Model oxidative modification of fibrinogen and the influence on its function

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Introduction

Fibrinogen is considered as one of the most sought of targets of oxidative stress. Oxidative stress is linked with many pathophysiological conditions, e.g. cardiovascular diseases.

Materials & Methods

Three reagents of different oxidation strength were selected for fibrinogen modification: malondialdehyde, sodium hypochlorite and 3-morpholinosydnonimine. Confocal microscopy, fibrinolysis and interaction with platelets were used to characterize the function of modified fibrinogen. Extent of modification was evaluated by content of the created carbonyl groups and by liquid chromatography coupled with mass spectrometry. Molecular dynamics simulations of hydrated protein were performed in Gromacs and Amber software with force fields Gromos and Amber, respectively. Crystal structure 3GHG was used as a reference structure to which post-translational modifications were introduced manually in Yasara View.

Results

The highest count of newly formed modified amino acid residues was achieved by MDA; NaOCl caused the fastest modification. Impact of modification was linked with the extent and kind of modification. Oxidative changes affected formation and lysis of fibrin clot, fibrin net architecture as well as interactions between fibrinogen and platelets. The impact of post-translational modifications on the structure fibrinogen was described by two different force fields.

Conclusion

The study of influence of oxidative changes may lead to better understanding of fibrinogen function and interactions under oxidative stress condition.

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