The Nonlinear Susceptibility Tensor Changes in Myosin Filaments Detected by Polarization-Resolved Second Harmonic Generation Microscopy

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Abstract: Second harmonic generation (SHG) microscopy has been widely applied for visualizing noncentrosymmetric biomolecules. The SHG signal is directly determined by the nonlinear susceptibility tensor, which is a crystallographic structure-related optical property of a biomolecule. When polarization technique is used, the polarization-resolved SHG microscopy has the capability to retrieve the values of the second-order susceptibility tensor values (e.g., d_{33}/d_{15}) of a biomolecule and thus can be used to explore the crystallographic structure of the biomolecule. It has been confirmed that the molecular structure of a myosin filament changes with physiological and pathological states. In this work, we explore structural changes in myosin filaments reflected by the second-order susceptibility tensor obtained from cardiac muscles that experienced pressure/volume overload, which typically causes myocardial hypertrophy. The pressure overloaded samples were collected from adult mouse heart that experienced one-month transverse-aortic constriction. The volume overloaded samples were collected from hearts of mother rats, 3 days after delivery. All slices were sampled from the left ventricular free wall. We hypothesized that the changes in nonlinear susceptibility tensor values in the two overload models were caused by accumulated mechanical tension. We tested this hypothesis using a cell stretch model to mimic the accumulated tension in vivo.

Compared with those in normal rat myocardium (d_{33}/d_{15}=0.69), the nonlinear susceptibility tensor values of myosin filaments in both pressure overloaded (d_{33}/d_{15}=1.02) and volume overloaded myocardium (d_{33}/d_{15}=0.99) increased significantly. The results from cell stretch model demonstrated that the value of d_{33}/d_{15} increased with the extent of stretch (from 5% to 20%), from 0.47 to 0.68 for lateral stretch and 0.47 to 0.64 for longitudinal stretch. Our data demonstrates that polarization-resolved SHG can be used to explore structural changes at the crystallographic level in a pressure/volume overloaded hart. Our future research will be focused on the establishment of a quantitative relationship between the state of mechanical overload-induced hypertrophy (e.g., physiological or pathological) and the nonlinear susceptibility tensor so as to develop a SHG-based myocardium diagnostic technique.