From cells to circulating biomarker: BMP10 is a myocyte-secreted peptide with potential to detect atrial fibrillation

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Background: Early onset detection and recurrence prediction of atrial fibrillation (AF) may improve therapeutic decision-making, prognosis and long-term outcome. Plasma proteome analyses and mechanistic studies identified bone morphogenetic protein 10 (BMP10) as an atrial-specific secreted biomolecule for AF associated with reduced paired-like homeodomain transcription factor 2 (PITX2) expression.

Purpose: Our aim is 1) to confirm BMP10 synthesis and secretion by human atrial isolated myocytes, 2) to compare BMP10 secreted levels between right atrial, left atrial and left ventricular myocytes, and 3) to assess if BMP10 secretion is indeed associated with AF in human myocytes.

Methods: Right atrial (RA), left atrial (LA) and left ventricular (LV) myocytes were isolated from 16 tissues samples of patients undergoing open heart surgery which were currently in sinus rhythm (SR) or AF. Freshly isolated myocytes were resuspended in minimal essential medium (MEM, M1) containing fetal bovine serum (FBS) and plated in laminin coated dishes. M1 was collected after 3 hours of culture and substituted by FBS-free medium (M2), which was collected after 48 hours of culture. Cardiomyocyte-released BMP10 levels were measured in M1 and M2 by ELISA.

Results: Cardiomyocytes from twelve patients (68±2.7 years, 52±2.1 % ejection fraction, 17 % women, 50 % with AF, 50 % valvular surgery and 75 % bypass) were cultured and BMP10 secreted levels analyzed. BMP10 concentrations were high in medium from atrial cardiomyocytes (2.76±1.8 ng/µl) and negligible in medium from ventricular cardiomyocytes (0.01±0.005 ng/µl). Left atrial cardiomyocytes released less BMP10 than right atrial cardiomyocytes (LA 0.02±0.007 ng/µl; RA 3.50±2.3 ng/µl). In addition, BMP10 concentrations were higher in right atrial cardiomyocytes from patients with AF (3.76±3.6 ng/µl) than in the right atrial cardiomyocytes from patients in SR (0.97±0.9 ng/µl).

Conclusion: Our results provide a direct proof that BMP10 is secreted by human atrial myocytes, mainly right atrial myocytes. Furthermore, atrial myocytes from patients with AF secreted significantly more BMP10 than myocytes from patients in sinus rhythm. These observations validate the atrial cardiomyocyte origin of circulating BMP10, making BMP10 a potentially attractive atrial-specific cardiac biomarker.