Docket #: S15-422

Telomere Length as a Diagnostic Biomarker for Cardiomyopathy

Stanford researchers in the Blau Lab have discovered that telomere length can be used as a biomarker for cardiomyopathy diagnosis and drug screening with cardiomyocytes. In cases of hereditary cardiomyopathies without known mutations, this technology using quantitative fluorescent in situ hybridization (QFISH) to detect shortened telomeres can predict disease risk. It can be applied to cardiac biopsies, archived samples, or cardiomyocytes derived from patient blood via induced pluripotent stem cells (iPSCs). This telomere analysis enables stratifying patients for clinical trials and identifying potential cardiomyopathy therapies.

Stage of Research
Using quantitative fluorescence in situ hybridization (QFISH), the inventors have demonstrated greatly shortened telomeres (30-45% of normal length) in three heritable human diseases that are marked with cardiomyopathy. Telomere shortening was found in both primary cardiac biopsies as well as iPSC-derived cardiomyocytes from patient blood samples.

Applications

- **Cardiomyopathy diagnostic** - QFISH telomere assay on cardiac tissue or iPSC-derived cardiac myocytes to:
    - identify patients with increased risk of cardiomyopathy, particularly those with a family history of the disease and an unknown genetic mutation
    - stratify patients in clinical trials for drugs to treat cardiomyopathy
- **Drug discovery** - iPSC cardiomyocyte assay to:
    - identify compounds that may prevent or treat cardiomyopathy
    - screen for toxicity in cardiovascular drug candidates

Advantages

- **Independent biomarker** - could predict familial cardiomyopathy with idiopathic disease without identifying a specific genetic mutation
- **Compatible with archived samples** - QFISH assay has been optimized to handle paraffin samples collected decades ago
- **Easily incorporated into high throughput iPSC screens** for drug development

Publications

- Chang, A. C., & Blau, H. M. (2018). Short Telomeres—A Hallmark of Heritable Cardiomyopathies. *Differentiation.*
- Chang ACY, Chang ACH, Kirillova A, Sasagawa K, Su W, Weber G, Lin J, Termglinchan V, Karakikes I, Seeger T, Dainis AM, Hinson JT, Seidman J, Seidman CE, Day JW, Ashley E, Wu JC, and Blau HM. (2018) Telomere shortening is a hallmark of genetic cardiomyopathies. Proc Natl Acad Sci U S A. 115(37): 9276-9281. PMID: 30150400
- Chang ACY, Pardon G, Chang ACH, Wu H, Ong SG, Eguchi A, Ancel S, Holbrook C, Ramunas J, Ribeiro AJS, LaGory EL, Wang H, Koleckar K, Giaccia A, Mack DL, Childers MK, Denning C, Day JW, Wu JC, Pruitt BL, and Blau HM. (2021) Increased Tissue Stiffness Triggers Contractile Dysfunction and Telomere Shortening in Dystrophic Cardiomyocytes. Stem Cell Reports 16(9):2169-2181.

Patents

- Published Application: WO2017147132
- Published Application: 20190048420
- Issued: 11,597,976 (USA)

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