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Conference Abstract

Induced pluripotent stem (iPS) cells and somatic cardiac regeneration — An exploratory bioinformatic analysis

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Abstract

Background

Cardiac regeneration may be the future ultimate therapy for terminal heart failure. Nucleostemin (GNL3) plays a pivotal role in cardiac repair. Induced pluripotent stem (iPS) cells, induced by SOX2-OCT4-NANOG complex, may offer clues form regeneration. We would like to explore the interactions by bioinformatic approach. We identified the candidates that interacted with nucleostemin (GNL3), SOX2, OCT4 (POU5F1), and NANOG with NCBI online Entrez Gene and PubMed. The pathway networks were built with Ingenuity Pathway Analysis (IPA) 7.5 ®.

New information

In GNL3 network, molecules related to cardiovascular system development and function included CDKN2A, TP53 (tumor protein p53), ID3, NPM1, and IL2 (p=8.4e-4 ~ 9.9e-4 by right-tailed Fisher Exact Test). In canonical pathways, PPP2R5A involved in cardiac beta-adrenergic signaling and Fgf (fibroblast growth factor) involved in human embryonic stem

cell pluripotency. Nucleostemin and iPS networks had two common molecules: Fgf and TP53. Nucleostemin and iPS have interactions via tumor protein P53 and fibroblast growth factor, which would require future research.

Keywords

induced pluripotent stem (iPS) cells, nucleostemin, Ingenuity Pathway Analysis

Presentation event

Gold Prize of the Best Presentation of the Young Investigator Award, the Biennial Congress of the Association of Thoracic and Cardiovascular Surgeons of Asia (ATCSA) (http://www.atcsa2009.org), Seoul, South Korea, 2009.

Objective

Although there are clinical advances in mechanical circulatory support devices and heart transplantation, the ultimate therapy for a failing heart may be cardiac regeneration from reprogrammed somatic cells or induced pluripotent stem cells, which avoids the pitfalls in ethics of embryonic cells, device anticoagulants, or immunosuppressants (Heilmann 2008, Mauritz et al. 2008, Narazaki et al. 2008, Passier et al. 2008, Sauer 2008, Schenke-Layland et al. 2008, Siepe et al. 2008, Tulloch et al. 2008). Prior studies found nucleostemin (GNL3) may play a pivotal role in cardiac repair (Tjwa and Dimmeler 2008, Siddiqi et al. 2008). On the other hand, SOX2-OCT4-NANOG complex, the ectopically induced transcription factors for induced pluripotent stem (iPS) cells, is the key to stem cell pluripotency (Cyranoski 2008, Mauritz et al. 2008, Narazaki et al. 2008, Tulloch et al. 2008). We would like to explore their interactions by bioinformatic approach for future molecular biologists (Yosef et al. 2008, Garg et al. 2008).

Methods

Literature review was done with NCBI online Entrez Gene and PubMed to identify the candidate molecules that may interact with nucleostemin (GNL3), SOX2, OCT4 (POU5F1), and NANOG (Mauritz et al. 2008, Schenke-Layland et al. 2008, Siddiqi et al. 2008, Tjwa and Dimmeler 2008, Tulloch et al. 2008, Yosef et al. 2008). Ingenuity Pathway Analysis (IPA) 7.5 ® was then used to build the pathway networks exploiting the interplays of interactions with GNL3 and SOX2-OCT4-NANOG. Functional analyses of pathophysiological processes as well as canonical pathways were conducted and integrated.

Results

Functional pathway networks were built for nucleostemin (GNL3), with the interactions with the iPS (SOX2-OCT4-NANOG) network in the subcellular level (Fig. 1). In the GNL3 network, molecules related to cardiovascular system development and function were identified: CDKN2A, TP53 (tumor protein p53), ID3, NPM1, and IL2 (p=8.4e-4 ~ 9.9e-4 by right-tailed Fisher Exact Test). In canonical pathways, PPP2R5A involved in cardiac beta-adrenergic signaling and Fgf (fibroblast growth factor) involved in human embryonic stem cell pluripotency. Nucleostemin was found having interactions in common with NANOG of the iPS networks via two molecules: Fgf and TP53.

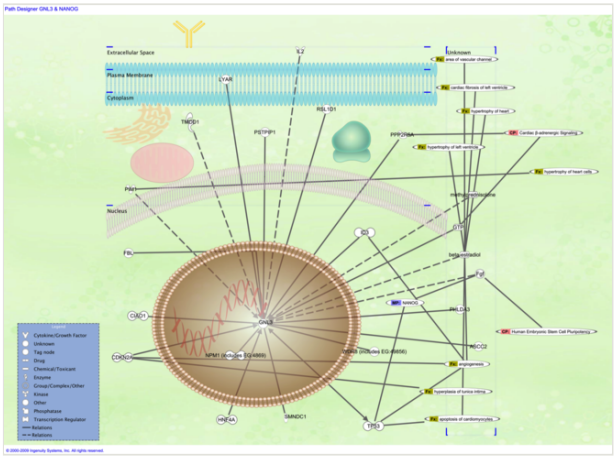

Figure 1.

Nucleostemin (GNL3) and iPS (SOX2-OCT4-NANOG) subcellular interaction network

Conclusion

In the exploratory analysis, the functional pathway networks of nucleostemin and iPS interact via TP53 (tumor protein P53) and Fgf (fibroblast growth factor), which could be further investigated to provide clues for the future research of postnatal cardiac regeneration (Huang et al. 2008).

Conflicts of interest

None.

References

- Cyranoski D (2008) Stem cells: 5 things to know before jumping on the iPS bandwagon. Nature 452: 406-408. [In eng]. DOI: 10.1038/452406a
- Garg A, Di Cara A, Xenarios I, Mendoza L, De Micheli G (2008) Synchronous versus asynchronous modeling of gene regulatory networks. Bioinformatics 24 (17): 1917-1925. DOI: 10.1093/bioinformatics/btn336
- Heilmann C (2008) Editorial comment: Myocardial regeneration by stem cells: still a black box. Eur J Cardiothorac Surg 34 (2): 255. DOI: 10.1016/j.ejcts.2008.03.032
- Huang T, Hsieh J, Wu Y, Jen C, Tsuang Y, Chiou S, Partanen J, Anderson H, Jaatinen T, Yu Y, Wang H (2008) Functional network reconstruction reveals somatic stemness genetic maps and dedifferentiation-like transcriptome reprogramming induced by GATA2. Stem cells (Dayton, Ohio) 26 (5): 1186-1201. [In English]. DOI: 10.1634/stemcells.2007-0821
- Mauritz C, Schwanke K, Reppel M, Neef S, Katsirntaki K, Maier LS, Nguemo F, Menke S, Haustein M, Hescheler J, Hasenfuss G, Martin U (2008) Generation of functional murine cardiac myocytes from induced pluripotent stem cells. Circulation 118: 507-517. [In eng]. DOI: 10.1161/CIRCULATIONAHA.108.778795
- Narazaki G, Uosaki H, Teranishi M, Okita K, Kim B, Matsuoka S, Yamanaka S, Yamashita J (2008) Directed and Systematic Differentiation of Cardiovascular Cells From Mouse Induced Pluripotent Stem Cells. Circulation 118 (5): 498-506. DOI: 10.1161/circulationaha.108.769562
- Passier R, van Laake L, Mummery C (2008) Stem-cell-based therapy and lessons from the heart. Nature 453 (7193): 322-329. URL: http://dx.doi.org/10.1038/nature07040
- Sauer , (2008) Recent advances using stem cell-derived cardiac and vascular cells for cardiomyoplasty. Xenotransplantation 15 (5): 306-306. URL: http://dx.doi.org/10.1111/j.1399-3089.2008.00488_14.x
- Schenke-Layland K, Rhodes K, Angelis E, Butylkova Y, Heydarkhan-Hagvall S, Gekas C, Zhang R, Goldhaber J, Mikkola H, Plath K, MacLellan WR (2008) Reprogrammed Mouse Fibroblasts Differentiate into Cells of the Cardiovascular and Hematopoietic Lineages. Stem Cells 26 (6): 1537-1546. DOI: 10.1634/stemcells.2008-0033
- Siddiqi S, Gude N, Hosoda T, Muraski J, Rubio M, Emmanuel G, Fransioli J, Vitale S, Parolin C, D'Amario D, Schaefer E, Kajstura J, Leri A, Anversa P, Sussman M (2008) Myocardial Induction of Nucleostemin in Response to Postnatal Growth and Pathological Challenge. Circ Res 103 (1): 89-97. DOI: 10.1161/circresaha.107.169334
- Siepe M, Akhyari P, Lichtenberg A, Schlensak C, Beyersdorf F (2008) Stem cells used for cardiovascular tissue engineering. Eur J Cardiothorac Surg 34 (2): 242-247. DOI: 10.1016/j.ejcts.2008.03.067
- Tjwa M, Dimmeler S (2008) A nucleolar weapon in our fight for regenerating adult hearts: nucleostemin and cardiac stem cells. Circ Res 103 (1): 4-6. [In eng]. DOI: 10.1161/CIRCRESAHA.108.179994
- Tulloch N, Pabon L, Murry C (2008) Get With the (Re)Program: Cardiovascular Potential of Skin-Derived Induced Pluripotent Stem Cells. Circulation 118 (5): 472-475. DOI: 10.1161/circulationaha.108.791442
- Yosef N, Sharan R, Noble WS (2008) Improved network-based identification of protein orthologs. Bioinformatics 24 (16): 200-206. DOI: 10.1093/bioinformatics/btn277