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Data in Brief

Functional high-resolution time-course expression analysis of human embryonic stem cells undergoing cardiac induction

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ABSTRACT

Cardiac induction of human embryonic stem cells (hESCs) is a process bearing increasing medical relevance, yet it is poorly understood from a developmental biology perspective. Anticipated technological progress in deriving stably expandable cardiac precursor cells or in advancing cardiac subtype specification protocols will likely require deeper insights into this fascinating system. Recent improvements in controlling hESC differentiation now enable a near-homogeneous induction of the cardiac lineage. This is based on an optimized initial stimulation of mesoderm-inducing signaling pathways such as Activin and/or FGF, BMP, and WNT, followed by WNT inhibition as a secondary requirement. Here, we describe a comprehensive data set based on varying hESC differentiation conditions in a systematic manner and recording high-resolution differentiation time-courses analyzed by genome-wide expression profiling (GEO accession number GSE67154). As a baseline, hESCs were differentiated into cardiomyocytes under optimal conditions. Moreover, in additional time-series, individual signaling factors were withdrawn from the initial stimulation cocktail to reveal their specific roles via comparison to the standard condition. Hence, this data set presents a rich resource for hypothesis generation in studying human cardiac induction, as we reveal numbers of known as well as uncharacterized genes prominently marking distinct intermediate stages in the process. These data will also be useful for identifying putative cardiac master regulators in the human system as well as for characterizing expandable cardiac stem cells.

1. Direct link to deposited data

Specifications	
Organism/cell line/tissue	*Homo sapiens/hESC line HuES6/Differentiating human embryonic stem cells*
Sex	*Female*
Sequencer or array type	*HumanHT-12 v4*
Data format	*Raw and processed*
Experimental factors	*Variation of cell signaling factor stimulation; Time-course expression profiling at daily intervals during hESC differentiation*
Experimental features	*hESCs maintained in chemically defined culture medium were replated at high density and simultaneously treated with cardiac mesoderm-inducing factors for one day (20 ng/ml FGF2, 1 ng/ml BMP4, 1 μM CHIR99021). At 48 h, the differentiating cells were treated with WNT inhibitor IWP-2 for 2 days (2 μM). Overall differentiation was performed on Matrigel-coated plates in chemically defined medium devoid of serum, serum albumin, insulin, and complex additives. Furthermore, for investigating the significance of stimulating the three pathways at the beginning of the protocol, three additional time-series were recorded. In these, one signaling factor each was omitted from the initial stimulation cocktail, to reveal its significance for cardiac induction through comparison against the standard condition, respectively.*
Consent	*Not applicable*
Sample source location	*Münster, Germany*

Deposited data can be found here: http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE67154.

2. Experimental design, materials and methods

2.1. Generation and processing of samples

hESCs, cell line HuES6 [1], were maintained in FTDA medium [2], on Matrigel™-coated dishes. Cardiac differentiation was induced as

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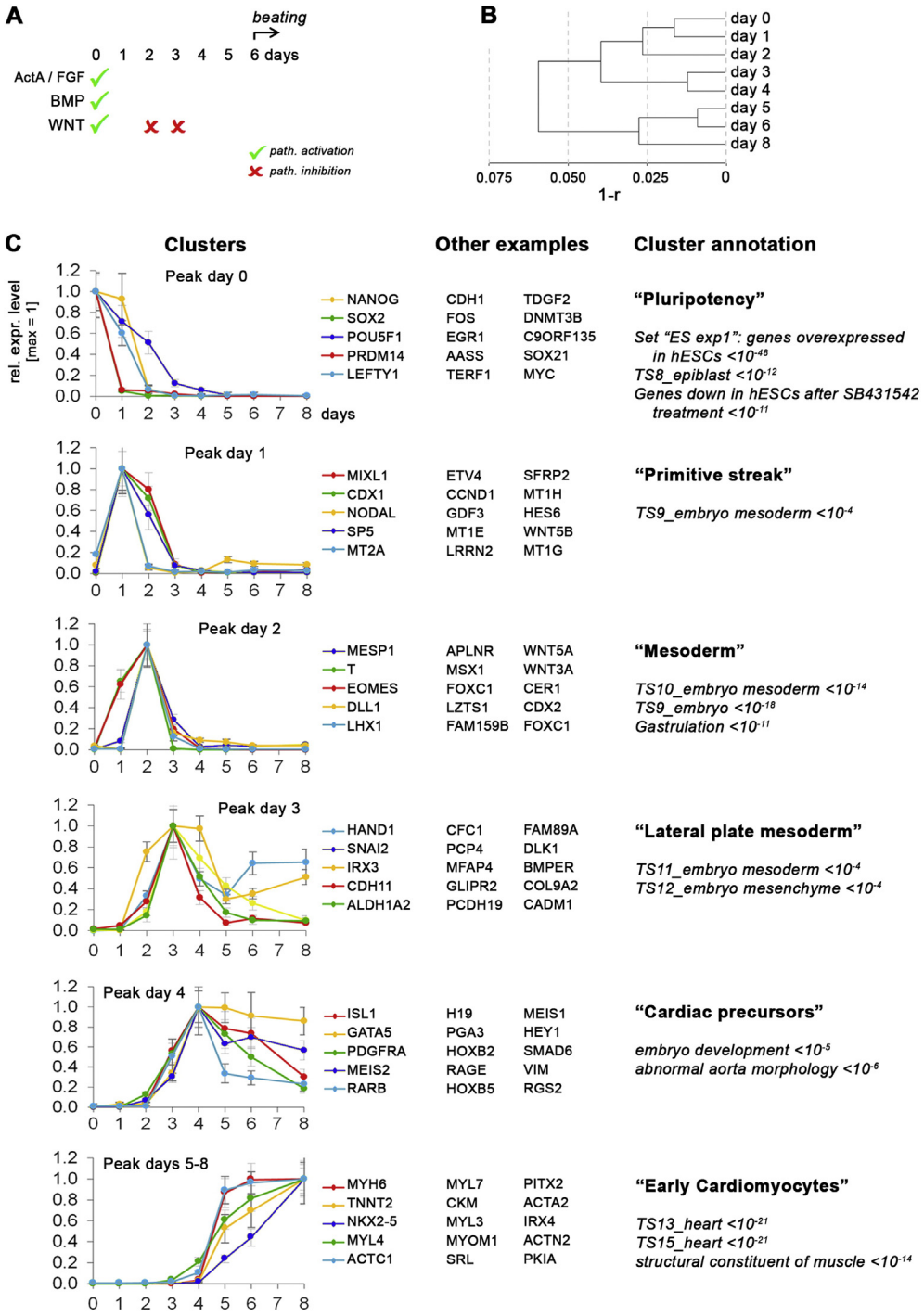

Fig. 1. Basic analysis of standard cardiac induction time-course. (A) Illustration of the signaling factor treatment protocol used for promoting cardiac induction. (B) Global correlation-based dendrogram of the time-course samples; r = linear transcriptome correlation coefficient. (C) Clustering of gene sets according to temporal expression kinetics. Selected representatives of each cluster are plotted on the left. Error bars indicate bead standard deviation. Selected annotation terms revealed by GREAT are shown on the right along with corresponding P values.

described [3]. In brief, fully confluent hPSC cultures were harvested using Accutase™, and replated onto Matrigel-coated 24-well plates (500,000 cells per well in 2 ml of day 0 differentiation medium). An aliquot of cells was used for RNA isolation ("day 0" = undifferentiated hESCs). Day 0 differentiation medium contained Knockout™ DMEM, insulin/transferrin/selenium, 10 μM Y27632, penicillin/streptomycin/L-Glutamine, 20 ng/ml FGF2, 1 ng/ml BMP4, and 1 μM CHIR99021 (3 - standard condition). Alternatively, FGF2, BMP4, or CHIR were selectively omitted from the signaling stimulation cocktail (factor withdrawal time-courses). Day 1 medium contained Knockout™ DMEM, transferrin/selenium, penicillin/streptomycin/L-Glutamine, and 250 μM phospho-ascorbate ("TS medium"). On days 2 and 3, cells were fed with TS medium supplemented with 2 μM of WNT inhibitor IWP-2 (Fig. 1A). Hence after, cells were maintained in basal TS medium. Spontaneous beating was observed from day 6 onwards. CM differentiation efficiency in the standard time-course was approximately 90% as judged by FACS analysis for cardiac troponin T [4]. Samples were collected from replicate cultures at daily intervals. Total RNA was isolated using Qiagen RNeasy columns with on-column DNA digestion.

500 ng of total RNA from each biological sample were used as input for the generation of biotin-labelled cRNA using an Illumina® TotalPrep ™ RNA amplification kit (Life Technologies). Following the