Corrado et al. 2011
Bauce et al. 2010	Ghosh and Haddad 2011
Delmar and McKenna 2010	Lahtinen et al. 2011
Elger et al. 2010	Lombardi and Marian 2011
Ellinor et al. 2010	Mezzano and Sheikh 2011
Fressart et al. 2010	Palmisano et al. 2011
J. Li and Radice 2010	Smith 2011
Lombardi and Marian 2010	van der Zwaag et al. 2011b
	Pieperhoff 2012

^a Animal model review^b This review contains information on a database from clinical research and other types of data on variants in genes causing arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVD/C)**Acknowledgement** We thank Werner W. Franke for his encouragement, critical comments and many discussions.**Open Access** This article is distributed under the terms of the Creative Commons Attribution License which permits any use, distribution, and reproduction in any medium, provided the original author(s) and the source are credited.

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