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Data Article

Data on the role of cardiac α-actin (ACTC1) gene mutations on SRF-signaling

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ABSTRACT

We recently reported a novel, heterozygous, and non-synonymous ACTC1 mutation (p.Gly247Asp or G247D) in a large, multi-generational family, causing atrial-septal defect followed by late-onset dilated cardiomyopathy (DCM). We also found that the G247D ACTC1 mutation negatively regulated serum response (SRF)-signaling thereby contributing to the late-onset DCM observed in human patients carrying this mutation ("A cardiac α-actin (ACTC1) p. Gly247Asp mutation inhibits SRF-signaling in vitro in neonatal rat cardiomyocytes" [1]). There are some ACTC1 mutations known to date, majority of which, though, have not been investigated for their functional consequence. We thus aimed at determining the functional impact of various ACTC1 gene mutations on SRF-signaling using SM22-response element driven firefly luciferase activity assays in C2C12 cells.

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Specifications Table

Subject	Cardiology and Cardiovascular Medicine
Specific subject area	Molecular cardiology (molecular mechanisms of dilated cardiomyopathy)
Type of data	Table Graph Figure
How data were acquired	Chemiluminescence was measured photometrically on an Infinite M200 PRO system (Tecan).
Data format	Analysed
Parameters for data collection	ACTC1 gene mutations mentioned in Table 1 were inducted by site directed mutagenesis and used to perform the luciferase activity. Data from all the mutant genes is compared with the wild-type ACTC1 to determine the functional impact of respective mutations.
Description of data collection	C2C12 cells were transfected with either wild-type or one of the mutant ACTC1 together with Renilla-luciferase and Firefly-luciferase. Media was changed post 6 h transfections and cells were further incubated for 48 h. Cells were then washed twice with PBS, lysed with the active lysis buffer and the assay was performed using dual luciferase reporter assay kit (Promega), according to the manufacturer's instructions. Bioluminescence was measured photometrically on an Infinite M200 PRO system (Tecan). All the experiments were performed in hexaplicate and repeated two times.
Data source location	Institution: University Medical Centre Kiel City/Town/Region: Kiel Country: Germany
Data accessibility	With the article
Related research article	Rangrez et al., A cardiac α-actin (ACTC1) p. Gly247Asp mutation inhibits SRF-signaling in vitro in neonatal rat cardiomyocytes. Biochem Biophys Res Commun. https://doi.org/10.1016/j.bbrc.2019.08.081.

Value of the Data

- Present data is a preliminary evidence of the differential functional impact ACTC1 genetic mutations on SRF-signaling
- These data provide a basis molecular cardiologists working on ACTC1 for further evaluation of these ACTC1 mutations for genotype-phenotype correlations
- Functional differences obtained here highlight the fact that different localizations of known or yet to be identified ACTC1 mutations affect the tertiary structure thereby affecting protein-protein interactions, which needs to be experimentally validated.

1. Data description

Cardiac α-actin is a fundamental structural protein necessary for the maintenance of myofibrillar integrity of the heart by forming thin filaments with tropomyosin and three troponins (C, I, and T). Several isolated ACTC1 mutations have been reported till date (Fig. 1) causing atrial-septal-defect, dilated and hypertrophic cardiomyopathy (Table 1). Majority of these ACTC1 mutants though have not been investigated for their functional consequence. Based on our findings from G247D mutation on SRF-signaling [1], we aimed here at deciphering the functional impact of ACTC1 genetic mutations

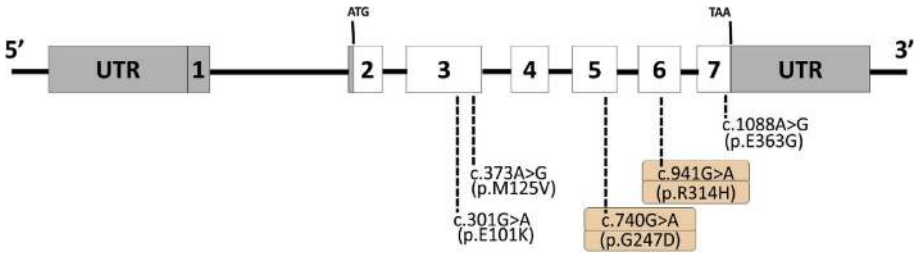

Fig. 1. Known human *ACTC1* gene mutations are depicted pictorially. Mutations are described as the nuclic acid change in the coding DNA and the resulting amino acid change in the protein in brackets. ATG = start codon, c = coding DNA, p = protein, TAA = stop codon, UTR = untranslated region.

Table 1
Location and associated cardiac phenotypes of human ACTC1 gene mutations. Listed are the description of the mutation on DNA and protein level as descripted in this article (and corresponding description according to the reference sequence from the NCBI database), the exon and the protein domain in which the mutation is located and reported cardiac phenotypes. ASD = atrial septal defect, ASD II = ostium secundum atrial septal defect, HCM = hypertrophic cardiomyopathy, LVNCC = left ventricular non compaction cardiomyopathy, MR = mitral regurgitation, RCM = restrictive cardiomyopathy.

coding DNA: nucleotide acid change (NM_005159.5)	exon	protein: amino acid change (NP_001091.1)	protein domain	clinical cardiac phenotype	references
c.301G>A	3	p.E99K (p.Glu101Lys)	subdomain 1	ASD, LVNCC, apical HCM, RCM, MR	Olson et al. 2000 [2], Arad et al. 2005 [3], Monserrat et al. 2007 [4]
c.373A>G	3	p.M123V (p.Met125Val)	subdomain 1, hydrophobic core	ASD-II	Matsson et al. 2008 [5]
c.740G>A	5	p.G245D (p.Gly247Asp)	subdomain 3	ASD-II, atrial arrhythmias, late onset DCM,	Frank et al. 2019 [6], Rangrez et al. 2019 [1]
c.941G>A	6	p.R312H (p.Arg314His)	subdomain 3, tropomyosin binding site	DCM	Olson et al.1998 [7]
c.1088A>G	7	p.E361G (p.Glu363Gly)	subdomain 3, Actinin binding site	DCM	Olson et al.1998 [7]

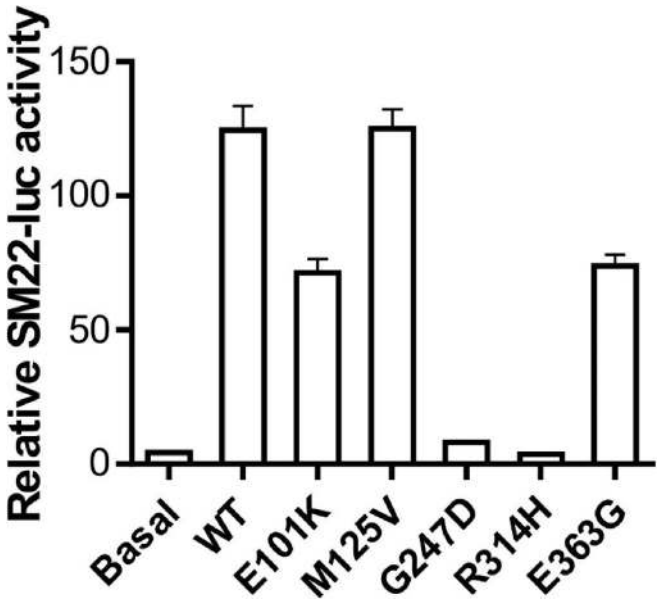

Fig. 2. Relative luciferase activity in C2C12 cells deduced from SM22 reporter-driven firefly luciferase for the human wild-type and ACTC1-mutant proteins. (n = 6/group).

on SRF-signaling using SM22-response element driven Firefly luciferase activity assay in C2C12 cells. The data is shown in Fig. 2 and the respective raw and analysed data is provided in a separate excel file.

2. Experimental design, materials, and methods

2.1. Cloning of wild-type and mutant ACTC1

Wild-type human ACTC1 gene was cloned into PDONR221 using Gateway technology (BP clonase II reaction, Life technologies) and subsequently recombined into mammalian expression vector pDEST47 (LR clonase II reaction, Life technologies). Site-directed mutagenesis for ACTC1 single nucleotide variants was performed using QuikChange XL Kit (Stratagene) according to manufacturer's instructions. All the constructs were verified by Sangers sequencing to confirm the ACTC1 genotypes.

2.2. Luciferase reporter gene assay

C2C12 cells at the confluency of approximately 50% in 12xwell plates were transfected with either wild-type or one of the mutant ACTC1 plasmids together with SM22-promoter driven Firefly-luciferase construct as well as Renilla luciferase under the control of a thymidine kinase promoter (pRLTK) to normalize for transfection efficiency. Media was changed post 6 h transfections and cells were further incubated for 48 h. Cells were then washed twice with PBS, lysed with 150 μl of the active lysis buffer by shaking the plates on a horizontal plate shaker for 20 min. Luciferase assay was performed with 20 μl of the lysates using dual luciferase reporter assay kit according to the manufacturer's instructions (Promega) in 96-well luminometry plates. Bioluminescence was measured photometrically on an Infinite M200 PRO system (Tecan). All the experiments were performed in hexaplicate and repeated two times.

Acknowledgments

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Conflict of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.dib.2019.105071.

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