LOW LEVELS OF GROWTH DIFFERENTIATION FACTOR 11 AND HIGH LEVELS OF ITS INHIBITOR FOLLISTATIN-LIKE 3 ARE ASSOCIATED WITH ADVERSE CARDIOVASCULAR OUTCOMES IN HUMANS

Poster Contributions
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Background: In mice, age-related decline in Growth Differentiation Factor 11 (GDF 11) leads to cardiac hypertrophy and vascular dysfunction, but information is lacking about its role in humans. We thus investigated the associations of GDF11 and its inhibitor Follistatin-like 3 (FSTL3) with cardiovascular (CV) outcomes (myocardial infarction, stroke, heart failure hospitalization, and death) in humans.

Methods: We measured plasma GDF11 and FSTL3 levels in 928 subjects with stable coronary heart disease (CHD) from the Heart and Soul Study cohort using modified aptamer-based proteomics. We used Cox proportional hazards to evaluate the association between GDF11 and FSTL3 with CV outcomes, adjusted for age, sex, and race.

Results: During 8.9 years of follow-up, 450 subjects (48%) experienced a CV event. The adjusted risk of the composite CV outcome was lower in the top vs. bottom GDF11 quartile (Q4/Q1 HR=0.40; 95% CI 0.30-0.53; p<0.001). Conversely, the adjusted risk was higher in the top vs. bottom FSTL3 quartile (Q4/Q1 HR=2.98; 95% CI 2.18-4.08; p<0.001). Subjects in the least favorable quartiles of GDF11 (lowest) and its inhibitor FSTL3 (highest) had 7-fold increased CV risk (HR=6.66; 95% CI 3.73-11.90, p<0.001) (Figure).

Conclusion: In subjects with stable CHD, low GDF11 levels or high levels of its inhibitor FSTL3 are associated with increased risk of adverse CV outcomes and these associations are additive. Our findings suggest that the GDF11 pathway is similarly cardio-protective in humans as in mice.